Chapter 6: A Semantically enabled formalism for the Knowledge Management of Parkinson’s Disease

6.1 Introduction

The explosion of clinical, histological, pathological, etiological and imaging data has become a minefield for medical practitioners and researchers alike looking for meaningful information. The presence of structured and semi-structured data in emails, spreadsheets and knowledge nuggets in different clinical and research institutions residing across heterogeneous data sources on different platforms in multiple geographic locations has warranted the usage of knowledge management as an efficient and intelligent tool in tapping the fountain of information into tangible knowledge. This has led to the development of ontologies, the foundation on which the Semantic web is built.

6.1.1 Knowledge map

The modeling of the ontology constructed in the previous chapter was then used to develop the knowledge base system. Domain experts were interviewed, information extracted relevant to the different facets of PD under consideration from web resources, documents, academic journals, patient information booklets and clinical books in consultation with the experts. The interview process was conducted in both a structured and semi-structured manner. The structured process involved asking a fixed set of closed questions while the semi-structured manner involved asking open questions allowing the domain expert to delve into his/her unique experience in solving the problem at hand.

Different typographies are used in the article. Concepts are represented in `Courier New` format to distinguish concepts such as `Carers` from general terms of 'carers'. The relations or attributes are presented in *italics*. The instances are represented in **bold format**. Medical terminologies like ***substantial nigra*** are presented in bold and italics format. We first describe the ontology developed, citing examples wherever appropriate, for a particular knowledge based system. The creation of axioms to add constraints and the ability to draw inferences from the knowledge base has also been illustrated. Finally, the mapping and the merging of the different knowledge bases are described before leading to the set of conclusions.

6.2 Methodology

6.2.1 Defining organizational knowledge

Consultant neurologist, doctors, specialist Parkinson nurses, the chartered physiotherapist, the speech and language therapist and the dietitian were interviewed from the Royal Surrey County Hospital NHS Trust and Guildford and Waverley Primary Care Trust to determine the scope and the extent of granularity of the knowledge. This formed the backbone of the ontology. Besides interviewing domain experts, ontology was also developed from other sources of knowledge like leaflets, training manuals and internet sources. Organisational knowledge of the Royal Surrey County Hospital dealing with PWPD was categorized in four areas: (a) symptoms and treatment, (b) physiotherapy, (c) speech and language therapy and (d) diet.

The knowledge map of the overall KBS is illustrated in figure 6.1. Knowledge is represented by nodes while the relationship that exists between knowledge is represented by edges. The nodes are shown by the rectangular boxes while the edges are displayed by arrows. This knowledge map enabled the capture of the explicit and tacit knowledge of the organisation's intellectual capital.

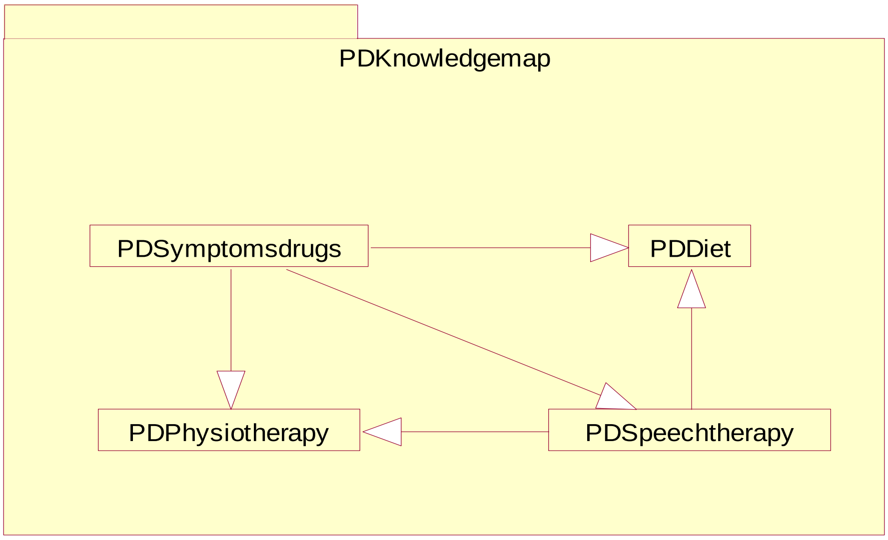

Figure 6.1 Diagram showing the knowledge map of PD

6.2.2 Background

Ontology can be regarded as the knowledge base that fills the knowledge with concepts and the relations in ontologies [107]. In elucidating the building blocks of ontology, Schulze-Kremer [107], regarded concepts together with instances, classes and predicates constitute the "semantic atoms" of ontology. Yet the semantic disambiguities of ontology persist even when human experts are involved in the development of the knowledge domain. Such ambiguities are inherent due to the terminological, syntactic and semantic differences that exist in the course of the development of our knowledge. Different experts used different terminologies to convey the same meaning in defining a concept. Experts were observed to use different concepts like `People With Parkinson's Disease` (PWPD) and `People With Parkinson's` (PWP) to convey the same meaning.   By limiting the use of grammatical constraints, the definition of concepts to four words, it was possible to make use of the context and the background knowledge of the human experts to mitigate the inherent ambiguities of ontology development.

The complexity of clinical, research, patient, imaging and published data makes it difficult to intelligently retrieve biomedical data, particularly neurological, across multiple biomedical resources. As such, the formalism of knowledge by ontology becomes essential. Since the purpose is to capture the knowledge of the experts in the neurological field, the clinical aspect of the development of Parkinson's Disease is being focused.

Yet, the *raison d'etre* of ontology is not just to create a knowledge base. It is essential to investigate the utility and usability of ontology [108] i.e. to verify whether the knowledge fits the application domain of our interest. Knowledge maps aid in the development of the knowledge base. Plumley [109] quoting French Caldwell of Gartner Group classified "knowledge maps" into 3 types: (a) procedural in which knowledge maps display knowledge mapped to a business process, (b) conceptual maps which arrange knowledge in a hierarchical manner and (c) competency maps that display the skills, positions and the career path of individuals. In this case, the procedural (or process) map that displays knowledge from the business perspective has been focused. Both tacit and explicit knowledge were regarded as inputs in the knowledge map.

6.2.2.1 Business Process Map

This is dictated by the overall process in the treatment of a patient and the different health care givers assigned to each stage of the disease. This map traverses in a systematic direction so that each of the actions triggered in the process is generated by the knowledge. This includes both explicit knowledge, knowledge that can be retrieved from manuals and other documentary sources, and tacit knowledge which is a combination of life experiences, intuition and know-how of the domain experts. The advantage of a process map is that it enables the tracing of the flow of knowledge within the knowledge map and facilitates sharing, capture, retention and packaging of knowledge [109].

The general nature of the overall ***cares pathway*** from the time a PWPD interacts with the General Practitioner (GP) in order to tap the inputs of both the tacit and the explicit knowledge of the domain experts for the purpose of building the knowledge base is shown in figure 6.2. Once the GP identifies or recommends the patient to the Neurologist or Parkinson's Disease Specialist Nurse (PDNS), they can either give their feedback directly to the GP or recommend them to the Allied Health Professions (AHP) of Speech and Language Therapy, Physiotherapy and Dietitian. Similarly, the AHP can refer the patients to the GP or refer them to each other. The knowledge inputs of Speech and Language Therapist, Physiotherapist and Dietitian, and Consultant neurologist and PDNS are harvested in the development of the knowledge base.

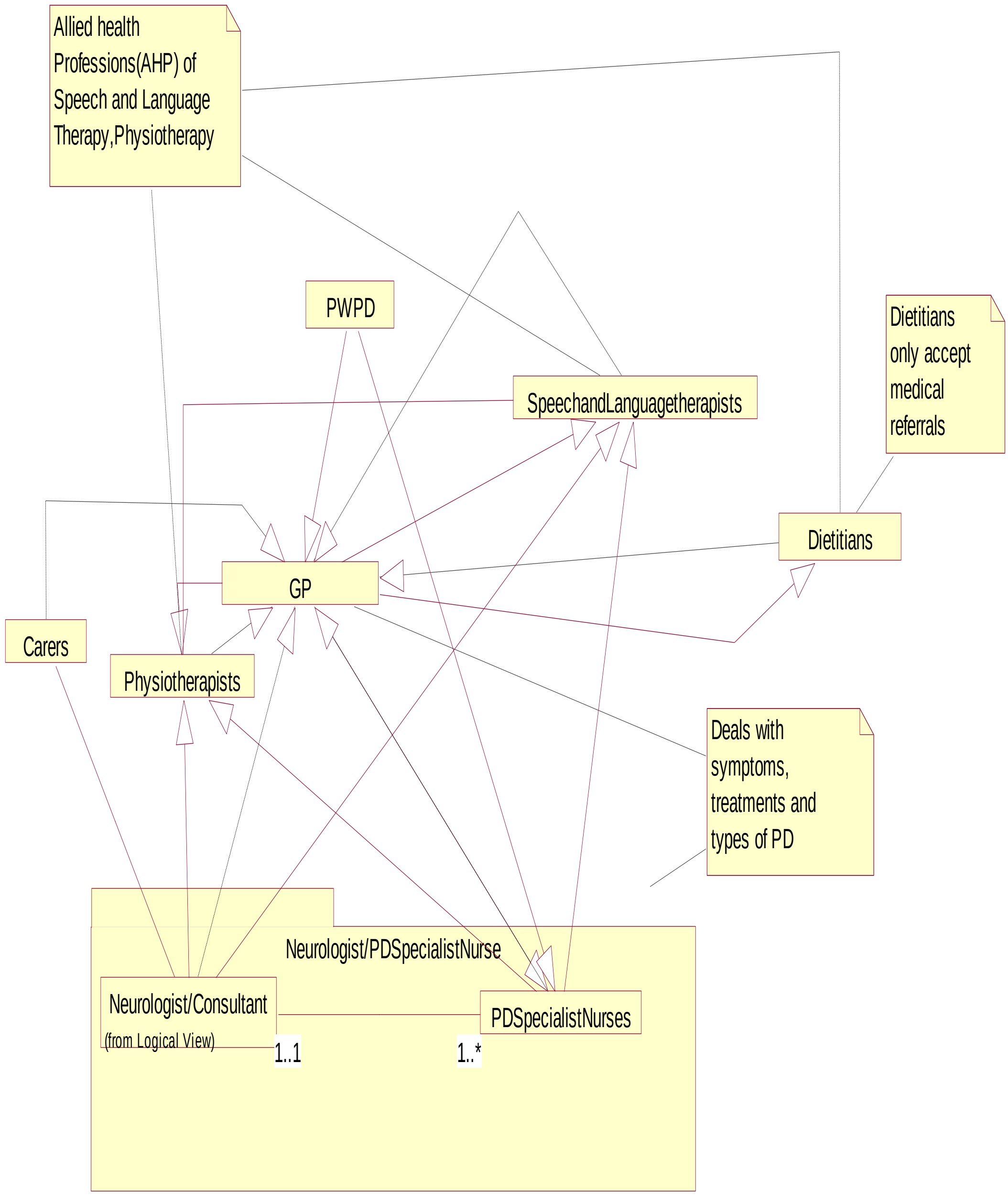

Figure 6.2 The knowledge process involved in People With Parkinson's Disease (PWPD)

6.2.2.2 Knowledge Extraction

Following the process map, knowledge is extracted by interviewing domain experts, from documents, manuals and from Internet using F-logic. The interviewing process was conducted in an unstructured manner and also in a semi-structured manner. The unstructured manner entails asking questions without any set formats while in the semi-structured process, a fixed set of questions but wherever necessary, based on the real-life experience of the experts and open-ended questions were also asked. In setting out for the construction of concepts in PDSymptomsdrugs, some of the questions asked are shown below:

(a) What are the kinds of symptoms that exist for PWPD?
(b) What are the different kinds of treatments available to patients with PWPD?
(c) What are the pharmacological treatments available?
(d) What are the different types of Parkinson Disease?

6.2.2.3 Knowledge Profile

Profiling knowledge entails describing the associative relations of the concepts, the symmetric, transitive and the inverse relationship between attributes, establishing synonyms of concepts. Symmetrical relationships are where 2 different attributes are identical. In the knowledge base of PDDiet, the relations between *juice* and *fruitjuice* are considered to be similar since the properties of juice and fruitjuice are the same. An inverse relationship is one where the converse of a property holds true in the relation e.g. the inverse of male is female. The interdependency of the clinical nature of Parkinson's Disease, however, precludes us of categorizing an inverse relation. The transitive relation is one which can be stated as if A is *part_of* B and B is *part_of* C, then A is *part_of* C. In case of PDSymptomsdrugs, *brandname*, *dosage* and *manufacturer* are transitive relations of the concepts `DopamineAgonists` and `Levodopa`.

The usability of the knowledge base was checked by the creation of inferred knowledge. This was possible by the creation of rule-based systems using F-logic, also known as Frame Logic. These rules can then be reused when new concepts are added to the set of primitives or referenced as parameters within newly created rules. F-logic, which is an extension of Datalog, includes primitives like classes, attributes, relations and instances that can be used to represent the knowledge base. It has been used for knowledge representation and reasoning with ontologies. The concepts in ontology can be represented in F-logic as `DopamineAgonists:: Pharmacologic` for the PDSymptosdrugs knowledge base which shows that `DopamineAgonists` is a subclass of `Pharmacologic`. Additionally, it allows axioms to constrain the interpretation of the model [110] and either use it to describe constraints or define new rules. The expressive power of F-logic allows for efficient reasoning with instances and a new set of rules that quantifies a whole set of classes [110].

6.2.2.4 Knowledge Verification and Validation

The knowledge is then verified and validated (also known as V & V) with the domain experts and associated health care givers. This is done only after the knowledge has been elicited and collated to create the knowledge base since the inspection and validation with the collaboration of the experts augments the knowledge acquisition process [111]. Gaps in the knowledge are identified, created knowledge is noted and redundancies eliminated, a knowledge network among domain experts established. Knowledge gaps can exist due to the failure of deploying knowledge that can conduct the business of the organization even though the knowledge is archived in the computer [112]. The questions asked are:

(a) Whether all the explicit knowledge has been unearthed and archived for the application knowledge?
(b) Whether new knowledge has been created?
(c) Whether there is consistency in knowledge profile?
(d) Whether there is redundancy in knowledge base?
(e) Whether it met the internal specifications of the knowledge base?
(f) Whether concepts and relations in the knowledge base are in any way in conflict with the definition of the ontology for the task in hand?

While these test-questions were used to assess the knowledge, the errors could be only identified with the help from the domain experts. As such, validation of knowledge can be both error-prone and tedious. While it is possible for problems to have multiple solutions, it is necessary to determine the behavioural nature of the domain experts to validate the context and the background in which the knowledge base is developed. Also, the goal in which the knowledge base is developed is taken into account in the determination of the errors [113] to preserve the ontological commitment of the knowledge base system [114].

6.3 Development of the Knowledge Base

The PD knowledge base acts as the federated knowledge base that comprises the knowledge bases on PDSymptomsdrugs, PDDiet, PDPhysiotherapy and PDSpeechtherapy and hence can act as the distributed knowledge base system. In each case, the knowledge map was used in the development of the knowledge base and the usability of the ontology was verified by inferring the knowledge. The PD knowledge base is being represented as

PDK= (PDSy,PDDi,PDPh,PDSp) ....(1)

Where PDK = PDKnowledge map,

PDSy= knowledge base of PDSymptomsdrugs,

PDDi= knowledge base of PDDiet,

PDPh= knowledge base of PDPhysiotherapy,

PDSp= knowledge base of PDSpeechtherapy

The ontologies were developed for practitioners and researchers in the area of Parkinson's Disease. Mindful of the evolving nature of knowledge, a concerted approach was taken in the construction of ontology for each of the KBS. The ontologies were classified as Canonical PWPD and Instantiated PWPD. The Canonical form of the ontology models the structural construct of the generalization/specialization of the concepts and their associated relationships while the Instantiated form represents the individual or multiple instances of the concepts.

The goal of making the knowledge base is to make it reusable. Primitive concepts were defined as abstracts in nature. This means that concepts cannot have any instances. Since knowledge is fluid, and can change with the passage of time, it should be possible to add new or edit existing concepts depending on any new discovery of knowledge. In developing the concepts for PDSymptomsdrugs the domain experts are asked the basic symptoms, treatments and types of Parkinson disease. The concepts are written starting with an upper case letter. As such, `Symptoms` and `Treatments` are created as abstract concepts so that any new symptoms or evolving treatments in the pathogenesis of PD can then be added to the knowledgebase. Since there are currently different kinds of treatments available, the type of treatments are classified as `NonPharmacologic`, `Pharmacologic` and `Surgical` which are all sub-classes of `Treatments`. `NonPharmacologic` treatment is being defined as any kind of alternative treatment, other than using pharmaceuticals and surgical procedures that helps in the treatment of PD. This included `Physiotherapy`, `Nutrition` and `AlternativeMedicine`. In the event it was necessary to add Homeopathy as an alternative medicine in the treatment for PD to the knowledge base, it can simply be added as a sub-class of `AlternativeMedicine`. Similarly, the `Pharmacologic` treatment has been classified as `DopamineAgonists`, `Levodopa`, `Amantidine`, `COMTInhibitors`, `MAOBInhibitor`. Drugs like ***antidepressants*** that exacerbate Parkinsonian symptoms should be avoided by PWPD, the concept, therefore, has been defined as `DrugsThatShouldAvoid`. Presently, there are four different surgical procedures and these are `Thalamotomy`, `Pallidotomy`, `ThalmicStimulation` and `BrainImplants`. This is shown diagrammatically in the accompanying figure 6.3.

OntoEdit, a commercial frame-based knowledge management tool, was used for the development, extraction, inference and mapping of KBS. All the information of the knowledge system in a frame based data structure is held in concepts that include attributes and the relationship between the concepts that form the Canonical form. For every entity that has an attribute there may or may not be a value. This pairing of attribute/value corresponds to the Instantiated form. F-logic, RDF/RDFS, DAML+OIL, and recently, OWL are languages that can be used to build an ontology. OntoEdit permits the construction of ontology with all the aforementioned languages except OWL. F-logic as mentioned before was used in the construction of axioms and in the inference of knowledge. OntoEdit facilitates the use of RDF/RDFS and DAML+OIL by either importing or generating a file in that format. A file generated in DAML+OIL format was used to import it on Protégé-2000, another frame based knowledge editor which is freely available (http://protege.stanford.edu) for automatic mapping of different knowledge bases.

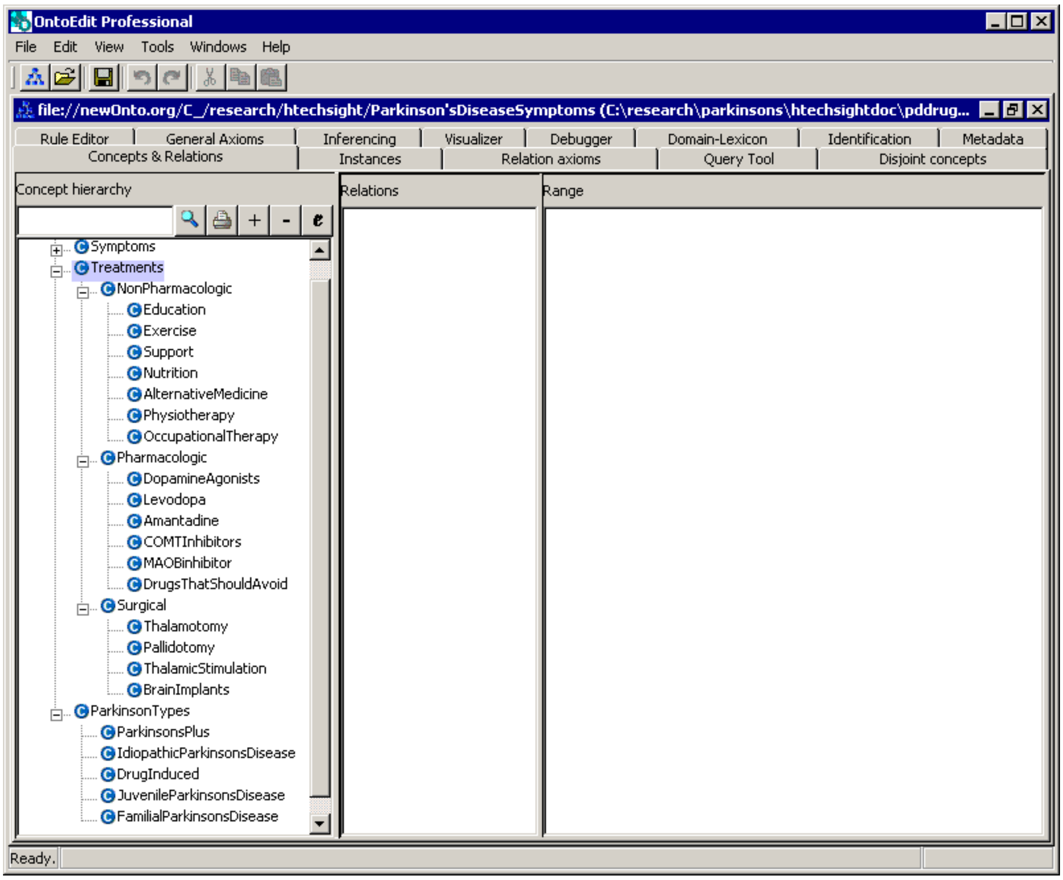

Figure 6.3 Diagram showing the KBS for PDSymptomsdrugs

The *inheritance* or *subsumption* of concepts represents the '*is-a*' relationship of knowledge representation in object-oriented form [89]. This means that `DopamineAgonists`, `Levodopa`, `Amantadine`, `COMTInhibitors`, MAOBInhibitor are instances of the class Pharmacologic which in turn is an instance of the primitive class Treatments. These instantiated classes would then inherit all the attributes of the parent class. Using the 1st order logic, an 'is-a' relationship can be represented generally as:

A *is-a* B = $\forall$ x (inst(x,A) $\rightarrow$ inst(x,B).. (2)

where the 1st order variables for x ranges over instances while that for A ranges over classes. The symbol $\forall$ means 'for all values' and '$\rightarrow$' means 'if … then...' and 'inst' is an axiom that is valid in all cases between an instance and a class and that no entity can be both a concept and an instance at the same time [84]. If for every instance of Pharmacologic, represented as inst(x,Pharmacologic), and for all values of instances as Levodopa, defined as $\forall$ x (inst(x,Levodopa), then it can be shown that Levodopa is an instance of Pharmacologic:

Levodopa *is-a* Pharmacologic = $\forall$ x (inst(x,Levodopa) $\rightarrow$ inst(x,Pharmacologic) .. (3)

One of the benefits of a subsumption relationship between 2 concepts is that it facilitates the union of 2 or more concepts, *A U B*, such that the superconcept ParkinsonTypes can be regarded as a combination of all the different kinds of Parkinson's Disease like ParkinsonsPlus, IdiopathicParkinsonDisease, DrugInduced and JuvenileParkinsonDisease.

The *relations or the attributes* of the concepts correspond to the '*has-part*' of the relationship. This structural relationship of attributes to concepts is demonstrated as:

B *has-part* A = $\forall$ y (inst(y,B) $\rightarrow$ $\exists$x (inst(x,A) & part(x,y))) .... (4)

Where $\exists$ represents "for some value of " and 'part ' constitutes the part relation among individual entities. Equation 4 states that B cannot exist except for the instance level parts of A.

The attribute *sideeffects* of the concept `Levodopa` can therefore be represented as follows:

Levodopa *has-part* sideeffects = $\forall$ y (inst(y,Levodopa) $\rightarrow$ $\exists$x (inst(x,sideeffects) & part(x,y))) .... (5)

The part relations can be transitive and reflexive. In this case, not all treatments which are pharmacologic in nature will have side effects but Levodopa like pharmacologic treatments has *sideeffects*. Transitive relations are those parts (also known as partonomies) that are represented as:

part(x,y) & part (y,z) $\rightarrow$ part (x,z) .... (6)

The concepts `Pharmacologic, DopamineAgonists` and `Levodopa` are related via the **dosage** relationship which is transitive in nature e.g. a `Pharmacologic` drug would show **dosage** for all drugs, `DopamineAgonists` would show dosage for all drugs of ***dopamine agonists*** and `Levodopa` would show dosage for all ***levodopa*** drugs. Reflexive relationships are relations where for every concept A, we have A '*is-a'* A. Such a relationship does not exist for the application domain. Symmetrical relationships are where two different attributes are identical. The different relationships are shown in figure 6.4.

The attributes can have n-ary relationships. For example, the *sideeffects* of administering **Sinemet, Madopar,** two kinds of Levodopa has multiple instances like 'nausea','vomitting' and 'low blood pressure'.

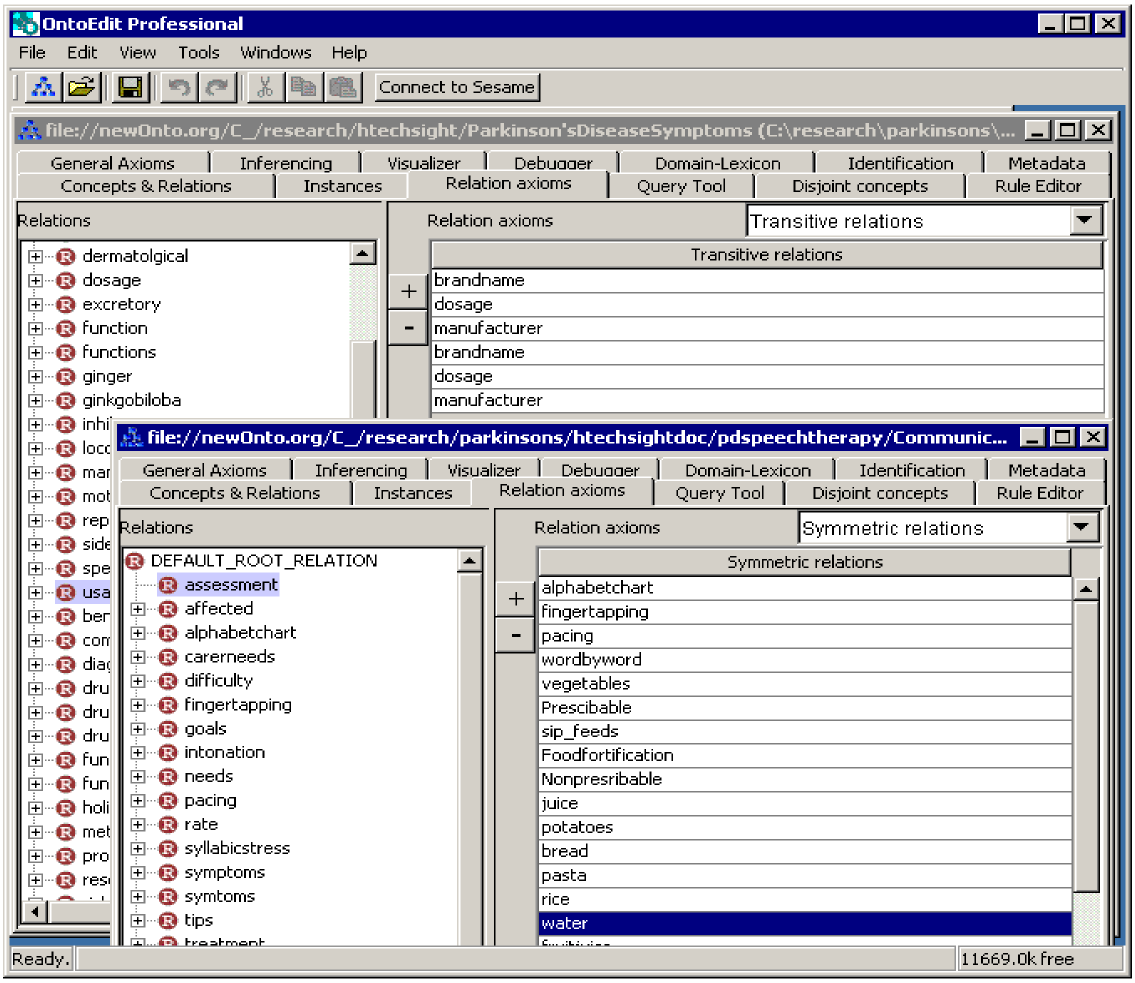

Figure 6.4 Transitive relations of the KBS of PDSymptomsDrugs and symmetric relations of the KBS of PDSpeechtherapy

Each of the knowledge bases was enhanced by the addition of non-structural relationships of concepts and attributes as synonyms. The concepts `ParkinsonPlus` is analogous to `Atypical Parkinsonism` and the synonym for `FoodFortification` is `High Calorie Diet`. This is illustrated in figure 6.5. Adding similar terms to the lexicon of the domain can expand the ontology further. The addition of synonym gives added meaning to the established concepts and where necessary filtering out erroneous synonyms [99]. Such normalization of ontologies was done during the knowledge validation stage in concurrence with domain experts. This would reduce the ambiguity of terms and eliminate any problems when integrating with external databases where such redundancy of data is abundant. Synonymous concepts enable queries to retrieve different terms that have the same meaning. While such terms and concepts can be stored in different languages, homonyms or a single concept having several meanings or criteria are not available.

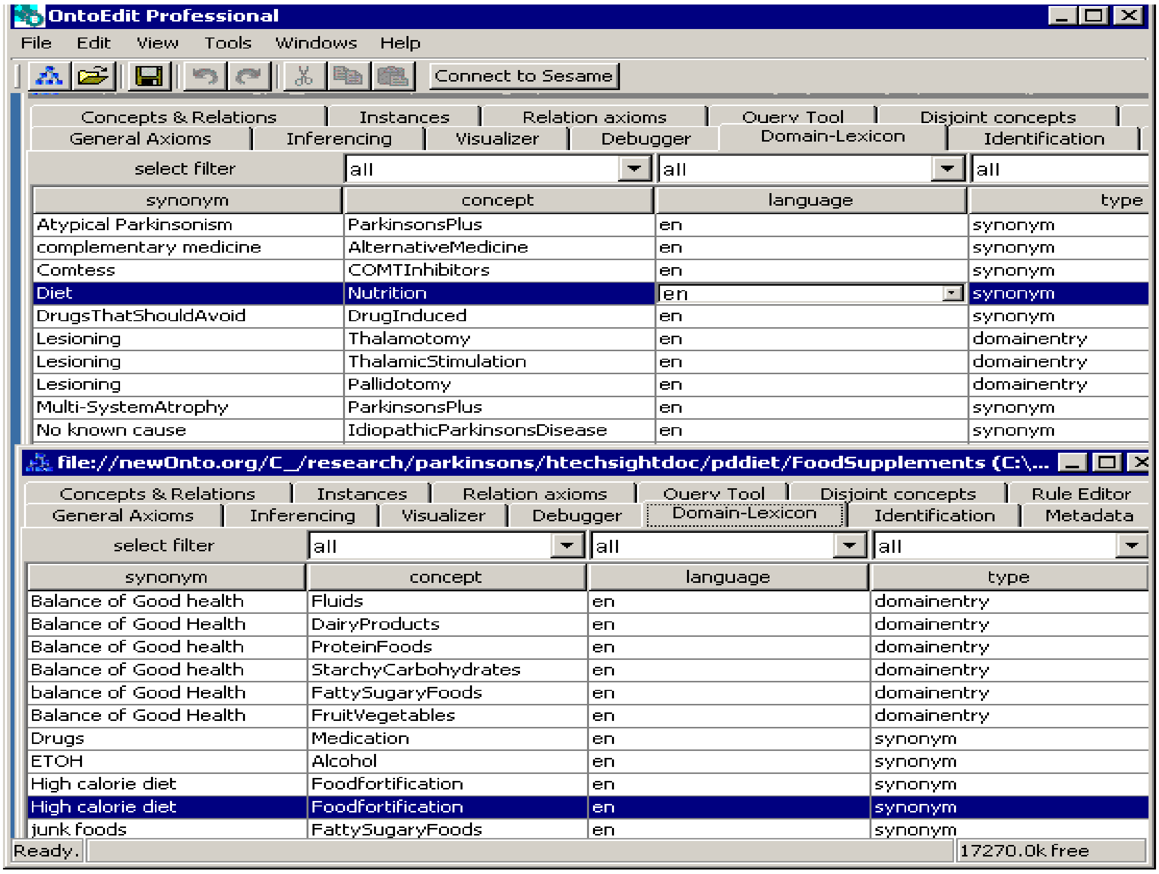

Figure 6.5 Synonyms of KBS of PDDiet and PDSymptomsdrugs

The instances of the concepts are known as facts. These facts are the individual items of the concepts. Several instances have been modeled for each of the knowledge bases that have been developed. In case of the PDSymptomsdrugs, there are 6 instances of ***dopamine agonists***. They are **Bromocriptine, Pergolide, Pramipexole dihydrochloride, Ropinirole hydrochloride, Cabergoline** and **Lisuride**. This is shown in figure 6.6.

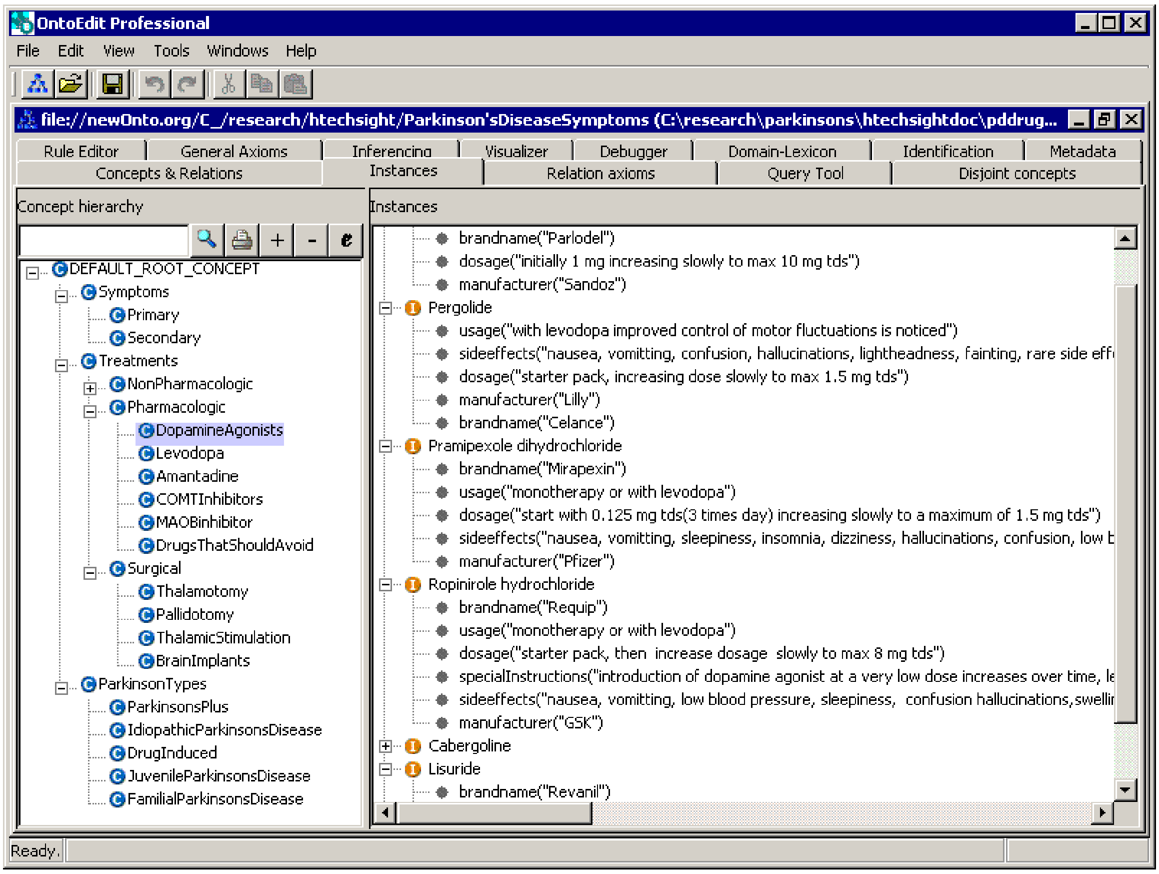

Figure 6.6 Instances of `DopamineAgonists`

6.4 Advanced Features and Knowledge Inference

The consistency and the purpose of the knowledge base can be enhanced by implementing logic in the knowledge base. This is facilitated by the use of F-Logic which acts as a bridge between the model and the logic since it covers ontological data and the rules [81]. This is made possible by the fact that every object in the ontology can be written in F-Logic atoms or molecules which in turn can be embedded into logical rules [115]. Axioms allow the knowledge base to function within the constraints of the business logic for the domain. Hence it allows for the integrity of the knowledge base. Axioms therefore serve as a brake to ensure that the knowledge base does not deviate from the behavioural goal of the knowledge base. It is also possible to reuse these axioms in other ontologies and make the development of ontologies more modular.

Different namespaces identifying the definitions of axioms of a domain specific ontology can then be loaded into a different ontology [110].

6.4.1 Implementation of Rules

The logical relationships between the concepts can be enhanced by the addition of new rules. These rules or axioms are implemented in the maintenance of specific integrity constraints. Here some of the axioms specified in F-Logic are shown:

(1) Hyponyms and Hypernyms

Both hyponyms and hypernyms can give rise to problems in mapping between ontologies where a concept in one ontology can be regarded as more general than a concept in another ontology. While hyponyms are objects which can have dual meanings, the objects of hypernym are being defined, in this case, as subconcepts of `Pharmacologic`, so that it would be possible to find all the subconcepts whose superconcept is `Pharmacologic`. This is also necessary in order to find all the drug treatments that are available for PD and can also be reused in other knowledge bases like PDDrugs where the dietary habits of the patients are linked to the kind of medications that are prescribed by the neurologists.

<u>Illustration</u>: The rule can be expressed as follows:

```
FORALL A,B ( A::B )
<- ( (Hypernym(A,B)
   and B::Pharmacologic) ).
```

(2) Consistency in domain-specific ontology

Axioms can also be used to enforce the consistency in domain-specific ontology. These axioms raise an alert whenever an inconsistency is either detected or derived and helps in the detection of local inconsistencies in the ontology. The relation h*asPart* can be enforced as a domain-specific relation of `AlternativeMedicine` in the PDSymptomsdrugs knowledge base such that `NonAllopathic` is a subclass of `AlternativeMedicine`.

Illustration: The *hasPart* is of the type `AlternativeMedicine` and would indicate a consistency violation if any attribute of Homeopathy is of type NonAllopathic and AlternativeMedicine and X is related to Homeopathy via itself:

NonAllopathic::AlternativeMedicine(hasPart).
FORALL X,R (undefined)
<- ((NonAllopathic(R)
and X[Homeopathy->X])).

(3) Concatenation of the string

The individual physiotherapy requirements for a PWPD consist of addressing the personal needs of the patient and talking to them privately.

Illustration: "Individual therapy requirements" of a patient with physiotherapy will succeed only after the patient has ***talked privately*** and has met the ***personal needs***. This is demonstrated with the use of in-built function "concat":
FORALL X,A,B (X:IndividualOrGroup)
<- ((X[talkprivately->A]
and (X[personalneeds->B]
and concat("individual therapy requirements",A,B)))).

(4) Enumeration of External Services

This example categorises all the features provided by the External Services team for physiotherapeutic services.

Illustration: In this case, the `ExternalServices` has several instances of the attribute *features* like "strong links between hospital and home settings","contact with physiotherapist on diagnosis","programme of long-term monitoring and on-going management","flexible frequency of physiotherapy review","self-referral to physiotherapy service by individuals and carers" and "commitment to on-going professional knowledge updating". This is making usage of the in-built function "message", expressed as follows:

FORALL X (message("The External Services team features offered by the physiotherapy services"))
<- (X:ExternalService[features->>{"strong links between hospital and home settings","contact with physiotherapist on diagnosis","programme of long-term monitoring and on-going management","flexible frequency of physiotherapy review","self-referral to physiotherapy service by individuals and carers","commitment to on-going professional knowledge updating"}]).

(5) Benefits of early referral

In this axiom, the numerous benefits of early referral by the consultant for physiotherapeutic services are being specified.

Illustration: The relation *earlyreferral* of the concept `Referral` has multi-valued instances of "address concerns about differential diagnosis","assessment and monitoring to allow early identification of movement problems","encourage participation through optimal conditioning of cardiovascular, musculoskeletal and neuromuscular systems","preventive management of secondary complications such as joint stiffness","introduce movement strategies for use","education of individuals and carers about physical management of PD" and "monitor drug efficacy to optimise motor performance. As such, the benefits accrued by referring early in the treatment are shown below:

FORALL X,Y (X[benefits->>Y])
<- (Y:Referral[earlyreferral->>{"address concerns about differential diagnosis","assessment and monitoring to allow early identification of movement problems","encourage participation through optimal conditioning of cardiovascular,

musculoskeletal and neuromuscular systems","preventive management of secondary complications such as joint stiffness","introduce movement
strategies for use","education of individuals and carers about physical management of PD","monitor drug efficacy to optimise motor performance"}]).

6.4.2 Logic based Inference

F-Logic can also be used to query the knowledge base, extract knowledge from external sources and add it to the knowledge domain. It is possible to extract instances and schema from the KBS. This inference of knowledge is done to test the validity of the knowledge base. This is essential to ensure that the behaviour of the knowledge base functions within the stated parameters of the application domain. At this stage the domain experts are consulted to verify the querying of the knowledge base. Any error in the retrieval of the query of the knowledge base is resolved in the context of the domain and the background of the knowledge. The following examples that aid in the inference of knowledge are cited below:

(1) Knowledge Extraction from Internet

Knowledge, at times, needs to be extracted from the Internet to add to the knowledge base. The data available can be in both structured and semi-structured format. The management of semi-structured format is performed better by the use of the FLORID system♣ an implementation of F-Logic, and for the mediation of Web data. F-Logic, in this case, extracts structured format from Internet portal PubMed.

Illustration: Health care workers looking to monitor the latest information on the *sideeffects* of the two Levodopa drugs of **Sinemet** and **Madopar** can retrieve 20 articles that will return the journal and the name of the authors by executing the following query:

FORALL X,Y,Z,A <-pubmed(["sinemet, madopar, side effects"], 1, 20, X, Y, Z, A).

♣ http://www.informatik.uni-freiburg.de/~dbis/florid

Output: A section of the output showing the name of the journal, the authors and the web-link is shown below:

"/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10617291"; "Castiello U, Bennett KM, Bonfiglioli C, Peppard RF."; "The reach-to-grasp movement in Parkinson's disease before and after dopaminergic medication.
Neuropsychologia. 2000;38(1):46-59.
PMID: 10617291 [PubMed - indexed for MEDLINE]"; "11"
"/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=2324754"; "Horstink MW, Zijlmans JC, Pasman JW, Berger HJ, van't Hof MA."; "Severity of Parkinson's disease is a risk factor for peak-dose dyskinesia.
J Neurol Neurosurg Psychiatry. 1990 Mar;53(3):224-6.
PMID: 2324754 [PubMed - indexed for MEDLINE]"; "11"
"/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=2586766";

………………….

(2) Names of drugs of Levodopa

There are times when the health care worker would like to find out the names of drugs. This is exemplified below.

Illustration: If the healthcare worker wants to find out the brand name of the drugs of Levodopa and their corresponding manufactures that are not manufactured by Dupont, then it can be represented as:

FORALL X, Y <- EXISTS A
A:Levodopa[BrandName->>X;Manufacturer->>Y] AND NOT equal(Y, "Dupont").

Output:
Madopar (levodopa + benserazide)";"Roche""

This output is correct since **Madopar** is the brand name for the ***levodopa*** drug that is manufactured by Roche.

(3) List of drugs that PWPD should avoid

Sometimes it becomes necessary to know the drugs that a patient should avoid since it can lead to Parkinson like symptoms.

Illustration: In order to find the list of drugs and their corresponding manufacturer's name that patients should avoid since it leads to ***Drug Induced Parkinsonism***, the following query can be executed

FORALL X, Y <- EXISTS A, Z
A:DrugsThatShouldAvoid[Manufacturer->>X;BrandName->>Y; SideEffects->>Z].

Output: A section of the output, as validated by the domain experts is shown below.

"Sanofi"; "Motival"
"Sanofi"; "Motipress"
"Sanofi"; "Stelazine"
"Sanofi"; "Parnate"
"Sanofi"; "Triptafen"
"Sanofi"; "Fluanxol"
"Sanofi"; "Depixol"
"Goldshield"; "Motival"
"Goldshield"; "Motipress"
"Goldshield"; "Stelazine"
....

(4) Dosage and usage of drugs

Often, consultants and specialist nurses need to know the dosage and the usage of the drugs that are prescribed to patients. This is exemplified in the following illustration.

Illustration: If the clinician wants to find out the list of drugs of DopamineAgonists, the corresponding brand name, the manufacturer other than Lily and their usage, then the following representation yields the correct results

FORALL A, B, C, D <- EXISTS X

X:DopamineAgonists[Dosage->>A; BrandName->>B; Manufacturer->>C;Usage->>D] AND NOT equal(C, "lily").

Output: The above query delivers the results for the each of the ***dopamine agonists*** drugs with their concomitant dosage, the brand name of the tablet, the corresponding manufacturer and their usage.

"start with 0.125 mg tds(3 times day) increasing slowly to a maximum of 1.5 mg tds"; "Mirapexin"; "Pfizer"; "monotherapy or with levodopa"
"starter pack, then increase dosage slowly to max 8 mg tds"; "Requip"; "GSK"; "monotherapy or with levodopa"
"1.0 mg/day increasing to max 6 mg/day"; "Cabaser"; "Pfizer"; "monotherapy or with levodopa"
"either as sub-cutaneous injections(max 10 mg) or infusion range 3-30 mg daily"; "Apo-go"; "Brittania"; "only available sub-cutaneous dopamine agonists used in fairly late disease"

6.5 Mapping and Merging of Ontologies

The mapping and merging of the different ontologies are performed manually in OntoEdit. Each of the KBS was manually mapped against each other. In consultation with domain experts, manual mapping was done using OntoEdit. Figure 6.7 shows the mapping of PDDiet and PDSymptomsdrugs to each other. This was mapped according to the equivalency of the two ontologies. In an equivalent mapping, ontologies which are conceptually similar are mapped to each other. The relations to the concepts were then mapped e.g. the mapping of the concept Medication in PDDiet to the concept Pharmacologic, a subsumption of Treatments in PDSymptomsdrugs. Medication was regarded as a kind of pharmacologic treatment by both the domain experts. Similarly, the concepts `BalanceOfGoodHealth`, `FoodSupplements`, `VitaminsMineralsAntioxidants` and `EatingPlan` in PDDiet KBS are mapped to `Nutrition` in the KBS of PDSymptomsdrugs. In order to avoid mismatches in granularity during the one-to-one mapping procedure it would be possible to specify a term, e.g. `Diet`, that would be the union of

`BalanceOfGoodHealth`, `FoodSupplements`, `VitaminsMineralsAntioxidants` and `EatingPlan`, and hence map easily to `Nutrition`.

The mapping of the relations to the concepts is shown in figure 6.8. The relation *exercise_opportunities* and *palliative_stages* were both affected by the food supplements, hence they are mapped to FoodSupplements. This kind of mapping facilitates in the database integration of the knowledge base. Once the concepts are mapped to each other, their corresponding attributes can then be mapped. This is shown in figure 6.9.

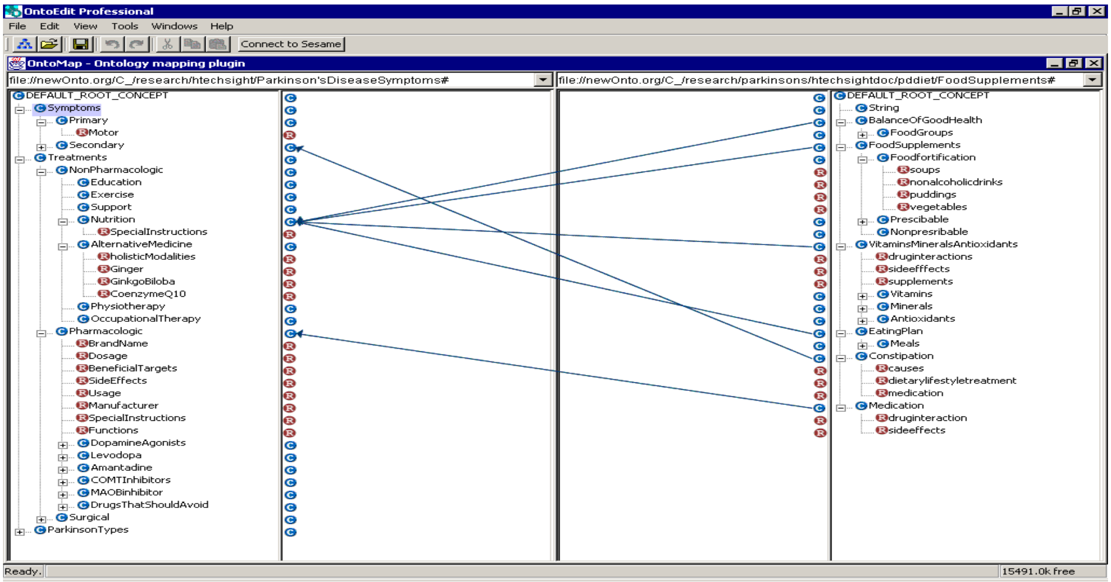

Figure 6.7 Mapping of the concepts between PDSymptomsDrugs and PDDiet

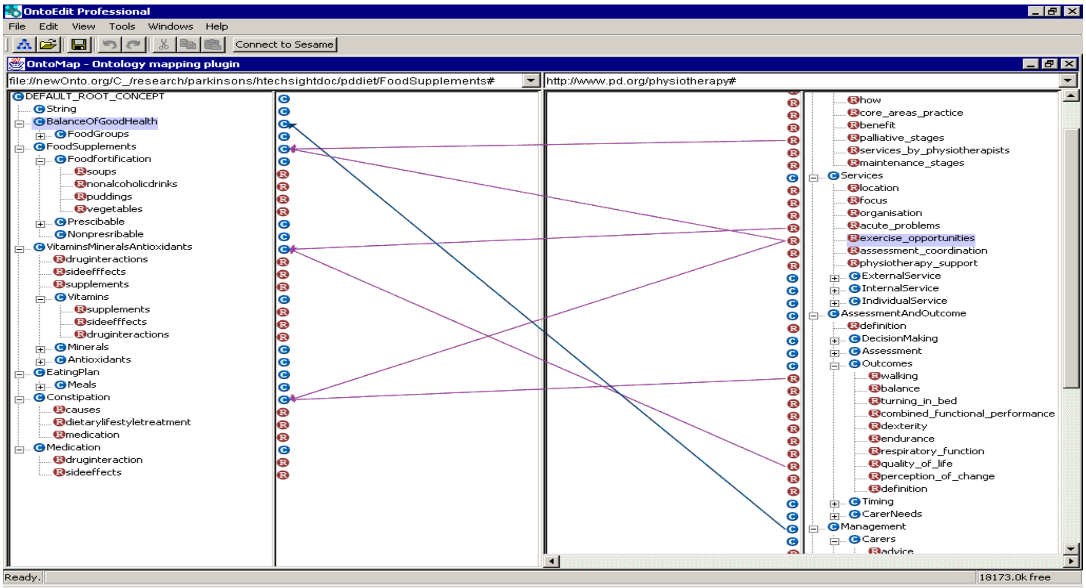

Figure 6.8 Mapping of relations to concepts between PDPhysiotherapy and PDDiet

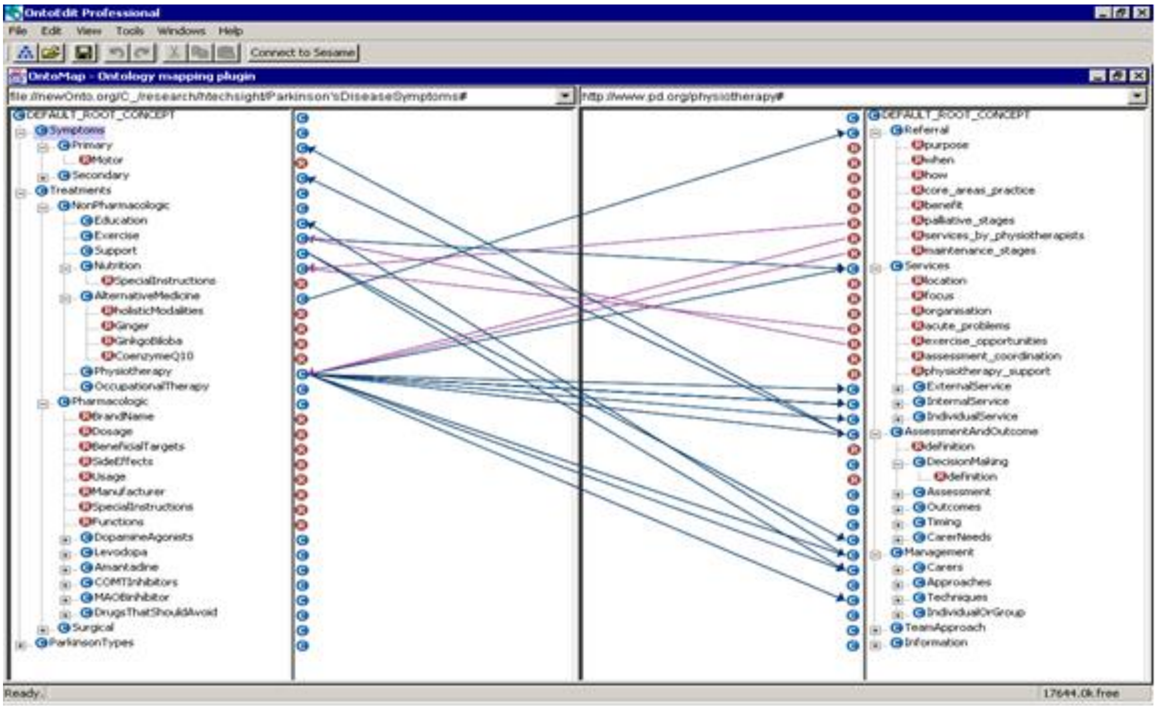

Figure 6.9 Mapping of the relations between PDSymptomsdrugs and PDPhysiotherapy

6.5.1 Merging of PDPhysiotherapy and PDSymptomsdrugs Ontologies using PROMPT

The component based architecture of Protégé 2000, allows users to add new features by installing plug-ins like PROMPT. The KBS of PDSymptomsdrugs and PDPhysiotherapy was exported in DAML+OIL format which was then imported into Protégé 2000.

The interface for the merging of the ontologies for PDSymptomsdrugs and PDPhysiotherapy is shown in figure 6.10. This provided the two source classes and their corresponding slots (attributes in OntoEdit) and their instances. The resulting ontology was obtained by merging the two ontologies. In the source class those classes that needed to be merged resulted in the generation of classes that already existed. It provided a list of the specific operations in its suggestions. This is illustrated in figure 6.11. The suggestions were made from both of the ontologies and contain the concepts or classes of the ontologies. While most of the suggestions were not valid, some even registered conflicts as shown in figure 6.12. The domain experts suggested the overwriting of the decisions of the tool. Another notable feature of the plug-in was that it allowed the corresponding instances of the source class to be seen. The completed merging of the KBS is illustrated in the accompanying diagram of figure 6.13.

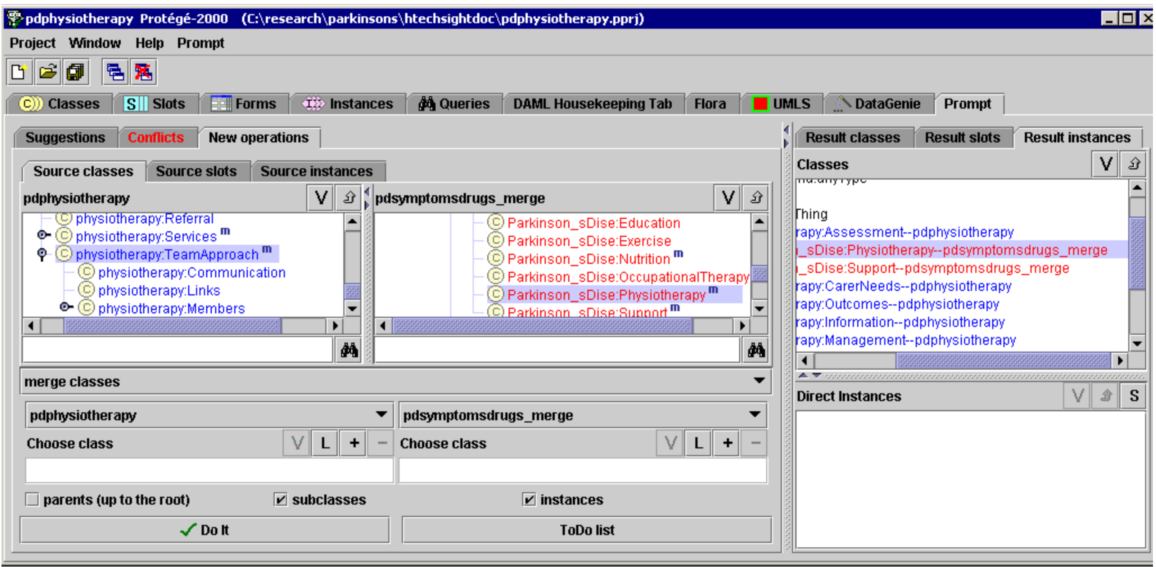

Figure 6.10 The merging operations of PDPhysiotherapy and PDSymptomsdrugs

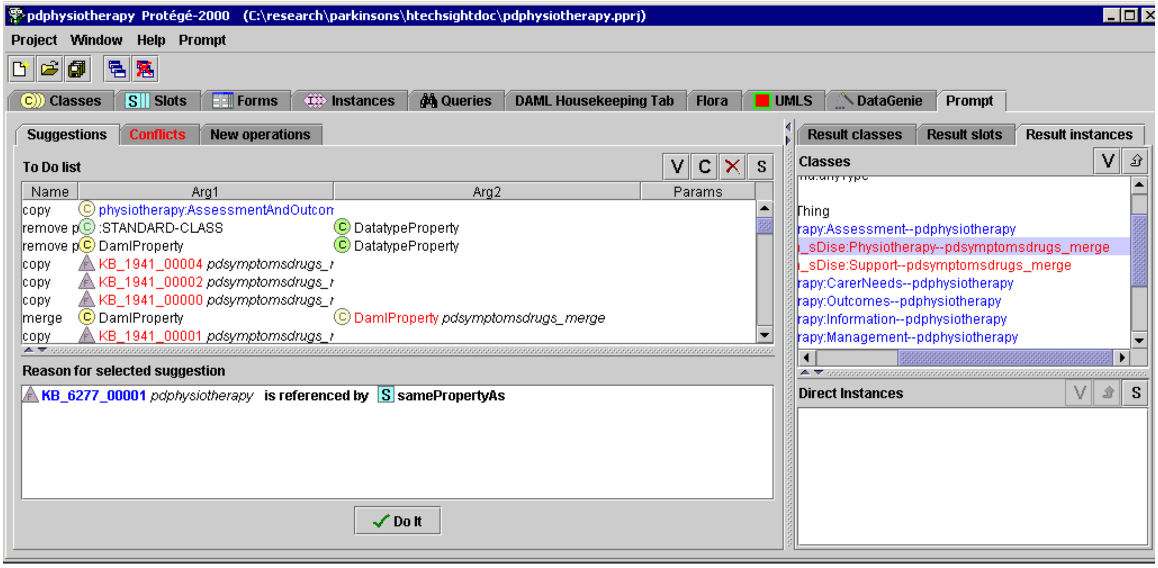

Figure 6.11 The suggestions made by PROMPT

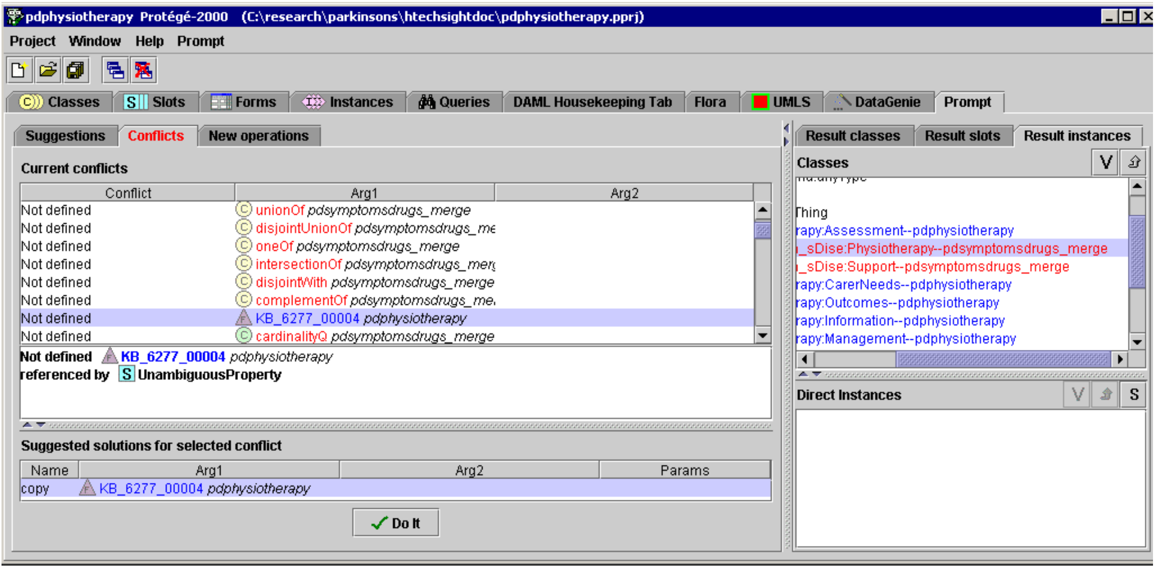

Figure 6.12 The conflicts of the proposed suggestions made by PROMPT

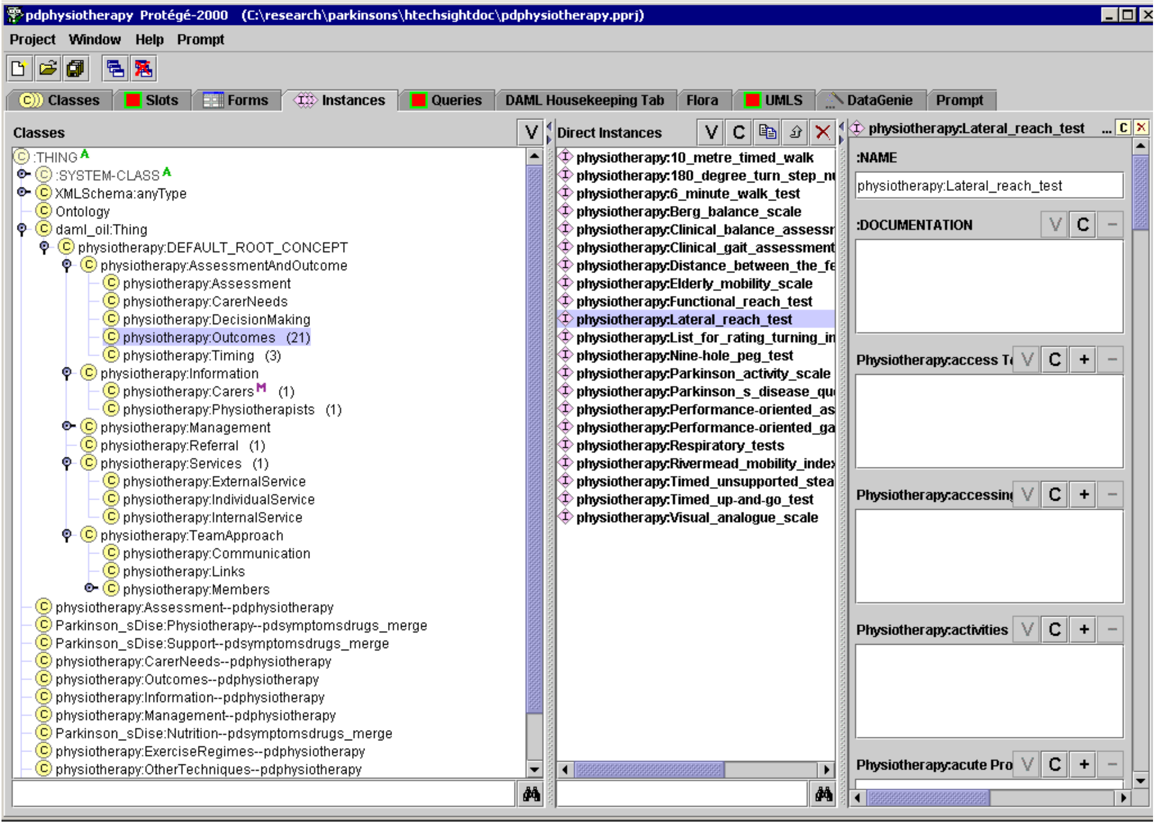

Figure 6.13 The completed merging of PDPhysiotherapy and PDSymptomsdrugs

6.6 Conclusions

The process of knowledge map was used in the development of the KBS for each of the knowledge bases. It is a step-by-step iterative process that helps to identify potential gaps in knowledge, generate knowledge creation, archive and extract the artifacts of knowledge, provide a basis for the storage of intellectual and intangible assets that can reduce the burden of experts by sharing knowledge in the biomedical domain of Parkinson's Disease. Considerable social capital needs to be expended in order to facilitate the process. A facilitator who can act as the bridge between the domain experts and the knowledge engineers can expedite the development process. Knowledge merging and mapping is one of the steps in knowledge mapping that should not only be performed after the knowledge validation step but is also a reiterative step that needs to be validated again after it is merged. A reusable knowledge base was created whereby researchers can add in new knowledge by making use of the primitive concepts. New axioms can be added to facilitate the creation of inferences.

The mapping of the knowledge was performed manually and merging was done by a semi-automatic process. The manual operation was tedious and time-consuming. Although the merging of the KBS was semi-automatic it gave rise to substantial conflicts which had to be resolved by further expert human input. A federated knowledge base that interacts with other loosely coupled knowledge bases was created out of this merging process.

The next chapter summarizes the conclusions and provides recommendations for future work.