

Ontological Inference of Treatment Plans from Psychiatric Clinical Guidelines

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Introduction



Motivation

Clinical practice guidelines (CPGs)

Benefits of CPGs:

- Reduce medical errors
- Better cost-efficiency
- Standardised workflows

In practice: Gap between evidence-based medicine and their actual use.

Potential barriers:

- Organisational context: Lack of time
- Social context: Disagreements with colleagues; Social routines
- Professional context: Information overload; Complexity of guidelines
- Professional context: **Information overload; Complexity of guidelines**

Addressed by Clinical Decision Support (CDS)

Previous Work

Proof of concept for a CDS system, called CGM/F20:

- Clinical Guideline Module (CGM)
- Formulates parts of German *Schizophrenia* guideline in OWL (diagnostic code F20).
- Saves medical record of patients in OWL

The system has been able to infer:

- Recommendations regarding diagnosis and measures.

Previous Work

CGM/F20 ⊞ ⌵

Patient

Recent history | Past history | Guideline assistant

Event	Type	Start date	End date
Symptom	Commenting voices	17.02.2015	
Symptom	Skin rash	03.03.2015	
Symptom	Mild fever	05.04.2015	
Suspected diagnosis	HIV	21.04.2015	
Measure	Test for HIV	22.04.2015	
Diagnosis	Acute schizophrenia	23.04.2015	

Additional information:

Question	Answer
----------	--------

(a) Apply symptoms, diagnosis and measures to medical record of patient

Previous Work

The screenshot shows a software interface for a patient named 'CGM/F20'. The interface has tabs for 'Recent history', 'Past history', and 'Guideline assistant'. Below these tabs is a table with three columns: 'Matched recommendation', 'Status', and 'Guideline sections'. The table contains two rows of data. Below this table, a 'Missing Information' dialog box is open, containing a table with three columns: 'Question', 'Answer', and 'Guideline section'. The dialog box also has 'Yes', 'No', and 'Done' buttons at the bottom.

Matched recommendation	Status	Guideline sections
Diagnosis: Acute schizophrenia	Possible (missing information)	DPGG SG (1)
Measure: Test for HIV	Recommended	DPGG SG (2)

Question	Answer	Guideline section
Is the patient undergoing a detoxification?	yes	DPGG SG (1)
Does the patient have a nonorganic psychotic disorder?	yes	DPGG SG (1)
Is the patient intoxicated?	unknown	DPGG SG (1)
Does the patient have a brain disorder?	unknown	DPGG SG (1)
Does the patient have a substance induced psychotic disorder?	unknown	DPGG SG (1)
Does the patient have an organic induced psychotic disorder?	unknown	DPGG SG (1)

(b) Infer recommendations for patient

Topic of my thesis

Extending the CGM/F20 framework by:

1. Covering a larger part of *Schizophrenia* guideline.
2. Generating individual treatment plans.

Benefits:

1. Displaying not only immediate recommendations but rather a complete treatment plan for an ongoing therapy
2. Treatment plan can adjust dynamically and use existing knowledge to be as specific as possible

Implementation



Introduction to *Web Ontology Language* (OWL)

General understanding

- Knowledge representation language
- Based on description logics (*ALC*, *SROIQ*)
- Use-cases: Defining the structure of knowledge for domains of interest

Basic blocks of OWL

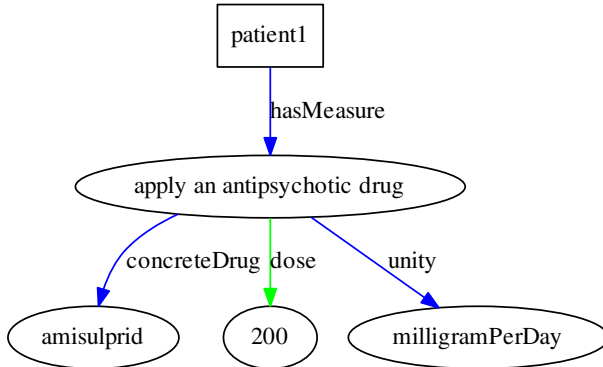
- Instances: Objects (e.g., tim, lisa)
- Classes: Set of objects (e.g., Human(tim), Human(lisa))
- Properties: binary relation between objects (e.g., hasParent(tim,lisa));
different logical features: *transitive*, *symmetric*, *inverse*

Ontological Design



Ontology Design I – Drug Application

According to guideline application of drugs is essential for a successful therapy:



Ontology Design I – Drug Application

Guidelines defines *starting* and *targeting* dose for patients:

Class: Startdose_Atypical_Aripiprazole

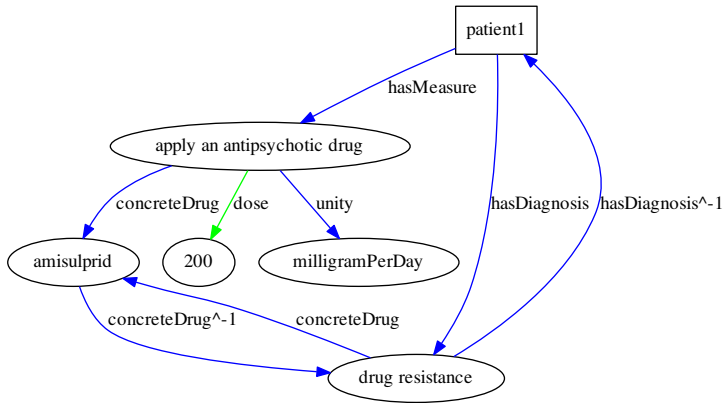
```

EquivalentTo:
  (concreteDrug some Aripiprazole) and
    (((unity some GramPerDay)
      and (dose some xsd:double[>= "0.01"^^xsd:double ,
        <= "0.015"^^xsd:double]))
    or ((unity some MilligramPerDay)
      and (dose some
        xsd:double[>= "10.0"^^xsd:double ,
        <= "15.0"^^xsd:double]
      )
    )
  )

```

Ontology Design II – Therapy resistance

Representation of a therapy resistance:



Ontology Design II – Therapy resistance

Class: TherapyResistance_ActiveDrugApplication

EquivalentTo:

```
hasMeasure some
  (ApplyAntipsychoticDrug
   and time:CurrentEvent
   and (concreteDrug some (concreteDrugInverse some
     (DrugResistance
      and time:CurrentEvent
      and (hasDiagnosisInverse some Patient))))))
```

SubClassOf:

```
Definite_ResistanceCurrent2ApplyStart ,
RecommendHavingTherapyResistance ,
hasFutureRecommendedMeasure only
  ((not (Condition_Resistance2CurrentDrug))
   or (time:is_theoretical_next_step_but_not_recommended
      value R_Condition_HadClozapineApplication)),
hasNonRecommendedMeasure value R_ApplyTargetDose ,
hasNonRecommendedMeasure value R_IncreaseorDecreaseDoseOfAntipsychotica ,
hasRecommendedMeasure value R_MarkDrugApplicationAsNotSuccessful ,
hasRecommendedMeasure value R_StopCurrentDrugApplication
```

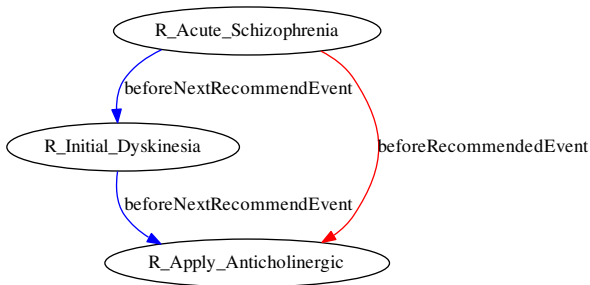
Treatment plans



Chronological Order of Events

- As an **event** we treat measures, diagnosis and symptoms.
 Generation of a treatment plan requires a *temporal relationship* between events.

Introduce two new object properties:



Future recommendations

Missing: A relation signalling that a recommendation may be relevant for the therapy of a patient

⇒ Introduce new object property `hasFutureRecommendedEvent`

Create classes for patients that infer these relations to specific recommendations, e.g:

```

Class: :FutureAcuteSchizophreniaRecommendations

EquivalentTo:
  :hasFutureRecommendedDiagnosis some :AcuteSchizophrenia

SubClassOf:
  :hasFutureRecommendedMeasure value R_Liver_First_Week ,
  :hasFutureRecommendedMeasure value R_Condition_HasInitialDyskensia ,
  :hasFutureRecommendedMeasure value R_MakePhysicalExamination
  
```

Future recommendations

Class: :FutureAcuteSchizophreniaRecommendations

EquivalentTo:

:hasFutureRecommendedDiagnosis some :AcuteSchizophrenia

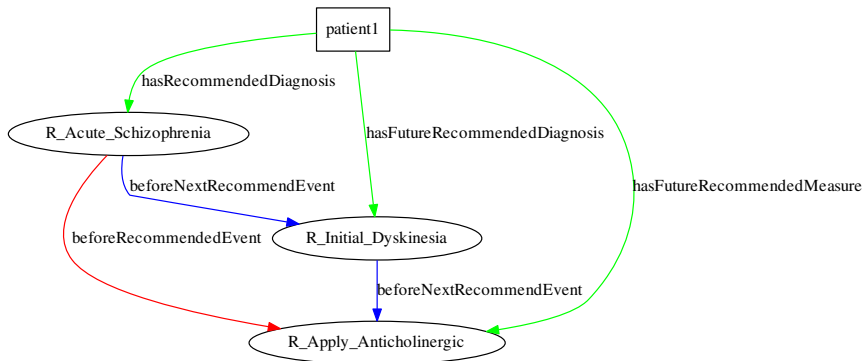
SubClassOf:

:hasFutureRecommendedMeasure value R_Liver_First_Week,
 :hasFutureRecommendedMeasure value R_Condition_HasInitialDyskensia,
 :hasFutureRecommendedMeasure value R_MakePhysicalExamination

The following applies: **hasRecommendedEvent \sqsubseteq hasFutureRecommendedEvent**

⇒ Patients that have an immediate recommendation for a diagnosis of acute schizophrenia are member of : FutureAcuteSchizophreniaRecommendations!

Future recommendations



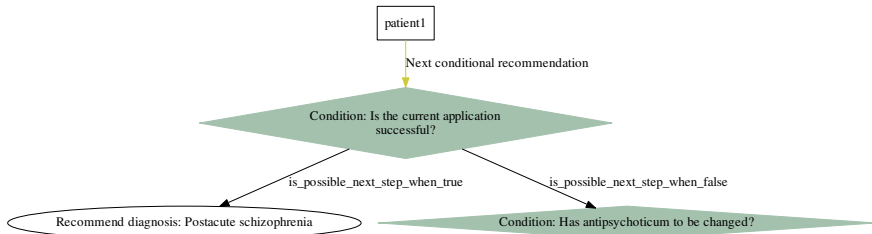
⇒ Future recommendations propagate along a chain of patient classes

Conditional events

Clinical guidelines consist of many conditions, like:

- In case X is diagnosed then do A ...
- In case Y has been applied without success then do B ...
- In case an application Z needs to be changed then do C ...

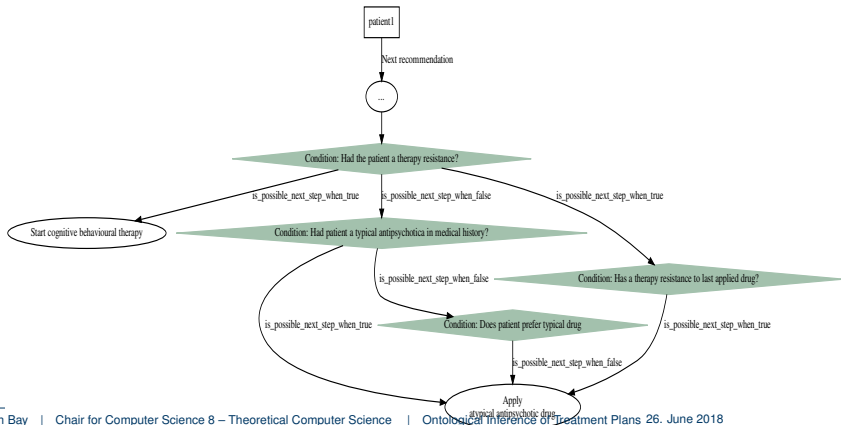
⇒ Introducing conditional events and object properties for **true** and **false** case:



Definite knowledge

Treatment plan needs to adjust dynamically whenever possible.

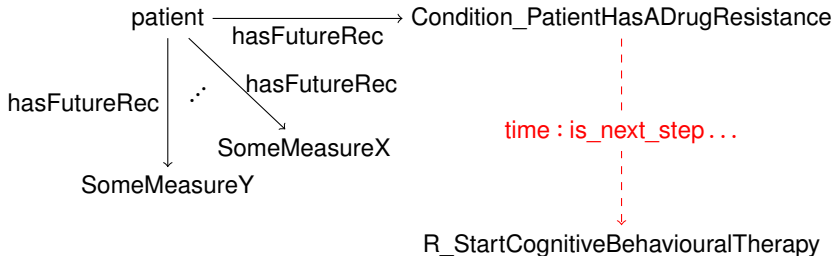
Plan when therapy resistance information is **not provided**: Plan when therapy resistance information is **provided**:



Definite knowledge

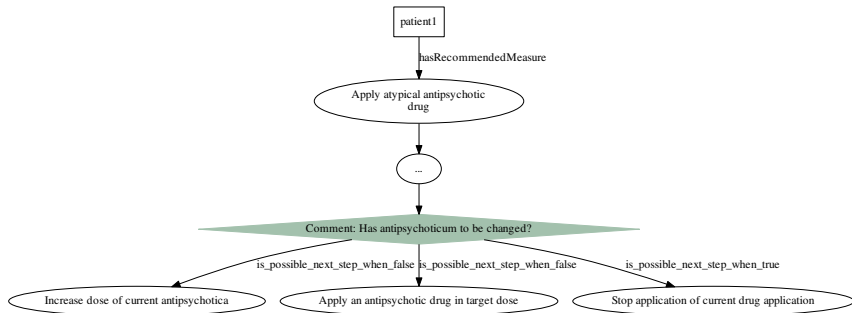
Infer Knowledge

\forall hasFutureRecommendedEvent.
 $(\neg(\text{Condition_PatientHasADrugResistance}) \vee$
 $(\exists \text{time : is_next_step_because_condition_is_true.}$
 $\text{R_StartCognitiveBehaviouralTherapy}))$



Multi-Level Conditions

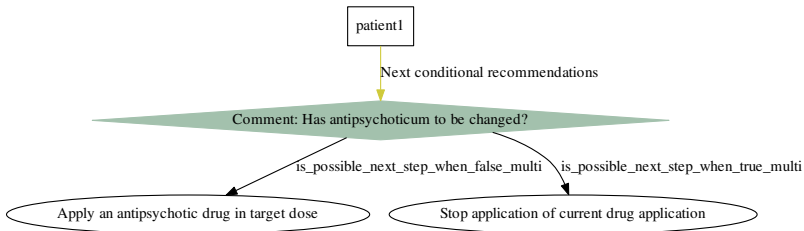
Some conditions depend on other factors, as well:



Multi-Level Conditions

Therefore, introduce another pair of object properties:

`is_possible_next_step_when_{true,false}_multi`

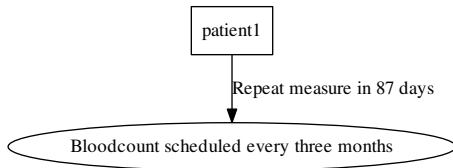


Repeating Events

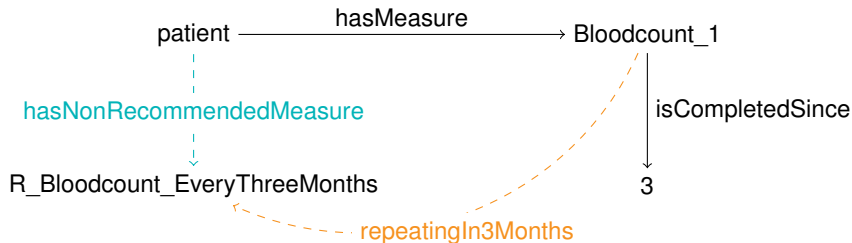
Measures repeat in specific time steps, e.g. Blood count

Measure	Start	after 4 weeks	after 3 months	every 3 months
Blood count	x	x	x	x

Treatment plan should display prediction of next schedule:



Repeating Events



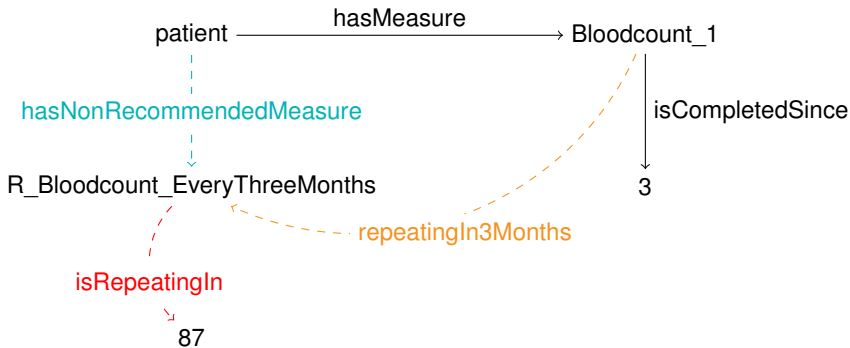
```

1 Class: Opposite_Repeating_BloodCount_EveryThreeMonths
2   EquivalentTo:
3     (hasMeasure some (Bloodcount_4Weeks
4       and (time:isCompletedSince some [< "90"])))
5
6   SubClassOf:
7     hasMeasure only
8       ((not (Bloodcount and (time:isCompletedSince some [< "90"])))
9         or (time:repeatingIn3Months value R_Bloodcount_EveryThreeMonths)),
10    hasNonRecommendedMeasure value R_Bloodcount_EveryThreeMonths
  
```

Repeating Events

SWRL Rule:

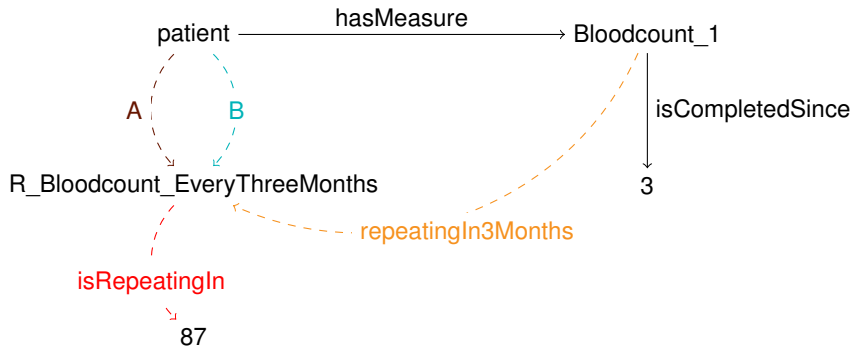
```
time:repeatingIn3Months(?a, ?rec) ∧ time:isCompletedSince(?a, ?completed) ∧
swrlb:sub(?rep, 90, ?completed) → time:isRepeatingIn(?rec, ?rep)
```



Repeating Events

```
:hasNonRecommendedEvent(?patient, ?ev) ^ time:isRepeatingIn(?ev, ?x) →  

:hasRepeatingRecommendedEvent(?patient, ?ev)
```



Queries I

Querying is done via SPARQL:

- A language similar to SQL.
- Able to query inferred knowledge-base.
- Closed-World assumption.

Query for repeating measures:

```

PREFIX :<http://www8.cs.fau.de/research:cgm/schizophrenia#>
PREFIX time:<http://www8.cs.fau.de/research:cgm/time#>

SELECT ?treatment (MAX(?timestamp) as ?greatestTimestamp)
  WHERE {
    ?patient :hasRepeatingRecommendedMeasure ?treatment.
    ?treatment time:isRepeatingIn ?timestamp.
  }
  Group By ?treatment
  
```

Queries II

For receive necessary information for the treatment plan the following query is used:

```

PREFIX <http://www8.cs.fau.de/research:cgm/schizophrenia#>
PREFIX time:<http://www8.cs.fau.de/research:cgm/time#>

SELECT ?treatment ?next ?nextFalse ?nextTrue ?definiteFalse ?definiteTrue
       ?pathFalse ?pathTrue ?non_recommended
WHERE{
  ?patient :hasFutureRecommendedEvent ?treatment .
  OPTIONAL {?treatment time:beforeNextRecommendedEvent ?next}
  OPTIONAL {?treatment time:is_possible_next_step_when_false ?nextFalse}
  OPTIONAL {?treatment time:is_possible_next_step_when_true ?nextTrue}
  OPTIONAL {?treatment time:is_next_step_because_condition_is_false ?definiteFalse}
  OPTIONAL {?treatment time:is_next_step_because_condition_is_true ?definiteTrue}
  OPTIONAL {?treatment time:is_possible_next_step_when_false ?externalFalse}
  OPTIONAL {?treatment time:is_possible_next_step_when_true_multi ?externalTrue}
  OPTIONAL {?treatment time:is_theoretical_next_step_but_not_recommended ?non_recommended}
}

```

Treatment plan generation

```

1: procedure CREATETREATMENTPLAN(Patient p)
2:   recs ← queryForRecommendations(p)
3:   futureRecs ← queryForFutureRecommendatins(p)
4:   g := newGraph()
5:   q := newQueue()
6:   visited := newSet()
7:   g.addVertex(p)
8:   for rec ← recs do
9:     g.addEdge(p, rec)
10:    q.add(rec)
11:    while !q.isEmpty() do
12:      nextRec ← q.pop()
13:      if visited.contains(nextRec) then
14:        continue
15:      else
16:        visited.add(nextRec)
17:        succs ← getAllNecessarySuccessors(nextRec, futureRecs)
18:        for succ ← succs do
19:          g.addEdge(nextRec, succ)
20:          q.push(succ)
  
```

▷ Ask for next recommendations
 ▷ Ask for future recommendations
 ▷ Add next recommendations
 ▷ Loop until no more recommendations are left
 ▷ Filter successors

Case Study



Case Study I

Recent history					
Past history		Guideline assistant			
Event	Type	Start date	End date	Drug	Dose of drug
Symptom	Negativism	01.01.2018			
Symptom	Audible thoughts	28.02.2018			
Symptom	Delusion of influence	02.03.2018			

Case Study II

Recent history					
Past history					
Guideline assistant					
Event	Type	Start date	End date	Drug	Dose of drug
Symptom	Negativism	01.01.2018			
Symptom	Audible thoughts	28.02.2018			
Symptom	Delusion of influence	02.03.2018			
Diagnosis	Acute schizophrenia	04.05.2018			
Measure	Inform the patient about pharmacotherapy	05.05.2018	05.05.2018		
Measure	Get patient's approval for pharmacotherapy	07.05.2018	07.05.2018		
Measure	Antipsychotic therapy	07.05.2018			
Measure	Make a MRT and CT of brain	08.05.2018	08.05.2018		
Measure	Bloodcount after therapy starts	10.05.2018	10.05.2018		
Measure	Apply antipsychotic drug	10.05.2018		Quetiapine	50.00 mg/d

Case Study III

Recent history					
Past history					
Guideline assistant					
Event	Type	Start date	End date	Drug	Dose of drug
Symptom	Negativism	01.01.2018			
Symptom	Audible thoughts	28.02.2018			
Symptom	Delusion of influence	02.03.2018			
Measure	Diabetes screening	02.05.2018	11.05.2018		
Diagnosis	Acute schizophrenia	04.05.2018			
Measure	Inform the patient about pharmacotherapy	05.05.2018	05.05.2018		
Measure	Get patient's approval for pharmacotherapy	07.05.2018	07.05.2018		
Measure	Antipsychotic therapy	07.05.2018			
Measure	Make a MRT and CT of brain	08.05.2018	08.05.2018		
Measure	Bloodcount after therapy starts	10.05.2018	10.05.2018		
Measure	Apply antipsychotic drug	10.05.2018	11.05.2018	Quetiapine	50.00 mg/d
Measure	Breast cancer screening	11.05.2018	11.05.2018		
Diagnosis	Drug resistance	11.05.2018		Quetiapine	
Measure	Apply antipsychotic drug	11.05.2018		Quetiapine	300.00 mg/d

Case Study IV

Recent history						Past history		Guideline assistant	
Event	Type	Start date	End date	Drug	Dose of drug				
Symptom	Negativism	01.01.2018							
Symptom	Audible thoughts	28.02.2018							
Symptom	Delusion of influence	02.03.2018							
Measure	Diabetes screening	02.05.2018	11.05.2018						
Diagnosis	Acute schizophrenia	04.05.2018							
Measure	Inform the patient about pharmacotherapy	05.05.2018	05.05.2018						
Measure	Antipsychotic therapy	07.05.2018							
Measure	Get patient's approval for pharmacotherapy	07.05.2018	07.05.2018						
Measure	Make a MRT and CT of brain	08.05.2018	08.05.2018						
Measure	Bloodcount after therapy starts	10.05.2018	10.05.2018						
Measure	Apply antipsychotic drug	10.05.2018	11.05.2018	Quetiapine	50.00 mg/d				
Diagnosis	Drug resistance	11.05.2018		Quetiapine					
Measure	Apply antipsychotic drug	11.05.2018	11.05.2018	Quetiapine	300.00 mg/d				
Measure	Apply antipsychotic drug	11.05.2018		Amisulpride	200.00 mg/d				
Measure	Breast cancer screening	11.05.2018	11.05.2018						

Future Work & Thanks



Future Work

- Find a way to deal with cycles in treatment plans
- Try approach in clinical practise
- Infer treatment plans by using OWL-S
- Integrate standard medical terminology such as OpenGalen

Thanks

