Ontological Principles of Disease Management from Public Health Perspective: a Tuberculosis Case Study

Patty Kostkova

City ehealth Research Centre

City University

London, UK

patty@soi.city.ac.uk

Anand Kumar

IFOMIS

Faculty of Medicine

University of Leipzig

Leipzig, Germany

anand.kumar@ ifomis.uni-leipzig.de

Anjana Roy

MIM & City ehealth Research Centre

City University

London, UK

A.Roy-1@city.ac.uk

Julius Weinberg

City ehealth Research Centre

City University

London, UK

J.R.Weinberg@ city.ac.uk

Gemma Madle

City ehealth Research Centre

City University

London, UK

G.C.Madle@ city.ac.uk

Ewart Carson

MIM

City University

London, UK

e.r.carson@ city.ac.uk

ABSTRACT

Formal ontological representation of clinical conditions and disease management is a key methodology ensuring that the complex knowledge of disease treatment, control and prevention can be represented, stored and accessed in the most appropriate way to help the medical professionals in their decision making. This is of particular importance for the public health domain where the concern is about the affect of the disease on populations rather than individuals.

The existing evidence-based knowledge can best be used by professionals if incorporated into care pathways (formal or informal) which relate the sequence of actions necessary for accurate management of diseases to the progression of the illness and treatment.

Therefore, there is a need for an ontological framework to be built around care pathways in order to allow the professionals to access the most relevant information at the time of making a decision. In this paper we will illustrate a Tuberculosis (TB) care pathway, as developed at City University, and show how a formal ontological representation can, in principle, serve the needs of information retrieval around this particular disease.

General Terms

Care Pathways, Digital Libraries, Ontologies, Evidence-Based Care

Keywords

Tuberculosis, Disease Management, National electronic Library of Infection, HL7, Snomed CT

1 INTRODUCTION

Use of formal ontological principles in order to represent the entities which constitute the biomedical world provides a framework which is helpful towards life-sciences data integration and inferences made over the data.

In this paper, we present a representation including the way tuberculosis and related disorders are classified within standard terminology systems like Snomed CT[1] from the formal ontological perspective and apply it on the information present on a TB care pathway prototype website developed at City University with tuberculosis care and evidence-based medicine pathways[2] in order to show how the formal ontological representation can be used on a real disease management. In addition, care pathways and ontological representations could only fulfill their purpose if these assist the healthcare professionals in accessing the key medical knowledge and can provide them with the essential action points retrieved form evidence-based quality-assured portals and databases, such as the National electronic Library of Infection, we are developing and using for this project.

This paper starts by giving a brief overview of TB, our case study, (section 2), then we focus on the underlying formal ontology that is illustrated on TB, in section 3. Section 4 brings an overview of the NeLI project, providing a knowledge base for the defined framework that will be presented to professionals through the ontological model. Finally, in section 5 we discuss future work and in section 6 we conclude.

2 TB CASE STUDY

In order to define a formal ontology to represent a disease management from a public health perspective, we have developed a TB care pathway case study to allow us to test the formal model.

---

[1] http://www.nhsia.nhs.uk/snomed/pages/default.asp
[2] http://topcat.soi.city.ac.uk/Lucky.nsf/t12?OpenPage

The high-level representation of the care pathway showing an interactive graphical representation of a TB care pathway is shown below.
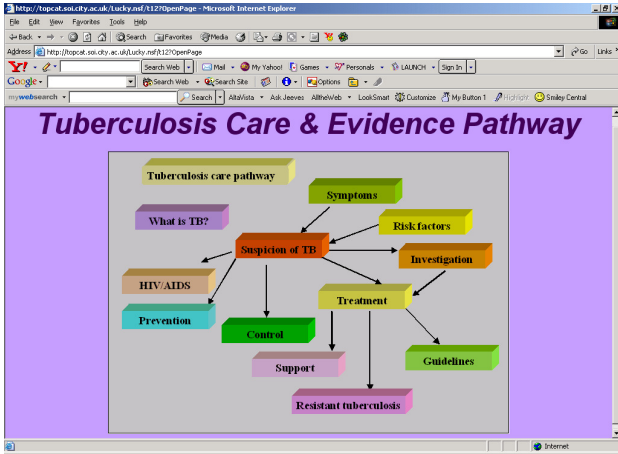

Figure 1: The TB care Pathway[3]

There are a number of entities and processes that need to be defined for the actual TB disease. This will be done in this section, while in the next sections, these concepts will be formally generalized by the proposed ontological framework.

The care pathways consists of the key following entities and processes: disease, investigation, prevention, treatment and control.
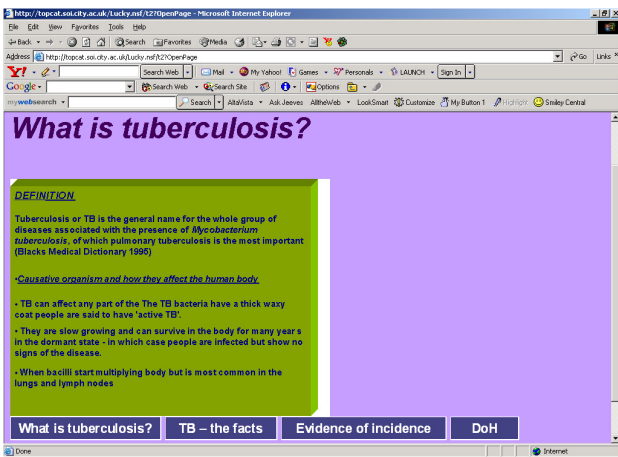
2.1   Disease: What is TB?

Figure 2: The TB care Pathway: What is TB Page

As shown above, this page gives a brief introduction about TB. Tuberculosis is an infectious disease caused by the bacterium *Mycobacterium tuberculosis*. TB is a contagious disease and usually spread by air, can affect any part of the body, but is most common in the lungs and lymph glands. Usually, when a healthy person inhales the bacteria their immune system destroys these bacteria and consequently has no effect. In some cases not all the bacteria are destroyed and remain dormant in the body. Later when the body develops any form of illness which weakens the body, specially one which weakens the immune system, the bacteria start multiplying rapidly and the individual develops "active TB".

2.2   Investigation of TB

If one is identified with the possibility of having TB then further investigations will be performed for screening of TB. Screening will consist of a skin test to determine whether the system recognizes TB. Heafs or Mantoux test are the two commonly used screen tests. Most people who have had the BCG vaccination will have a mildly positive screen test result. If the screen tests are strongly positive, then further investigation will be followed by a chest X-ray. If TB bacilli are found in the sputum of the patient, then it is confirmed that person is suffering from TB. According to the severity of the disease, close and casual contacts will be routinely screened. When all tests strongly indicate or confirm TB, specialist doctors will investigate further and decide on the course of treatment.

2.3   Prevention of TB

Tuberculosis can be prevented at various stages: BCG vaccinations is given to babies and children to reduce the risk of TB. The effect of the vaccination lasts for around 13-15 years. There is some controversy over the protective efficacy of BCG, however it probably protects against the most severe forms of the disease such as TB meningitis.

Early detection of TB can start early treatment of the disease which will prevent TB from developing to its most severe form. Individuals in high risk groups e.g. in close contact with the patient, can be administered prophylactic treatment even in the absence of "active TB".

The most obvious, but important method of prevention is treating those people with TB who are infectious. People suffering from the infectious form of the disease can pass the infection to others, until they have started treatment. After two weeks of being on medication for treatment of TB they are no longer infectious to other people. If left untreated each person with active pulmonary TB will affect on average 10-15 people.

2.4   TB Treatment

Before the treatment of tuberculosis, one needs to use the representations outlined above – those related to human beings, pathologies at various levels of granularities, disease, disease spread, geographical regions and spaces, organizational structures and so on.

---

[3] http://topcat.soi.city.ac.uk/Lucky.nsf/t12?OpenPage

The various therapies available for tuberculosis are usually based on antibiotic pharmacotherapy with adjuvant medications. The drugs by themselves are manufactured products usually, which are substances with specific roles which are inherent within the drug and which helps it to act against tuberculosis bacteria, for example effects on the bacterial DNA or bacterial cell wall; or with the role to supplement the body with nutrition which is needed during the period other drugs are acting against bacteria. The pharmacodynamics and pharmacokinetics of the drugs are a collection of processes which take place at various granularities within the human body. The measurement of the action of the drug is again targeted at various granularities within the human body, and the effects of the drugs can be measured.

There are specific regimes of drug administration. The very act of administering the drug by a suitable route is an again a process, with various temporal properties which specifies when, how frequently, and for how long the drug should be administered. Together with such administration goes the Potential Order Definition, Intent, Order, Criterion and Goals behind the act of administration.

2.5   TB Control

Various recommendations have been put forward in order to draw practice guidelines to guide health care professionals, paramedics, government bodies, non-profit organizations, and commercial establishments for prevention and control of tuberculosis. We considered the recommendations by Joint Tuberculosis Committee of the British Thoracic Society (Joint Tuberculosis Committee of the British Thoracic Society 2000) [1] in order to demonstrate what one requires of their representation.

1. public health law in relation to tuberculosis: Requires the collection of human beings which form the law bodies, the law itself which is a potential function to be applied on the groups of human beings which together form the society, and also the document which attests the law, which is a physical object with associated defining acts by legal bodies to represent its legality.
2. the organizational requirements for tuberculosis services.
3. measures for control of tuberculosis in hospitals, including segregation of patients: Requires the representation of hospital as a geographical space, with different departments as its parts. The rooms then form parts of those departments, and contain the groups of human beings within them performing or with the potential to form healthcare-related roles. The humans in the organization have their own hierarchy which is based on their roles as agents. Then the measures are those plans within the minds of administrators or expressed as a legal document or carried out physically are processes within the geographical space of hospital.
4. the requirements for health care worker protection, including HIV infected health care workers: Needs additional representation of the HIV infection pathology, disease and pathological processes.
5. measures for control of tuberculosis in prisons: Apart from the representations mentioned above, one requires prisons to be represented as a geographical region.
6. protection for other groups with potential exposure to tuberculosis: Requires the geographical regions and spaces to be represented.
7. awareness of the high rates of tuberculosis in the homeless together with local plans for detection and action: The incidence and prevalence of tuberculosis as a phenomenon, which depends on the population, the causative organism, environment including the geographic regions involved in various contexts as mentioned above.
8. detailed advice on contact tracing: Requires the representations above plus the formal relationship of disease spread. Disease spread is a phenomenon and the actual spreading is the process.
9. contact tracing required for close contacts of bovine tuberculosis: Apart from the above representations, requires the representation of disease carriers, who themselves are preserve their identity through time and have a particular role.
10. management of tuberculosis in schools: Additional representation of schools as geographic regions.
11. screening of new immigrants and how this should be performed: Immigration is a specification of movement with a temporal factor. The movement of human beings or a collection of human beings into a well-defined geographical region is the phenomenon here and their stay at that new location (the human being contained within the new geographical space) represents the immigration in physical terms. That physical change is then reflected within the local environment and the contact which exists within the groups of humans in the new location. The screening procedure is a process carried out by groups of human beings with a role of doing the screening in order to conceptualize if the physical pathology at different levels of granularity and the disease at the organism level is present or not.
12. outbreak contingency investigation: Representation as above.
13. BCG vaccination and the management of positive reactors found in the schools programme: BCG vaccine is a substance with a role of immunization, which can be considered either the intrinsic property of the substance itself (the property to provide immunity) or an intended act of the health practitioner or a standardizing body (a substance which is being used with an intention to vaccinate). Positive reactors are human beings which show a particular property to react which is recognized by the practitioner. Other representations remain as in the above cases.

3   ONTOLOGICAL REPRESENTATION OF CARE PATHWAYS

Public health informatics is one of those fields of the life-sciences which combines the domains of biology, medicine, public administration, social sciences, psychology and the informatics counterpart of these fields of the sorts of bioinformatics, medical informatics and so on. There are various aspects involved in classifications and relations between classes and therefore various professional groups maintain their own classification criteria and ontologies. These aspects of classification can be taken care of by considering these classifications based on criteria, which form partitions. For example, classification can be on the basis of either (i) an agent causing a disease; (ii) speed of disease progress or (iii) period of life involved are examples of the partitions on which different types of disease classifications can be useful for different purposes. The formal basis for such classifications is provided in [2, 3]. Thus with the broad scope of public health informatics, a framework based on the formal ontological

principles will help achieve the objective of data integration and inferences drawn on those data which come from public health informatics. In the work presented here, we consider a test-case of tuberculosis and its management in order to give an insight into the formal ontology.

3.1   Entities to be represented

The entities which need to be represented as a part of the test-study include:

a. Tuberculosis as a disease and as a diagnosis
b. Tuberculous pathology with the accompanying pathological processes
c. Symptoms and signs present in a person suffering from tuberculosis
d. Investigation, risk factors, prevention, support and treatment of a person suffering from Tuberculosis
e. Use of evidence-based medicine by adhering to the clinical practice guidelines provided to manage a person suffering from tuberculosis.

Based on our discussion in the previous section, we will now look at the ontological model for the key entities and processes at the framework level.

3.2   TB: Disease, Pathology, Pathological processes

Snomed CT classifies tuberculosis as a disease. Diseases have associated pathology which have many dependent pathological processes. Based on this notion, we treat disease and pathology as phenomena, and disease course and pathological processes as processes. In order to make our case, we use the term "Tuberculosis" to represent a disease, "Tuberculous pathology" to represent the associated pathology and "Tuberculous pathological processes" to represent the associated pathological processes.

Pathology can be described at each or most of these levels of granularity. In case of tuberculosis pathology, we can distinguish them into the following levels: (i) sub cellular level pathology with tuberculosis related inclusion bodies (ii) cellular pathology related to cell destruction (iii) tissue level pathology related to granulomas (iv) there is an organ part and organ level pathology related to tuberculous nodules (v) an organ system pathology related to the organ system affected, usually respiratory system, or others like digestive system, nervous system and (vi) organism level in the form that the patient has a pathology.

Diseases are present at the level of organism. At the level of organism, like the complete human body taken together, diseases are identical to pathologies. Note that we do not draw the distinction between the physical reality in the human body and the general agreement within professional bodies as to what a disease is. In a formal sense, the physical phenomena undergoing within the human body and the conceptualization of that phenomena are not identical. In the case of disease, diseases are present within the human body while the diagnosis of that disease is conceptualized within the mind of the medical practitioner. This is a complicated issue and within this paper we do not deal with it. Going by what is present within the human body, a pathology of lung is present at the organ level of granularity and a disease of lung is a conglomeration of pathologies which originate from the lung and can be either restricted to the lung or

spread further, thus being present at the organism level of granularity.

3.3   Investigation: Manifestations of TB

Manifestations of a disease, for example a manifestation of tuberculosis, in the form of cough with sputum, breathlessness, weight loss etc. are again present at the organism level. Manifestations present at the lower levels of granularity will thus be the manifestation of the tuberculous pathology. Manifestations of tuberculosis include symptoms, signs and results of various investigations. Symptoms are manifestations reported by the patient, signs of which are confirmed by the medical practitioner. Clinical and laboratory investigations interpreted by the pathologists are the results.

3.4   Prevention of TB

The steps taken for prevention of tuberculosis include :

1. Vaccination: As discussed above BCG vaccine is a substance with role.
2. Ensuring that all close contacts of people with TB are seen promptly in the chest clinic. Requires this representation of collection of human beings in which at least one human has tuberculosis. Chest clinic needs a representation as a part of a hospital (geographical region with organizational aspects) or as an interdependent clinic (again geographical region with organizational aspects) depending on the situation.
3. Treating all people with TB disease: This is discussed below.
4. Isoniazid for prevention: Isoniazid is a medical product, a substance with roles. Its chemical composition provides a potential for it to be used as a preventive agent for TB. The drug is prescribed by the physicians and public health administrators based on its potential prophylactic properties.

3.5   TB Treatment

As the general ontology level, we will draw from the HL7 RIM[4]. providing various moods for the associated Treatment Acts.

a. The definitional mood - defines what needs to be done. e.g. defining which drug needs to be administered, for example isoniazide.
b. An intent mood - an intention to carry that act. e.g. intending to administer the drug.
c. A request mood - to request or order that the act is carried out. e.g., requesting or ordering to administer the drug.
d. An event mood is actually doing the act. For example, the act of administering the drug.
e. A criteria mood - criteria which one has in mind in order to provide a certain value to the outcome. e.g. whether that drug has been administered or not.
f. A goal mood - specifies the goal. e.g. the goal of completing the drug regime.

A planned pharmacotherapy can be specified based on these moods associated with an act. The pharmacokinetics and

---

[4] http://www.hl7.org/library/data-model/RIM/C30202/rim.htm

pharmacodynamics of the drug then follow within the human body at various levels of granularities.

3.6 TB Control

In order to represent the epidemiology of tuberculosis within the human population, one needs to introduce the notion of a collection of human beings. There are various risk factors which play a role in the spread of tuberculosis from one individual to other.

   a. People in contact with tuberculosis patients: Requires this representation of collection of human beings in which at least one human has tuberculosis.
   b. Those whose immune system is weakened by HIV or steroids: Organism and organ system level specification of the pathology.
   c. People living in cramped environment: Requires the representation of human beings, collection of human beings and the environment.
   d. Homeless: Requires the notion of human beings and environment.
   e. Alcoholic: Organism level specification
   f. Young and elderly: Organism level specification with the temporal stages of life.

Infection and transmission of tuberculosis are dealt at different levels.

   a. From a regional perspective, the population of the region is the group of human beings under consideration. That population is given a location within the geographical space of the region.
   b. While, from a national perspective, the population of the country is the group of human beings under consideration and it is the sum of regional population; and the location of that population is the geographical space of the country and it is the sum of the geographical space of various regions.
   c. For an international body like the World Health Organization (WHO), the world population and geographical space of the world is under consideration.

Such a relation of parts and sums is seen within the reports and descriptions generated by bodies dealing with different perspectives. One of the main concerns by the WHO is the movement of people which is helping to spread the tuberculosis. Global trade, air travel, refugees are all factors adding to this cause[5]. Their representation requires the relation between geographical spaces, the relation between populations, a phenomenon of movement of population as a phenomenon and the moving process as a process. Processes themselves are always dependent entities, and in this case, depends on the (i) bearers (ii) the human beings and their groups (iii) the geographical locations which are the origin, route and the end destinations and finally (iv)the phenomenon of movement which is being executed by the moving process. Some of types of entities we discussed can be summarized in Table 1.

Entities	Types
Disease	Phenomenon
Spread of disease	Phenomenon
Spreading of disease	Process
Pathology	Phenomenon
Pathological structure	Substance
Pathological process	Process
City, Province, Country	Region, Location with space
Immigration	Phenomenon
Immigrating process	Process
Hospital	Region, Location with space
School	Region, Location with space

Table 1. Some entities and their types

4 EVIDENCE-BASED KNOWLEDGE

The care pathways provide the professionals with the key evidence for decision making in each step of the pathway. Therefore, an evidence-based knowledge source is necessary to underline a successful implementation of the pathway.

The main sources of medical evidence are books, journals, and internet-based sources. These include: Health Protection Agency[6], Cochrane database[7], NHS Centre for Reviews and Dissemination, Effective Health Care Bulletins, British National Formulary, CDC, BMJ and others.
However, the quality, reliability and "non-biased-ness" of the provided information significantly vary. For example, studies of Mulrow [4], Oxman and Guyatt [5] have revealed how unreliable some editorials and review articles can be if they are not prepared systematically. In particular, although readers rely on journal review articles and editorials, the scientific evidence of these is inherently unreliable and biased towards a positive and optimistic view of the effectiveness of intervention.

As the quality of the medical knowledge on the Internet significantly varies, a National electronic Library for Health[8] (NeLH) was set up in the UK to provide a single-point portal to the best available evidence.

Our team is responsible for development of the NeLI[9] [6], the Infectious Disease branch of the NeLH. This is a single information gateway, a portal, to evidence-based information related to communicable disease with respect to all user groups – clinicians, GPs, public health professionals, environmental health officers, infectious control nurses, general public and others.

The key aim of the NeLI is to provide quality-assured evidence-based medical knowledge, reviewed by professionals in the UK, on clinical and non-clinical subjects, medical teaching material, lectures and slides.

---

[5] http://www.who.int/mediacentre/factsheets/who104/en/

[6] http://www.hpa.co.uk

[7] www.cochrane.co.uk

[8] www.nelh.nhs.uk

[9] www.neli.org.uk

4.1 NeLI Coding System

There is no common agreement on ontology, nor agreed standards in health care (coding standards, data representation standards and common legal and ethical recommendations).

Despite international standardisation initiatives, there is no common internationally accepted clinical coding scheme – currently, several coding systems are being used by different organizations: MESH, CTLV3/SNOMED and ICD10. This is not only a UK but an international issue. MESH[10] – Medical Subject Headings was chosen as the underlying medical ontology for indexing documents in the library as it is the most commonly used among medical librarians in the UK and is the standard used for indexing in Medline, however, Snomed CT might be adopted to better meet the international standards.

Besides, rigorously formalized ontologies need time to be developed as quite a lot of the work is manual to begin with, and their maintenance with the changes in medical knowledge is an ever-demanding issue. Natural Language Processing could be used to supplement solving this problem. In any case, a well-defined formal ontology is easier to update than one which is not.

The best-available method to develop such ontologies is the Protégé-OWL framework based on description logic. Large ontologies build upon Description Logic tend to be highly resource consuming and this a translation of once-formalized ontology into database is a less-ideal albeit practical approach. Physicians and other users who would be at the client side will not be exposed to the rigors of the ontology but to simple and useful interfaces which would be driven by the ontology on the server side.

5 FUTURE WORK

5.1 Further Development of the TB case study

We are now looking at further exploring the TB case study in order to develop the interoperable layer and customizable search to link the pathway to the underlying knowledge available on NeLI and other medical portals.

5.2 Customization the Knowledge to Decision Makers

One-size-fits-all solution is not satisfactory – the ontological model and the actual need to retrieve the appropriate knowledge for the person seeking the information. In particular, different information about disease management, in the form of essential action points, needs to be given to the decision makers in different roles: doctors, ~~(NURSES ARE ALSO CLINICIANS!),~~ nurses, school headmasters, directors of community centres, etc. This type of customization, in collaboration with the Health Protection Agency, UK, will be investigated by our future research.

5.3 Generalization of the Ontology Representation

The representation of care pathways, the disease treatment, control, prevention have similarities among diseases important to public health. By using formal ontological principles, those entities can be represented in a way that they are useful across the spectrum of infectious diseases. The entities within public health, as within other portions of physical reality, are based on substances, their properties, functions and processes. The recognition of those entities by practitioners are based on observations of various types (symptoms, signs, public surveys) and actions of agreements and following physical acts in order to treat, control or prevent the diseases. Thus, use of ontological principles in order to represent entities in public health is generic and would lead to life sciences data integration dealing with public health.

6 CONCLUSION

In this paper we defined a formal ontological model around a TB care pathway, as a case study, that can help medical professionals to access and retrieve the best available evidence from underlying medical databases, such as the NeLI portal.

7 ACKNOWLEDGEMENTS

8 REFERENCES

[1]Joint Tuberculosis Committee of the British Thoracic Society. Control and prevention of tuberculosis in the United Kingdom: code of practice 2000. Thorax. 2000 Nov;55(11):887-901. Review.

[2] Bittner, T. and Smith, B. A Theory of Granular Partitions", Foundations of Geographic Information Science, M. Duckham et al., eds., London: Taylor & Francis, 2003, 117–151.

[3] Grenon, Pierre, Barry Smith: SNAP and SPAN: Prolegomenon to Geodynamic Ontology. in: Spatial Cognition and Computation, 4: 1 (March 2004), 69–103.

[4] C.W. Mulrow. *The medical review article: state of the science.* Ann. Intern. Med., **106**, pp 485-8, (1987).

[5] A.D. Oxman, G. H. Guyatt. *Guidelines for reading literature reviews.* Can. Med. Assoc. Journal, **138**, pp 697-703, 1988.

[6] P. Kostkova et al. Agent-Based Up-to-date Data Management in National electronic Library for Communicable Disease. In SI: "Applications of intelligent agents in health care", J. Nealon, T. Moreno Ed, in Whitestein Series in Software Agent Technologies, in press, pages 103-122, 2003

---

[10] www.nlm.nih.gov/mesh/2002/index.html