Application of Modelling Methods from Informatics in Evidence Based Health Care.

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Abstract

The paper introduces the idea to use modelling methods from informatics for the further development of the Evidence Based Health Care (EBHC) in terms of both: its technology support as well as an aid for the development of its methodology.
In the paper we briefly introduce the contents of the EBHC and its predecessor Evidence Based Medicine (EBM), their evolution, current state, its main limitations and consequent challenges. We also briefly introduce the principle of modelling in informatics and those semi-formal modelling methods and techniques which we regard as relevant for the given purpose, namely conceptual modelling, object life cycle modelling, and business process modelling. Using the example, based on existing EBHC practical guidelines for febrile seizures, we then illustrate the possibilities of the use of modelling techniques for an improvement of the EBHC processes and also the related possibilities of the exploitation of modelling techniques from informatics for further development of the EBHC methodology.
In conclusions section we then summarize main opportunities of the application of modelling techniques from informatics in the field of EBHC and outline the needed future work.

Keywords: Evidence Based Health Care, Ontology, Conceptual Modelling, Object Life Cycle Modelling, MMABP, Unified Modelling Language.

Introduction - Evidence Based Health Care

The term "Evidence-based medicine" was introduced in the medical literature in 1991 [8]. Accroding to [4] an original definition suggested "an ability to assess the validity and importance of evidence before applying it to day-to-day clinical problems" [15,9]. The initial definition of evidence-based practice was within the context of medicine, where it is well recognised that many treatments do not work as hoped. Since then, many professions allied to health and social care have embraced the advantages of an evidence-based approach to practice and learning. [4] proposes that “the concept of evidence-based medicine be broadened to evidence-based practice to reflect the benefits of entire health care teams and organizations adopting a shared evidence-based approach”. This statement emphasizes the fact that evidence-based practitioners may share more attitudes in common with other evidence-based practitioners than with non evidence-based colleagues from their own profession who do not embrace an evidence-based paradigm.

The initial focus on critical appraisal led to debate on the practicality of the use of evidence within patient care. In particular, the unrealistic expectation that evidence should be tracked down and critically appraised for all knowledge gaps led to early recognition of practical limitations and disenfranchisement amongst some practitioners. The growing awareness of the need for good evidence also led to awareness of the possible traps of rapid critical appraisal. Process of Evidence Based Practice includes translation of uncertainty to an answerable question, systematic retrieval of best evidence available, critical appraisal of evidence for validity, clinical relevance, and applicability, application of results in practice, and evaluation of performance.

Evidence-based medicine, like other models, has limitations, and further innovation and study are required to resolve the issues raised in this paper. In particular, efforts need to be directed toward improving clinicians' access to evidence at the point of care; developing better methods of describing evidence to patients in order to facilitate shared decision-making; and conducting studies to test whether and how evidence-based medicine affects processes of care and patient outcomes [22].

The work presented in this paper aims to the enrichment of the EBHC practices with the power of modelling techniques from informatics, particularly the conceptual modelling complemented with modelling the dynamics of objects in the form of "object life cycles". Currently, EBHC methods are mainly based on collecting the information about "best practices" in the given field, evaluating, generalizing and sharing it. Conceptual model contains, besides basic EBHC facts, also an additional information about general logical relationships among objects which increases the knowledge about them with basic options of their possible combinations. Life cycle model captures, in addition, the basic logic of object's dynamics, i.e. possible time sequences of events related to the given object. Existing methods for modelling dynamics in medicine are usually mathematical and focused mainly on infectious diseases and epidemiology. There are also some publications about modelling the disease development with algorithmic-like models ([10] for instance), but none of them in connection with the contextual conceptual model.

The paper is divided into three main sections. In the first section, after this introduction, we briefly explain the formal models and related methods from informatics, relevant to this topic. The following section contains the explanation of the proposed approach, using the EBHC example in the field of Febrile Seizures together with the basic discussion of the most important features of the approach. In the conclusions section we summarize the main ideas of the paper, further discuss the opportunities of the application of modelling techniques from informatics in the field of EBHC and outline the needed future work.

Formal Models in Informatics

There exist more actual attempts to apply the modelling methods from informatics, especially conceptual modelling in the field of health care, like [6,12,23] and others. Existing works vary in the subject of modelling, in the depth of analysis, in the degree of technology orientation, and in other aspects. Nevertheless, the common feature of all approaches is the use of informatics for supporting the needed evidences by information technologies, for supporting the data management. The unique feature of the approach, presented in this paper, is the use of the "cognitive power" of informatics modelling methods for possible improvement of the internal EBHC methodology. Particularly, the use of object life cycles as a tool for the stimulation of research questions can be regarded as novel and unique.

The work presented in this paper is based on the methodology MMABP [18]. MMABP is a methodology for modelling business systems, based on the formal meta-model [2] and continuously being developed [14]. By the concept *business system* we mean any domain of the Real World which is influenced by human activity, so also the health care domain. MMABP aims to cover both basic dimensions of the Real World description: ontology of the Real World and processes (business processes) in the Real World. Ontology represents the essential rules of the Real World in terms of so-called modal logic while processes represent the organized sets of actions for the implementation of some intention, for achieving some goal. Therefore it can be said that MMABP aims to describe the Real World domain (business system) as an equilibrium of intention and causality [17]. For all models MMABP uses standard modelling languages; UML [24] for the ontological / conceptual model and BPMN [1] for the process model. The work, presented in this paper, is currently oriented just on the ontological dimension of the modeled domain, nevertheless we plan also the use of process descriptions in further development of the research.

In following two sub-sections we roughly characterize basic methodological fields which the presented work is based on: Ontology Engineering and Conceptual Modelling together with Object Life Cycles Modelling.

1.1. Ontology Engineering and Conceptual Modelling

Conceptual modelling is a traditional informatics technique for description of the real world modality. The origin of conceptual modelling is closely connected with the database technology. The original purpose of the *technique for data modelling* was to create the concept of the database which structure is so flexible to be able to accept as much as possible needed future changes. The need for future changes of the database comes from the changes in the real world. As the real objects and their relationships are naturally changing, the contents of the database should change as well. The root motivation for data modelling is the need to design the database which would be able to accept as much as possible necessary changes in the real world without the need to change its own structure. In [3] Peter Chen expressed the crucial idea that these criteria best fulfills such structure of the database which is similar as much as possible to the structure of the real world concepts. Therefore, the modelling technique has to be primarily aimed on analyzing the structure of the real world concepts. For that purpose he proposed a data model, called the *entity-relationship model*, which incorporates the important semantic information about the real world by modelling the real world concepts and their relationships. The work of Peter Chan crossed the border between just technically oriented design of the database and fully-fledged semi-formal method for the description of the modality of the Real World by identifying the essential real world objects, expressed with concepts, and their essential relationships – a *Conceptual Modelling*.

At mid-nineties the informatics community accepted as a standard tool for conceptual modelling the *Class Diagram* from the UML [24]. Conceptual model made with Class Diagram describes the static structure of the given domain as a system; in the form of classes and relationships among them. Class Diagram is a basic diagram of the whole UML repertoire of diagrams. In the following decades there have come the new generation of the real world modelling which can be also regarded as a successor of the traditional conceptual modelling: *ontology modelling* and *ontology engineering*. Ontology engineering brought very important focus on the identity of real world objects and, consequently on the ways of ensuring it across different models with use of Internet technologies known as linked data approach. Strong focus on concepts and their identity also caused the natural reduction of ontology engineering mainly to essential classification of concepts which is just a part of the needed description of the modality of the real world. In 2005 the first formal step to the needed reintegration of ontology engineering with its natural predecessor conceptual modelling has been made in the form of so-called OntoUML methodology [7]. A comprehensive description and explanation of relationships among the conceptual modelling, ontology modelling and UML can be found in [7].

Particular object classes in the conceptual model represent concepts which identify possible real world objects from the given domain. Relationships among object classes then identify possible links among real objects in the domain. In principle, this “system-oriented” view of objects can simply recognize their existence and mutual context, not their dynamic details. Nevertheless, both real objects and their mutual links are naturally dynamic in the real world; they are changing in time. These dynamic aspects cannot be described in the Class Diagram as it principally describes the system of objects, i.e. the system of mutually parallel processes of changes of linked objects. To model the object's dynamics it is necessary to complete the Class Diagram with the set algorithmic models, each focused on just one particular object in terms of its so-called “life cycle”. This approach is described in the next section.

1.2. Modelling Object Life Cycles

Object life cycle expresses the internal dynamics of each object of given class. It describes the mechanism of the object evolution during the time. As the tool for the Object life cycle description, the MMABP methodology uses the State Chart diagram from the UML [24]. MMABP regards the State Chart as a most suitable tool from the Unified modelling Language for the purpose of the object life cycle description. Nevertheless, the State Chart has not been originally intended as a tool for description of life cycle. Its roots are in the field of state machines theory, and it is closely connected with the concept of so called 'real-time processing'. However, the concept of the state machine in general is not substantially reducible to just the area of real-time processing. There is also a need for recognizing the states and transitions among them in the area of data processing. The best proof of this idea is the concept of the object life cycle itself – once we think about the objects generally (i.e. in terms of their classes), then we have to strongly distinguish between the class and its instance. In the case of the object life this requires determining those points in the life of all objects of the same class, which we will be able to identify, and which it is necessary to identify in order to describe the synchronization of the object life with life cycles of other objects. Such points of the object life are its states. So each object instance “lives its own life” while the common, general structure of lives of all instances of the same class is described as a life cycle of the object class. Each described life cycle has to correspond to the particular object class in the Class Diagram. In such way the State Chart specifies the general mechanism of the life of all possible instances of the given class. Described states and transitions among them consequently correspond to the attributes and methods of the class. Life cycle states represent some kind of the special attribute of the class. This “state” attribute exists implicitly, by the definition, and therefore it should not be expresses in the conceptual model as an attribute of the class, similarly to the object identifier which follows from the definition of the meta-concept class where the identity of the object is defined as implicit. Like the “value of identity” represents particular object (class instance), the “value of state” represents the particular state in the object life cycle in which the given object stands at the moment. Each transition between life cycle states then represents the use of the particular class method.

One of the main reasons for using the UML Class Diagram as a standard is the fact that this diagram, as a part of the consistent system of UML diagrams, allows direct linking with the detailed object models – object life cycles in the form of UML State Charts.
As an example of the description of class life cycle with the State Chart can be used the model at Figure 3. Every transition between states is described there by the attribute which represents the reason for the transition. The reason for the transition is an event, ie. some external influence of the given object.

Combination of the traditional conceptual model in the Class Diagram with the description of life cycles of selected objects increases the traditional extent of the conceptual model, focused on just static modality with the description of the dynamics in modality. In other words, this way we are able to describe also some part of the real world causality which is not possible in the traditional conceptual modelling.

Example – Febrile Seizures

For the example of the possible application of modelling techniques from informatics we use the problem of Febrile seizures which; one of topics processed in the form of practical guidelines [5,16].

Febrile seizures are defined as seizures occurring in association with a febrile illness in children between the ages of six months and five years It is important to differentiate febrile seizures with fever from complex febrile seizures secondary to central nervous system infections. Febrile seizures are relatively benign as compared to complex febrile seizures that have serious sequale, longer duration, and require further medical follow-up [19]. The motivation for practical guidelines in this field underlines also the fact that simple febrile seizures are relatively prevalent conditions that often causing avoidable anxiety to the children and their parents [11].

The model at Figure 1 expresses the information about febrile seizures, and some other closely related phenomena. The information has been gathered from several resources, primarily the Simple Febrile Seizures Evidence-Based Guidelines [5]. Additional resources have been used for completion of the contextual information about related topics of febrile seizures, epilepsy, diseases of the nervous system in general, etc [20,11,13]. For various reasons, this model contains just a fragment of the complex information about febrile seizures. First, by means of conceptual modelling which description possibilities are naturally limited it is impossible to make a complete picture of such a complex phenomenon, as any medical field is. Second, the model describes a subset of internal relationships among used concepts, selected according to their relevance to the given purpose: to address primarily the problem of simple febrile seizures which is a subject of the source guidelines. Necessary limitation to just a subset of all possible relationships among object classes is also a typical feature of the conceptual model. Nevertheless, despite the above discussed limitations, it is obvious that such way of description of the “modal logic of the given field” is much more powerful than the traditional text description currently used as a basic form of Evidence-Based Guidelines.

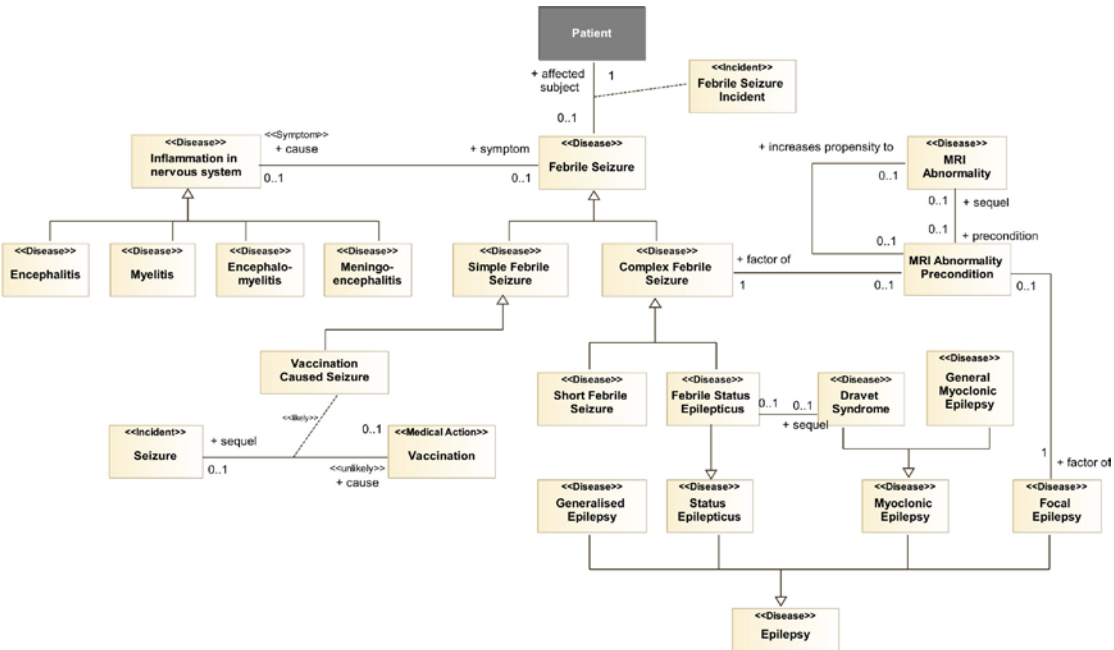

Fig. 1. Febrile Seizures conceptual model - a fragment.

The central concept in the model is *Febrile Seizure*. It expresses the particular disease (see the stereotype *<<Disease>>*) as a generic concept consisting of two basic subtypes: *Simple* and *Complex Febrile Seizure*s. There is some further classification of subtypes of the *Complex Febrile Seizure* for the purpose of expressing an important relationship to another disease – *Epilepsy* which is related just to the specific subtype of febrile seizure: *Febrile Status Epilepticus*. A strong form of febrile status epilepticus can also lead in the *Dravet Syndrome* which is another specific subtype of the myoclonic kind of *Epilepsy*. As in the context of febrile seizures also the risk of intracranial pathology is frequently discussed, this possible problem is also caught in the model. According to [16] “Neuroimaging has provided evidence that hippocampal injury can occasionally occur during prolonged and focal febrile seizures in infants who otherwise appear normal. It has been speculated that a preexisting abnormality increases the propensity to focal prolonged seizures and further hippocampal damage. …....

However, MRI abnormalities were related to a specific subtype of complex seizures: focal and prolonged. The most common abnormalities observed were subcortical focal hyperintensity, an abnormal white matter signal, and focal cortical dysplasia.”. Cited information from [16] is expressed in the model with the use of an abstract concept *MRI*[1] *Abnormality Precondition* representing the mandatory relationship to both the *Complex Febrile Seizure* and *Focal Epilepsy* (i.e. the disease manifesting itself as a focal seizure). At the same time it can be caused by the *MRI Abnormality* in terms of the mentioned speculation that “preexisting abnormality increases the propensity to focal prolonged seizures and further hippocampal damage”[16]. The mentioned reflection can be interpreted as a cyclic dependency between a cause (*MRI Abnormality → MRI Abnormality Precondition*) and a precondition (*MRI Abnormality Precondition → MRI Abnormality*) which corresponds to the expression “...further hippocampal damage”. Nevertheless, Class Diagram is not the best, nor a sufficient tool for expressing mentioned relationships of given concepts as a cyclic causal dependency as it can express the modality of the universe of discourse just in a static manner. Therefore it is useful to complement the model with detailed description of the causality connected with the given object in the form of “object life cycle”, using another diagram from UML language: State Chart. In this case we can describe the life cycle of objects of the class *Febrile Seizure Incident* (see Figure 3).

Left side of the model describes some of important problems connected with the simple febrile seizures in terms of the Simple Febrile Seizures Evidence-Based Guidelines [5].

According to [16] “*Debate exists between the relation of febrile seizures and childhood vaccinations. Seizures are rare following administration of childhood vaccines. Most seizures following administration of vaccines are simple febrile seizures*”. The model reflects this information as a relationship between an incident *Seizure* and medical action *Vaccination* which is stereotyped as <<*unlikely*>>. This stereotype is used for expressing that the relationship is rare. Nevertheless, if the relation between the seizure and vaccination exists, it is in most cases related to simple febrile seizure. Therefore, this relationship is expressed as an association class *Vaccination Caused Seizure* which is a special kind of the *Simple Febrile Seizure* and this assignment is stereotyped as <<*likely*>>.

In the model we use various stereotypes of classes in order to specify the meaning of the role which the object plays in the given context. Possible stereotypes are defined in the Health Care Domain Meta-Model. Figure 2 shows a fragment of the Health Care Domain Meta-Model, focused on those types of concepts which are used in the model at Figure 1.

1 Magnetic resonance imaging.

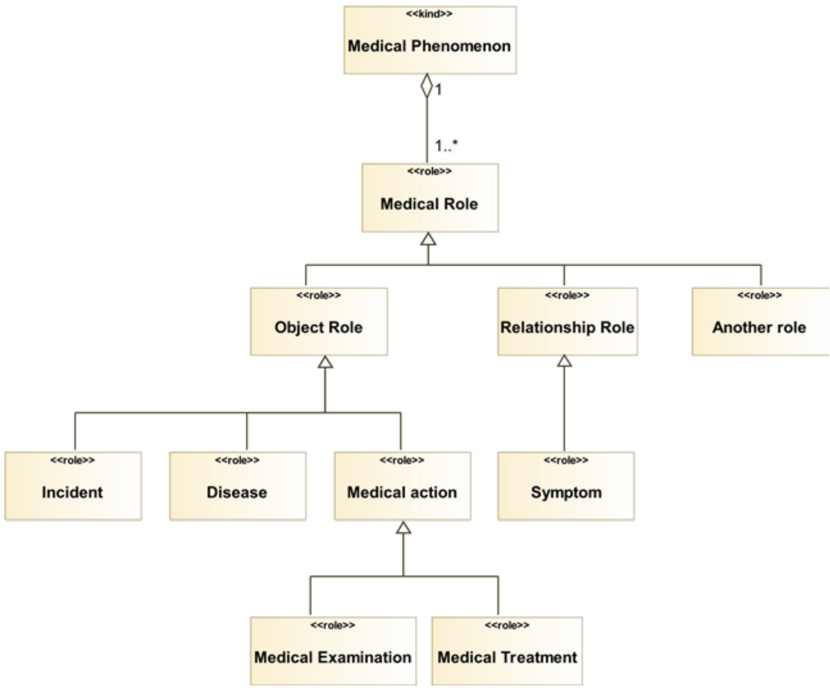

Fig. 2 Health Care domain meta-model – classification of essential concepts.

Health Care domain meta-model defines special meta-objects, needed for creating conceptual models in the field of health care. Meta-model itself is based on the very general meta-model, so-called meta-ontology OntoUML [7], and specializes it for the field of health care. Classes, defined in the meta-model, are named in accordance with existing clinical ontology standards, primarily with the SNOMED [21] as a dominant ontology in the field of healthcare.
SNOMED CT is a clinical terminology created by a range of healthcare specialists to support clinical decision-making and analytics in software programs. It is owned, administered and developed by the not-for-profit organization SNOMED International in order “to ensure that SNOMED CT can be routinely integrated into healthcare information systems so that users can record patient data more accurately and comprehensively and then use tools and analytics to provide better patient care and health management” [21]. SNOMED is based on the professional standards in the field of ontology engineering which guarantees the compatibility with other related ontologies as well as the perspective of the future development. From the point of view of our approach, its compatibility with the meta-ontology OntoUML [7] is especially significant. In the Health Care domain meta-model we use SNOMED as a basic source of the clinical terminology.

The classification at Figure 2 can be read as follows:
Medical Phenomenon is an essential real object (stereotype *<<kind>>* from the OntoUML [7]). At the same time it is a collection of one or more possible *Medical Roles* (stereotype *<<role>>* from OntoUML). *Medical Role* can be either a role of *Object*, or *Relationship* between objects, or some *Another* kind of role. *Object Role* can be either *Incident*, or *Disease*, or *Medical Action* which can be either *Examination* or *Treatment.* The fragment at Figure 2 contains just one role of the relationship: a *Symptom* as only this relationship role is used in the model at Figure 1. At a glance, this model expresses the idea that the same medical phenomenon can play more different roles according to different contexts in which this concept is used in the model (or models). For example, the concept “seizure” can mean either a disease or a symptom or possibly yet another role (incident), depending on the context in which it is used in the particular model. Nevertheless, it is always important to keep in mind that in all its possible roles it is still the same essential phenomenon. The information from this fragment of the meta-model naturally influences creating of all possible models in the

given field. Particularly in this case, it means that each newly introduced entity in any model in this field, manifesting itself in some particular role, should be confronted with all other existing models in order to ensure the essential identity of the phenomenon which it represents. In other words, this rule stimulates the strong collaboration of creators of various models in the same field, in terms of common and exact understanding of used concepts. This principle is very close to the main principle of Ontology Engineering in general and Linked Data and Semantic Web in particular, and therefore it can be used as a bridge between existing medical ontologies and medical conceptual models as an advanced technology support in the field of Evidence-Based Health Care.

Model at Figure 3 describes the life cycle of possible objects of the class *Febrile Seizure Incident.* In the conceptual model at Figure 1 it can be found that this class is an association class, it expresses the association between the essential general class *Patient*[2] and the class *Febrile Seizure* as a disease (stereotype *<<Disease>>). Febrile Seizure Incident* thus represents an incident of febrile seizure which happens to the particular patient. The whole structure of mutually associated other classes is connected with the patient just by this association. The life cycle model at Figure 3 thus describes possible ways of the development of the disease starting with the (yet unclassified) febrile seizure according to the modal logic of the domain, following from the conceptual model at Figure 1. The life cycle model is focused on the essential causal relationships, i.e. possible time dependencies of relevant events, associated with the initial incident.

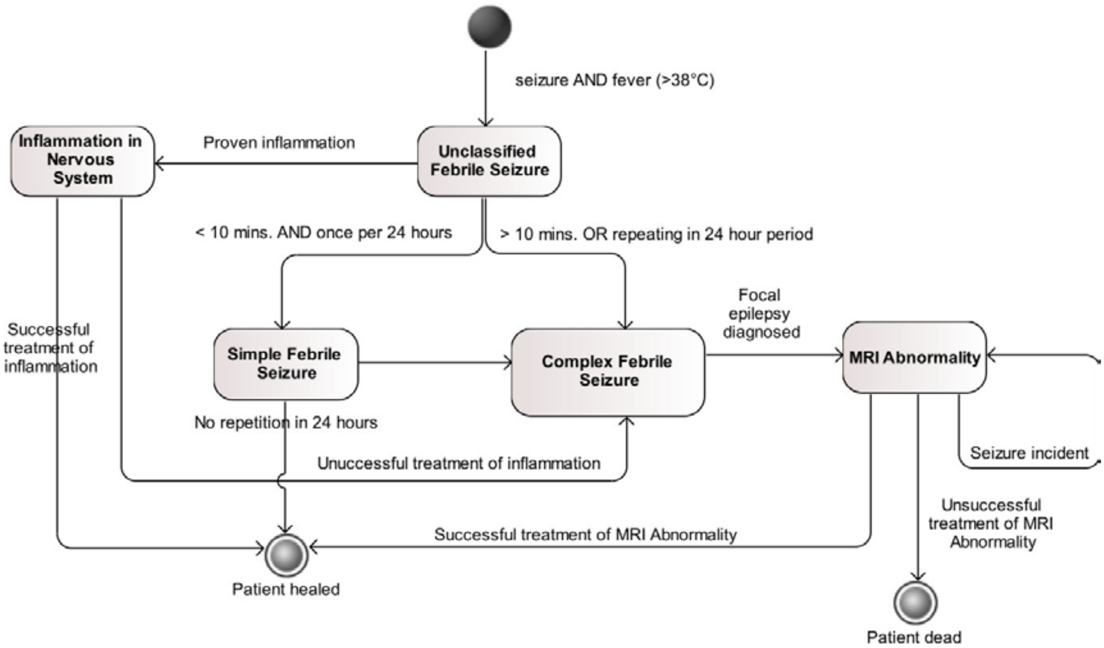

Fig. 3 Febrile Seizure Incident Life Cycle Model

The model should be interpreted as follows: the very first state of the life cycle is *Unclassified Febrile Seizure*. This state occurs after the febrile seizure attack what is characterized in the model as an input event *seizure AND fever* $>38^{O}C$. In the very first state the model expects three important possible events. Either the seizure ends within 10 minutes and it is not repeating within 24 hours; in such case the initial incident is classified as a *Simple Febrile*

2 From the point of view of the general medical ontology, *Patient* is a role of a *Person*. As this model is focused just on the problem of particular disease, only this kind of *Person* is relevant here. Therefore this class is used in the model without any stereotype as an essential real world entity.

Seizure and probably does not mean anything serious3. Otherwise it is classified as a *Complex Febrile Seizure* which represents completely different, more serious, possibilities of the further development. The third possible event in this state is the detection of the *Inflammation in Nervous System* which can explain both the seizure as well as the fever. If successfully treated this state can also result in nothing serious, nevertheless otherwise it can lead to the state of *Complex Febrile Seizure4*. The model also mentions possible state of *MRE Abnormality* which can follow the Complex Febrile Seizure if the focal epilepsy is diagnosed. This state can be progressively worsen by subsequent seizure incidents which is modeled here by the self-transition, representing the causal view of the cyclic associations between the concepts *MRI Abnormality* and *MRI Abnormality Precondition* in the conceptual model at Figure 1.

Conclusions

The paper introduces the idea to use modelling methods from informatics for the further development of the Evidence Based Health Care (EBHC). Unlike most of approaches to apply informatics in the field of healthcare our approach is not oriented just on the support of the evidence of facts. It is aimed on the use of modelling methods from informatics for the further development of the methodology in the field of EBHC. This way our approach follows the use of ontology engineering which also, even indirectly, contributes to the medical research methods and practices forcing them to use the systematic approach to the terminology and other connected aspects of the research.

Topics discussed in this paper also represent serious challenges for the future development of the methodology in the field of EBHC. For instance, MMABP technique for modelling the object life cycle includes the rules for achieving both completeness and correctness of the life cycle description. According to these rules all possible state transitions, including the transitions which are not present in the model, should be taken into the account and evaluated. This practice strongly evokes many new research questions which answering can significantly move forward the current knowledge. For instance, in the model at Figure 3 some possible relevant questions may be:

- Can MRI Abnormality cause Complex Febrile Seizure? If so, under which conditions, what is the related event, what are related medical actions?
- Can Complex Febrile Seizure turn back to Simple Febrile Seizure? If so, under which conditions, what is the related event, what related medical actions should be performed?
- Can Inflammation in Nervous System cause just the Simple Febrile Seizure? This question is related to the problem of potential neglecting of possible cause of consequent complex febrile seizure, discussed in the footnote 4.

The aim of the presented work is not the development of the software product for supporting the EBHC processes. Our product is rather a methodical approach, intended to be used by professionals in the field of EBHC and this way also evaluated, matured, and finally grounded

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3 In the case of children between 6 and 60 months of age, which is a relevant group of patients for the problem of simple febrile seizures, the seizure together with the fever can occur for many other “innocent” reasons, as natural phenomena associated with the quick development of the organism in this age.

4 This situation is a good example of the essential difference between the causality, modeled by the object life cycle, and the (medical) process. Object life cycle models just a general causality of the real world, which is not influenced by any intention, i.e. does not represent the way to achieve a goal. So there are no priorities of the further development in the given state, just the possibilities. In the model of respective medical process we should obviously recommend, as the first action, the check of possible inflammation in nervous system in order to exclude this possibility before eventual conclusion that the incident is just a simple febrile seizure, as such conclusion might mean, in the case of the inflammation, the neglecting of possible cause of consequent complex febrile seizure.

as a part of the EBHC methodology. After becoming the regular part of the EBHC practice it will have to be also supported with some software product. At the moment, it is primarily relevant to evaluate it in as broad as possible practical use which will also serve as a way of the development of the approach.

Our approach is currently oriented just on the ontological dimension of the modeled domain. In the future development we plan to take into the account also the process descriptions of the field of healthcare. Ontological conceptual models can be used for basic definitions of healthcare concepts and their mutual relationships, in terms of the modality of the domain, including also its causality in the form of objects' life cycles. Nevertheless, the healthcare domain, even the field of Evidence Based Healthcare, naturally contains also the process (intentional) dimension. So-called "best practices", an essence of the EBHC, are the best examples of the need to model also the intentionality (recommended practices, guidelines) in this domain. MMABP puts the great emphasis on the consistent integration of both ontological and process models of the Real World. Therefore, in the future steps of this research, we can expect, in this way, yet further significant methodological contribution to the field of EBHC.

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