

S92 CLINICAL A86G  
M31 RECORDS M1BO  
LB6 INTERACTIVE J  
5CO SEARCH RS90M



National Institute for  
Health Research



# Temporal Information Extraction from Clinical Narratives

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# About me

- **2012-2014:** MSc in Bioengineering, “health technologies” area (University of Pavia)
- **2014-2017:** PhD student in Bioengineering and Bioinformatics (University of Pavia, laboratory of BioMedical Informatics “Mario Stefanelli”)
- **Since Jan 2018:** postdoc at the Institute of Psychiatry, Psychology and Neuroscience (IoPPN), King’s College London

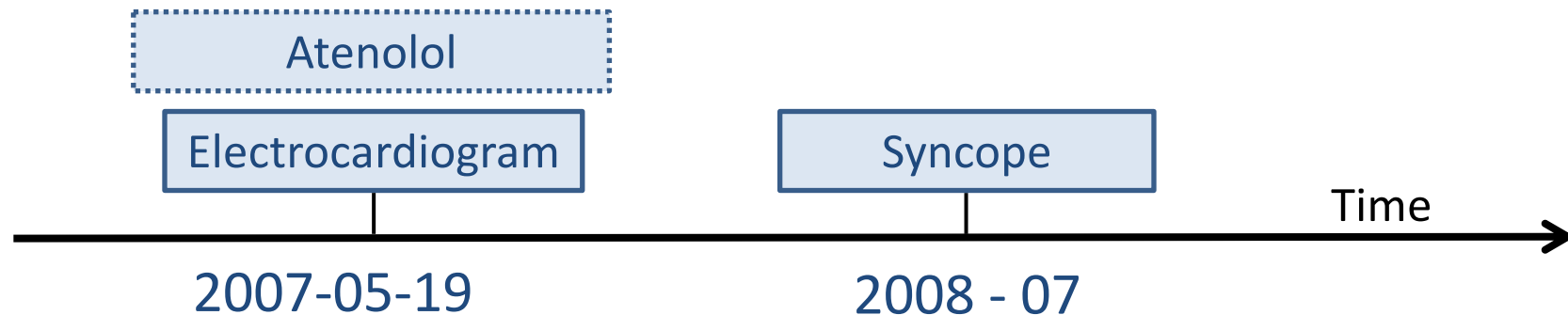
**Research interests:** clinical and temporal natural language processing

# Clinical text: unstructured information

On 19.05.2007 electrocardiogram and Atenolol dosage increased to 50 mg twice a day.

In July 2008 syncope during physical exercise.

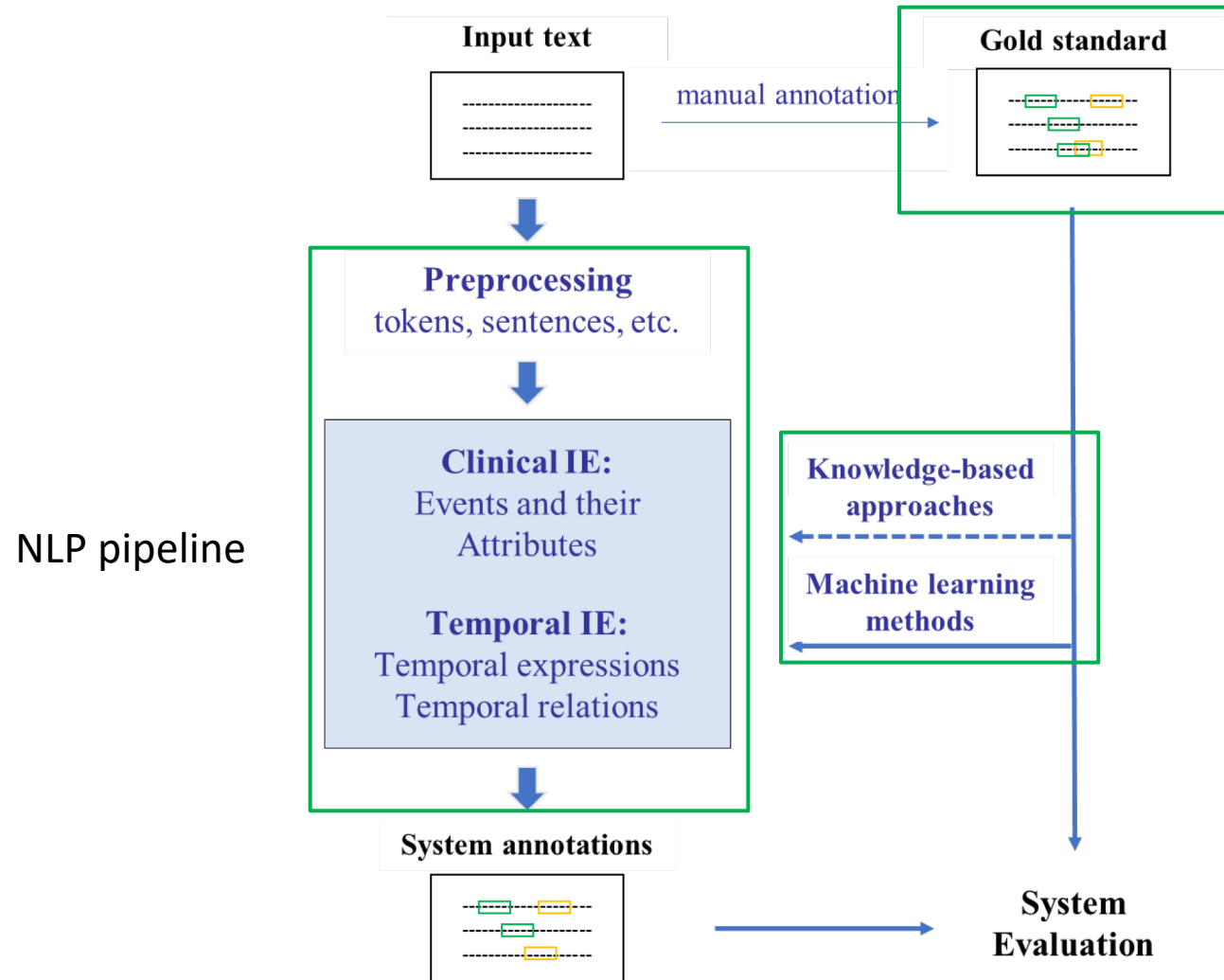
Denies any other symptom.



# Natural language processing

*<< Natural language processing (NLP) is the subfield of computer science concerned with using computational techniques to learn, understand, and produce human language content >>*

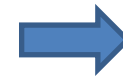
# Information extraction: basic steps



# Information extraction: methods

## Knowledge-based approaches

- External dictionaries and terminologies
- Rules and regular expressions, e.g. *"\d+ %unit\_of\_measurement"*



Require manual rule engineering

## Machine learning approaches

- Common classifiers (e.g., SVM, CRF)
- Deep learning approaches
- Need for annotated data



Need for many annotated data

# Information extraction in a non-English language: Italian

## Introduction and Background

# Clinical IE for the Italian language

## Challenges

- Lack of freely available annotated medical corpora
- Limited coverage of available clinical dictionaries
- Lack of medical-specific taggers

## Temporal IE

- Annotation efforts mostly in the general domain
- Only one medical corpus (semi-automatically) annotated

### Experiments in Identification of Italian Temporal Expressions

**Giuseppe Attardi**

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**Luca Baronti**

Dipartimento di Informatica  
Università di Pisa  
Largo B. Pontecorvo, 3  
I-56127 Pisa, Italy

**... No temporally annotated medical corpora!**



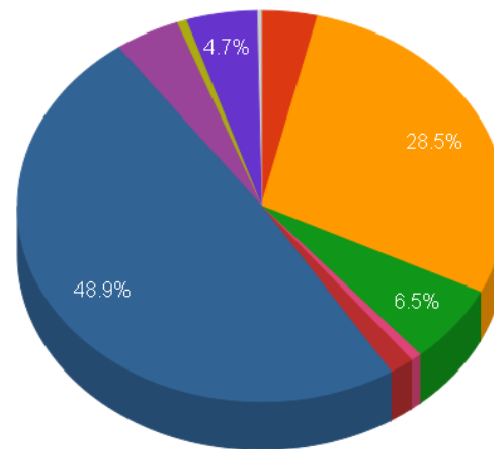
# Information extraction in a non-English language: Italian

## Materials and Methods

# Main CARDIO dataset



- Istituti Clinici Scientifici Maugeri Hospital (Pavia), Molecular Cardiology Unit
- Genetic variations in the field of inherited arrhythmogenic diseases
- 5432 medical reports



# Information to be extracted (1)

## Clinical events

- problems (“Brugada Syndrome”)
- tests (“ECG”)
- treatments (“Flecainide”)
- occurrences (“medical visit”)

Gli accertamenti eseguiti, in particolare, l'esito del test alla flecainide eseguito nel 2003, hanno portato a porre diagnosi di Sindrome di Brugada.

accertamenti

test alla flecainide

Sindrome di Brugada

ECG: Ritmo sinusale. FC 57 bpm; PR 156 msec; QRS 106 msec; asse QRS 40°; QT 430 msec; QTc 425 msec.

ECG

# Information to be extracted (2)

## Event attributes

- Test: results, findings
- Drug: dose, frequency
- ....

Gli accertamenti eseguiti, in particolare, l'esito del test alla flecainide eseguito nel 2003, hanno portato a porre diagnosi di Sindrome di Brugada.

ECG: Ritmo sinusale. FC 57 bpm; PR 156 msec; QRS 106 msec; asse QRS 40°; QT 430 msec; QTc 425 msec.

ECG

Ritmo: sinusale  
Frequenza cardiaca:  
57 bpm  
PR: 156 msec  
QRS: 106 msec  
Asse QRS: 40°  
QT: 430 msec  
QTc: 425 msec

# Information to be extracted (3)

## Temporal expressions (TIMEXes)

- dates (“16/09/2010”)
- times (“2pm”)
- durations (“two months”)
- sets (“twice a day”)

Gli accertamenti eseguiti, in particolare, l'esito del test alla flecainide eseguito nel 2003, hanno portato a porre diagnosi di Sindrome di Brugada.

2003

ECG: Ritmo sinusale. FC 57 bpm; PR 156 msec; QRS 106 msec; asse QRS 40°; QT 430 msec; QTc 425 msec.

# Manual annotation: 75 documents

**Annotation process: created specific annotation guidelines**

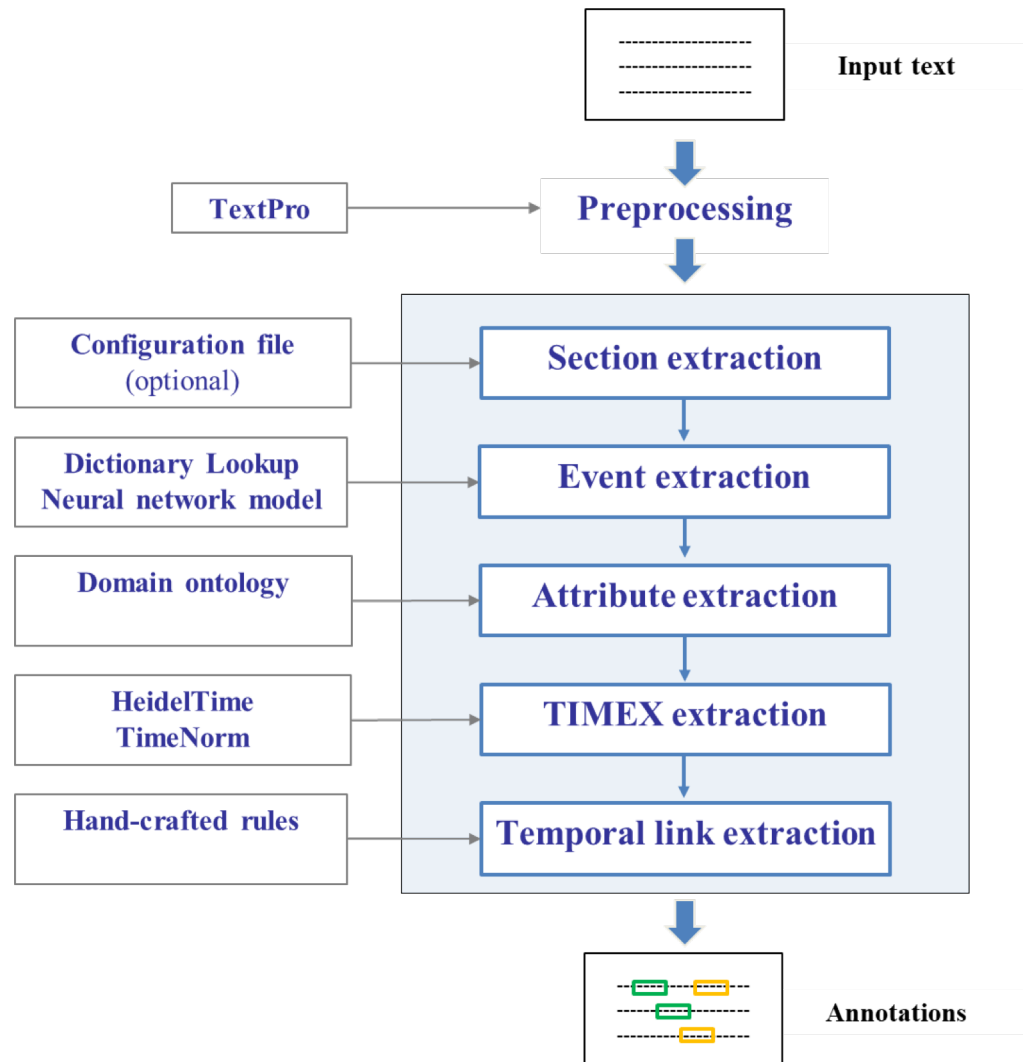
## **EVENTs**

- Semantic type (problem, ...)
- DocTimeRel (overlap, before, ...)
- Polarity (positive, negative)
- Modality (hypothetical, ...)
- Experiencer (patient, other)

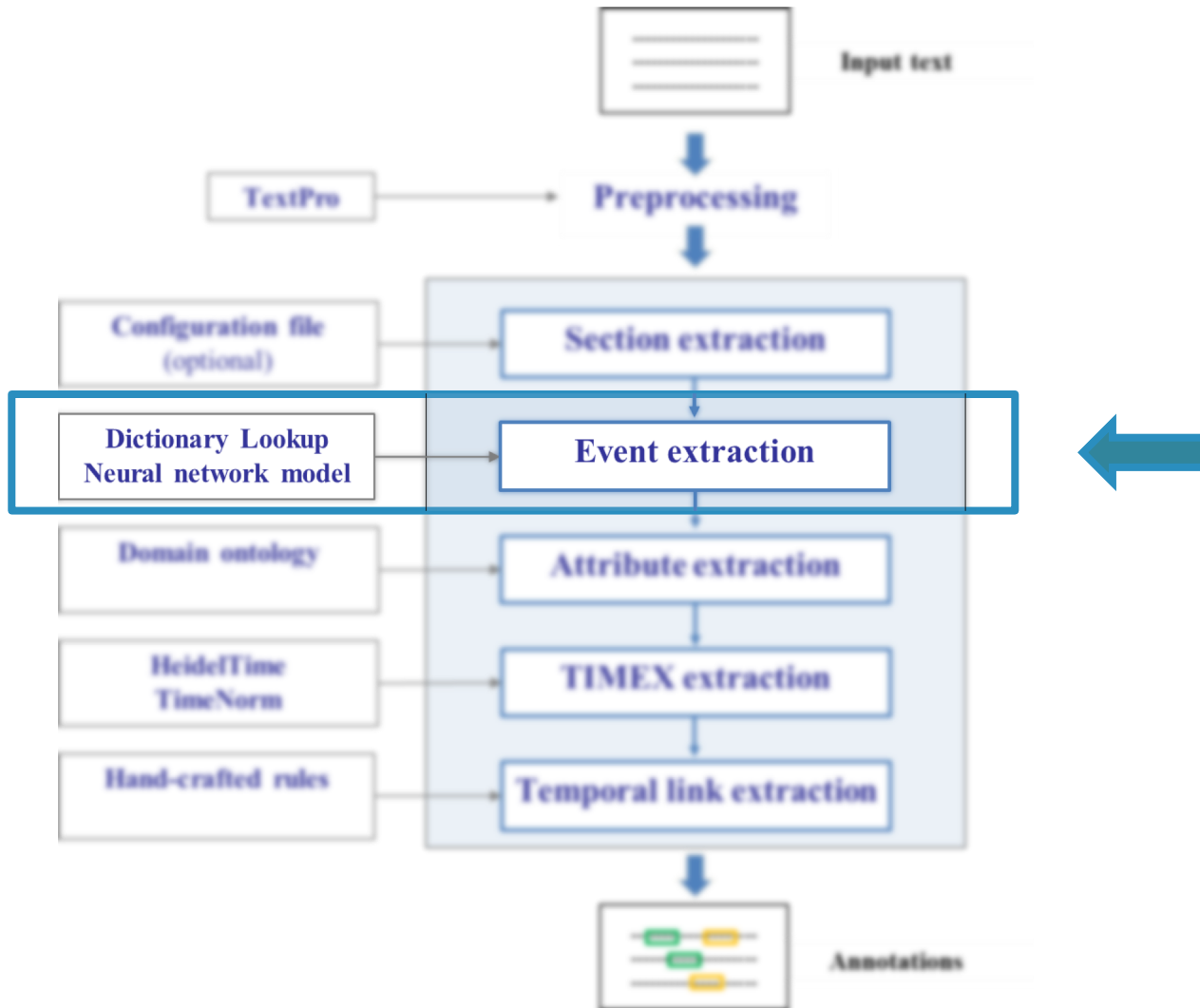
## **TIMEXes**

- Type (date, time, duration, set)
- Value
- Mod
- Quant (optional)
- Freq (optional)

# Information extraction pipeline



# Event extraction





# Dictionary lookup

- problems (“Sindrome di Brugada”, “episodi sincopali”)
- tests (“ECG”, “Test da Sforzo”)
- treatments (“Flecainide”, “Amiodarone”)
- occurrences (“ricovero”, “visita di controllo”)

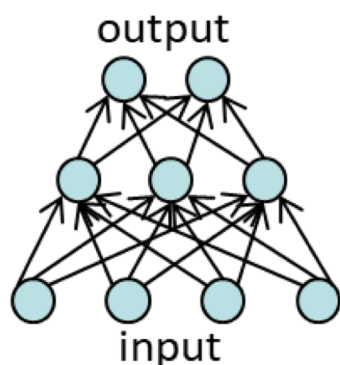
**Lookup:** search for dictionary entries in the text

- Dictionaries: UMLS, FederFarma, and two hand-crafted lexicons, acronyms
- TextPro for plural forms
- cTAKES UMLS Dictionary Lookup Fast Annotator

•Pianta E, Girardi C, Zanolli R. The TextPro tool suite. Proceedings of LREC, 6th edition of the Language Resources and Evaluation Conference, Marrakech, Morocco. 2008 May 28-30.

•Savova GK, Masanz JJ, Ogren PV, Zheng J, Sohn S, Kipper-Schuler KC, et al. Mayo clinical Text Analysis and Knowledge Extraction System (cTAKES): architecture, component evaluation and applications. J Am Med Inform Assoc JAMIA. 2010;17(5):507–13.

# Neural networks and entity recognition



## Neural network models

- Automatically extract features for supervised learning
- Applied to NLP tasks with promising results

## Sequence labeling problem

B (Beginning), I (Inside), O (Outside) tagging

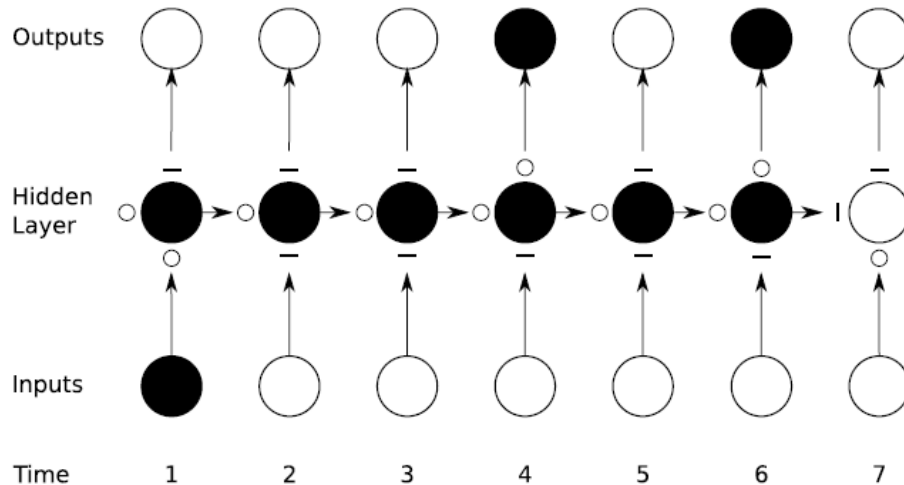
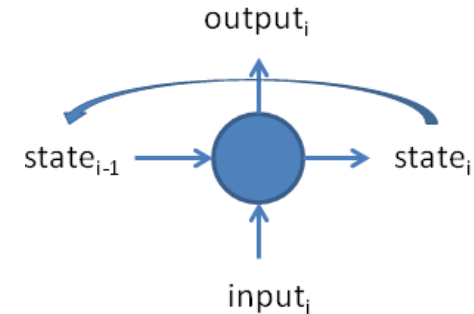
- Input: sequence of tokens
- Output: sequence of labels

Token	Tag
The	O
ECG	B-test
test	I-test
revealed	O
features	O
consistent	O
with	O
Brugada	B-problem
Syndrome	I-problem

# Recurrent neural network models

## Recurrent neural networks (RNNs)

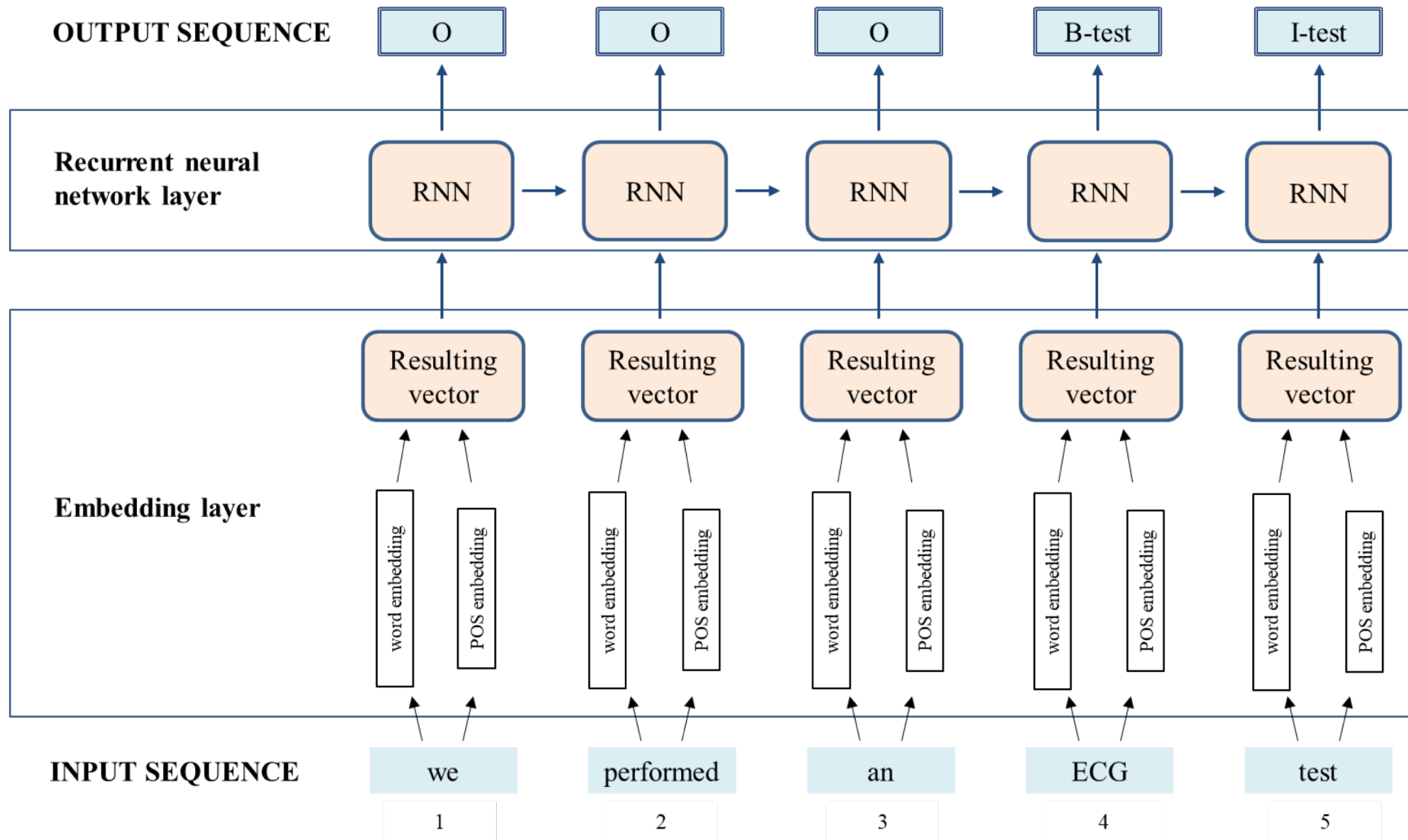
- Flexible use of context information
- Map from an entire history of previous inputs to each output



**Long Short-Term Memory (LSTM):** learn long-term dependencies

**Gated Recurrent Unit (GRU):** simpler variation

# Developed model for Event recognition



# Identification of Event properties

## DocTimeRel: SVM classifier

token	POS tag	section	verb temp tense	token -1	token +1	token -2	token +2
-------	---------	---------	-----------------	----------	----------	----------	----------



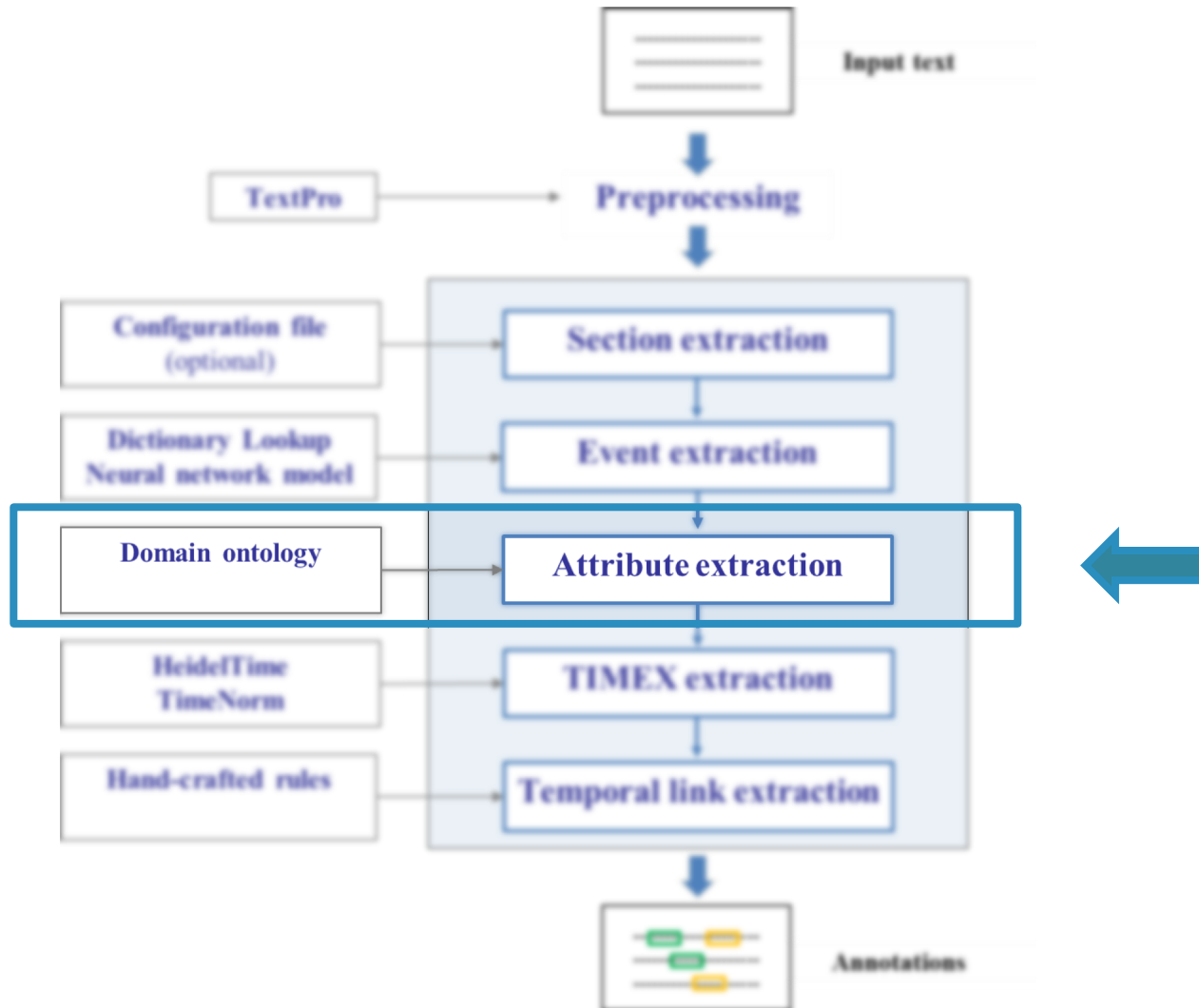
**DocTimeRel value** (overlap, before, before/overlap, after)

## Polarity, Contextual modality, and Experiencer: ConText

The patient did **not** experience any symptom

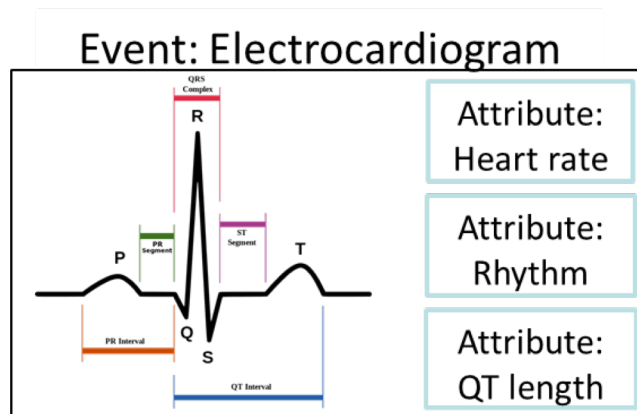
**Polarity: NEGATIVE**

# Attribute extraction

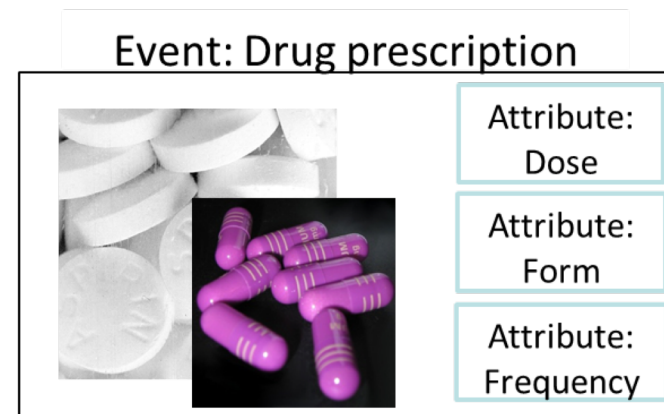


# Ontology-driven approach (1)

In clinical reports, it is frequent to find occurrences of events that are related to a set of attributes



Source: Wikipedia



Source: Wikipedia

## Ontologies: advantages

- can be easily updated to add/modify concepts
- can be enriched with new information
- regular expressions can be translated to other languages

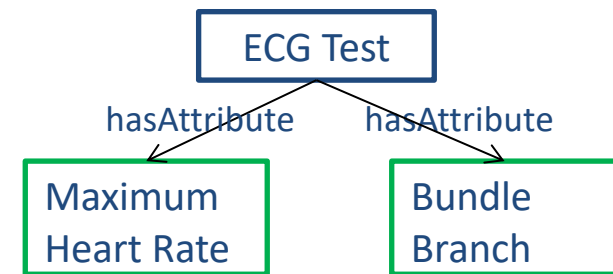
# Ontology-driven approach (2)

## Ontology-driven approach

1. Consider the medical problem to identify events and related attributes
2. Define a domain-related ontology containing events and attributes  
E.g. Cardiology domain
3. Automatically create an ontology-based configuration file

### Electrocardiogram

- Rhythm
- Maximum Heart Rate
- QT length
- Bundle Branch



```
<event>
  <type>test</type>
  <name>ECGTest</name>
  <regex>(ECG|[Ee]lettrocardiogramma)</regex>
  <attributes>
    <attribute>
      <name>BundleBlock</name>
      <regex>(BBD|[Bb]locco di branca destra|[Ee]miblocco
      <type>string</type>
      <pattern>(incompleto|completo)?</pattern>
    </attribute>
    <attribute>
      <name>HeartRate</name>
      <regex>(FC|[Ff]requenza [Cc]ardiaca)</regex>
      <type>integer</type>
      <value_min>40</value_min>
      <value_max>200</value_max>
      <um>bpm</um>
    </attribute>
  </attributes>
```

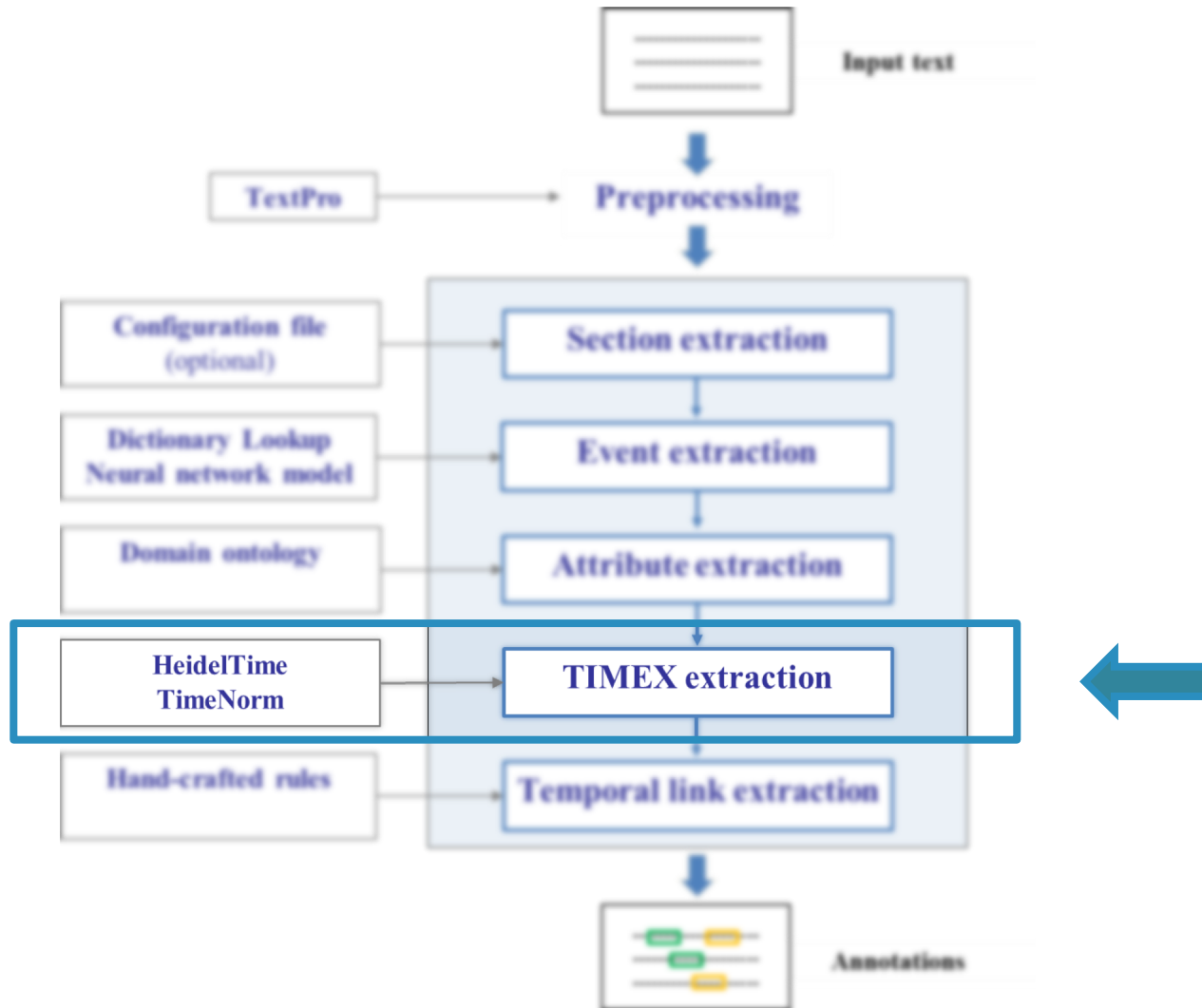


# Attribute annotation process

- Extracted events are linked to their attributes through the configuration file
- Attribute names and values (regular expressions) are looked for in suitable lookup windows

Event semantic type	Contextual information	Lookup window
Test	No sections available	One paragraph*
Test	Included in matching section	One section
Test	Not included in any section	One paragraph*
Test	Included in non-matching section	One sentence
Treatment	NA	One sentence*

# Temporal expression extraction



# HeidelTime and TimeNorm adaptation

## HeidelTime

- Rule-based tool
- TIMEX extraction and normalization
- Available also in Italian

## TimeNorm

- Tool based on synchronous context-free grammars
- TIMEX normalization
- Available also in Italian



## Adaptation to the clinical domain

- HeidelTime rules and TimeNorm grammar entries updated
- HeidelTime annotator modified to better deal with implicit TIMEXes (e.g. “the day after”)

• Strötgen J, Gertz M. HeidelTime: High Quality Rule-based Extraction and Normalization of Temporal Expressions. Proceedings of the 5th International Workshop on Semantic Evaluation. 2010:321-324.

• Bethard S. A Synchronous Context Free Grammar for Time Normalization. Proceedings of the Conference on Empirical Methods in Natural Language Processing. 2013:821-826.

# Main adaptations

- Extension of general domain rules: dates in the format DD.MM.YYYY, sets such as “every six months”, ...
- Creation of domain-specific rules

**IT**     *Atenololo: 1 cp x 2/die*

**EN**     Atenolol: 1 tablet twice a  
day



Type = SET

Value = P1D, Freq = 2X

**IT**     *Atenololo: 1 cp Ore 16*

**EN**     Atenolol: 1 tablet at 4 pm



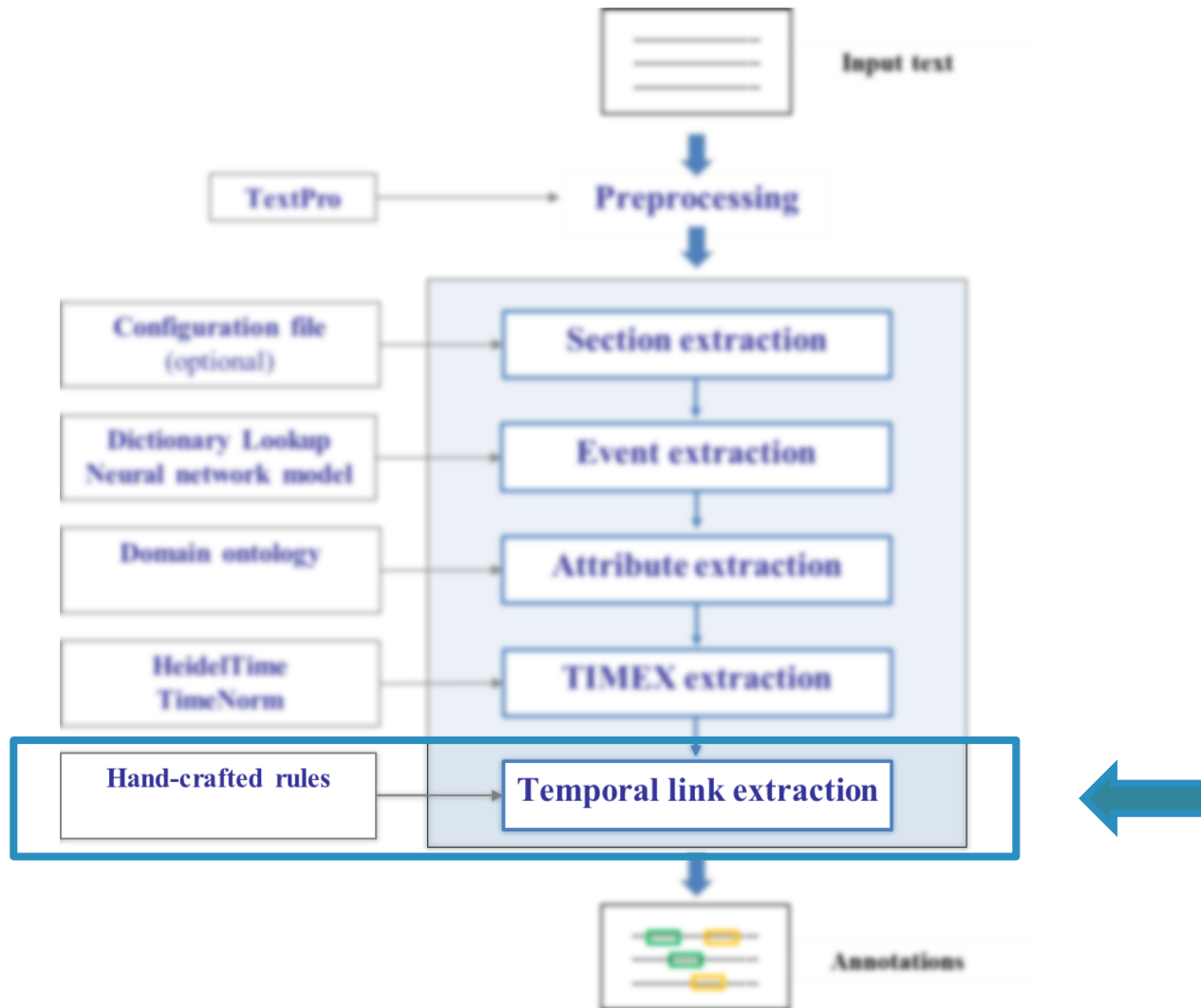
Type = TIME

Value = XXXX-XX-XXT16:00

• Strötgen J, Armiti A, Van Canh T, Zell J, Gertz M. Time for more languages: Temporal tagging of arabic, italian, spanish, and vietnamese. ACM Transactions on Asian Language Information Processing. 2014.;3(1):1–21.

• Mirza P, Minard A. FBK-HLT-time: a complete Italian Temporal Processing system for EVENTI-Evalita 2014. Proceedings of the 4th International Workshop EVALITA-2014. 2014:44–49.

# Temporal link extraction

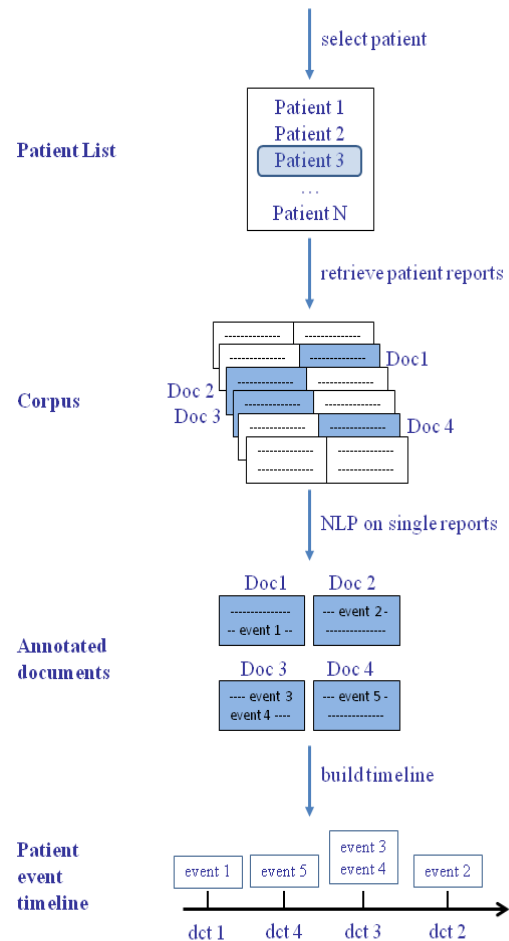


# Rule-based approach

- Links between Event-TIMEX pairs included in the same sentence
- Five possible links: BEFORE, BEGINS\_ON, ENDS\_ON, CONTAINS, OVERLAP
- Manual creation of rules, based on 12 features:

1. Event	7. TIMEX
2. Event section	8. TIMEX type
3. Event DocTimeRel	9. TIMEX value
4. Event semantic type	10. Temporal preposition
5. Event polarity	11. Verb temporal tense
6. Event-TIMEX distance	12. Temporal verbs

# Clinical timeline construction



The patient of interest is selected

The medical reports referred to the selected patient are retrieved

The NLP pipeline processes the retrieved documents

The events extracted from all patient documents are visualized on a timeline

# Information extraction in a non-English language: Italian

## Results and Discussion



# Statistics on the annotated corpus

	Training set	Test set	Corpus
Documents	60	15	75
Tokens	44115	13148	57263
Sentences	3347	941	4288
Events	3159	992	4151
TIMEXes	814	288	1102

Most events are Problems (42%), with an Overlap relation to the DCT (44%)

Most time expressions are Dates (61%)

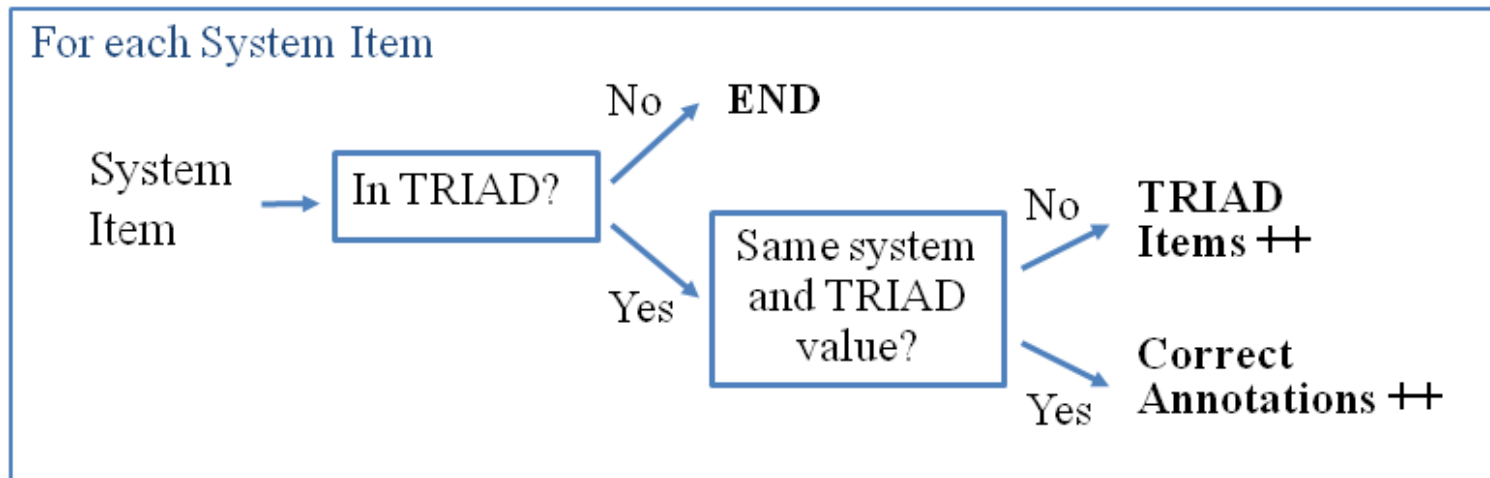
# Event extraction: results

Annotated test set (15 documents)

Extraction method	TP	FP	FN	P	R	F1
Dictionary lookup	548	118	444	82.3%	55.2%	66.1%
CRF classifier	795	189	197	80.8%	80.1%	80.5%
SVM classifier	748	103	244	87.9%	75.4%	81.2%
GRU classifier	844	111	148	88.4%	85.1%	86.7%
GRU classifier with POS input	863	107	129	89.0%	87.0%	88.0%
<b>Dictionary lookup + GRU classifier with POS input</b>	<b>895</b>	<b>114</b>	<b>97</b>	<b>88.7%</b>	<b>90.2%</b>	<b>89.5%</b>

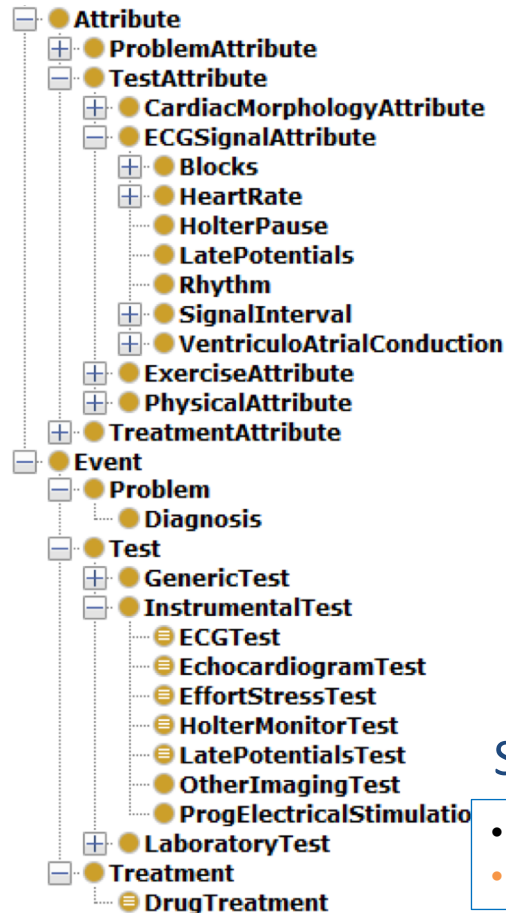
# Attribute extraction: evaluation

- **TRIAD**: database for clinical and genetic variations in the field of inherited arrhythmogenic diseases
- Data on diagnoses, genetic mutations, cardiac events, performed tests, prescribed treatments and device implants



# Attribute extraction: ontology

The developed ontology contains 11 events and 61 attributes



## EVENT: ECGTest

- **hasRegularExpression**: “ECG |[Ee]lettrocardiogramma”
- **hasAttribute**: BundleBlock
- **hasAttribute**: HeartRate
- **hasAttribute**: QT
- **hasAttribute**: Rhythm

## Numeric Attribute: AverageHeartRate

- **hasRegularExpression**: “FC |[Ff]requenza cardiaca”
- **hasUnitOfMeasurement**: “bpm”
- **hasNumericValue**: Integer >= 40 and Integer <= 200

## String Attribute: Rhythm

- **hasRegularExpression**: “[Rr]itmo”
- **hasStringValue**: “(sinusale)?[ ]\*bradicardico |(sinusale)?[ ]\*tachicardico |sinusale”

# Attribute extraction: results

SV	Set	Event	System item	TRIAD item	Correct annotations	Accuracy	
1	4429 reports	Main Diagnosis	4202	4077	3607	88.5%	
		Dev	ECG	26669	22546	21352	94.7%
		Holter ECG	26767	21538	19058	88.5%	
		Effort Stress Test	9683	3978	2367	59.5%	
		Prescribed Drug	8720	2436	2186	89.7%	
2	1003 reports	Main Diagnosis	927	913	845	92.6%	
		Test	ECG	7452	5070	4885	96.4%
		Holter ECG	7173	5127	4757	92.8%	
		Effort Stress Test	2543	1118	1064	95.2%	
		Prescribed Drug	1999	538	435	80.9%	

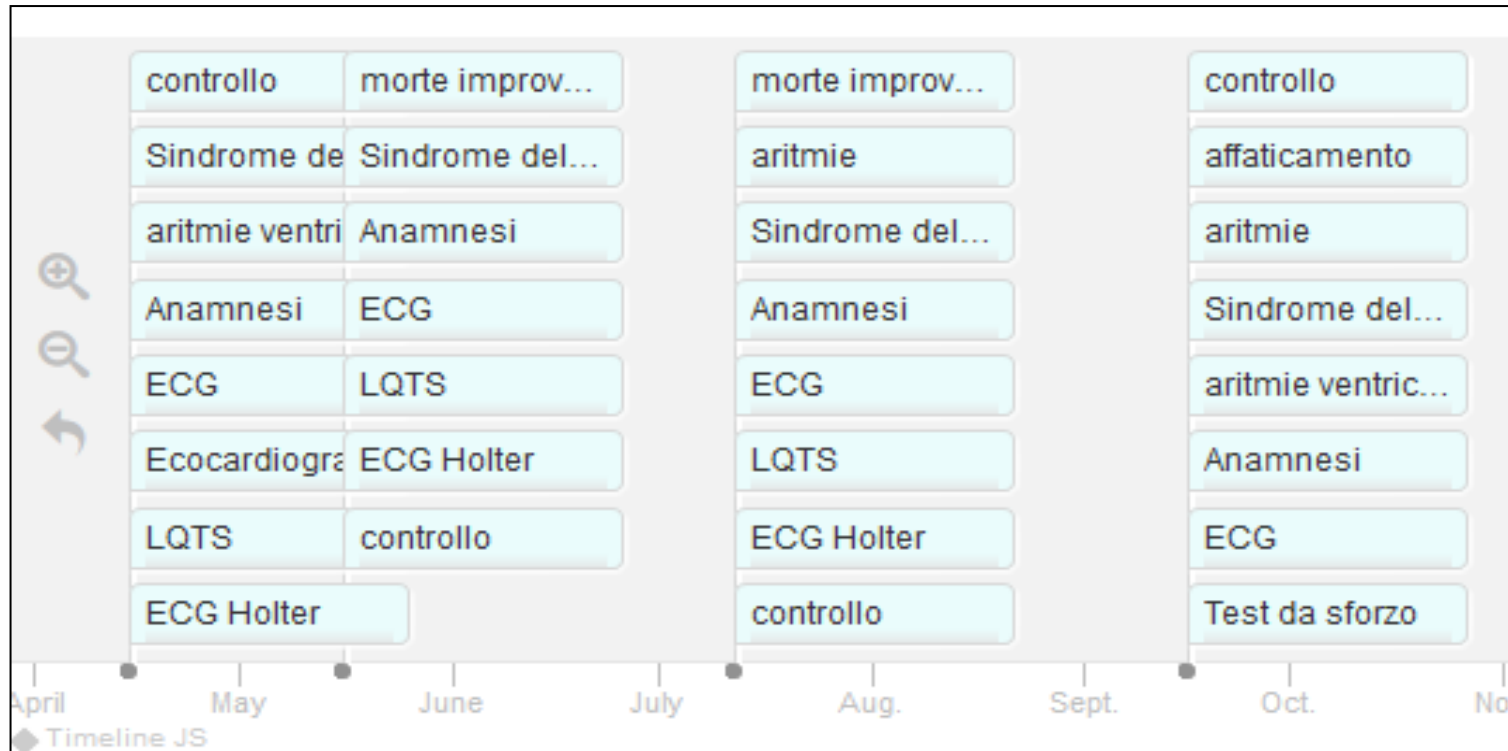
# Time expression extraction: results

Annotated test set (15 documents)

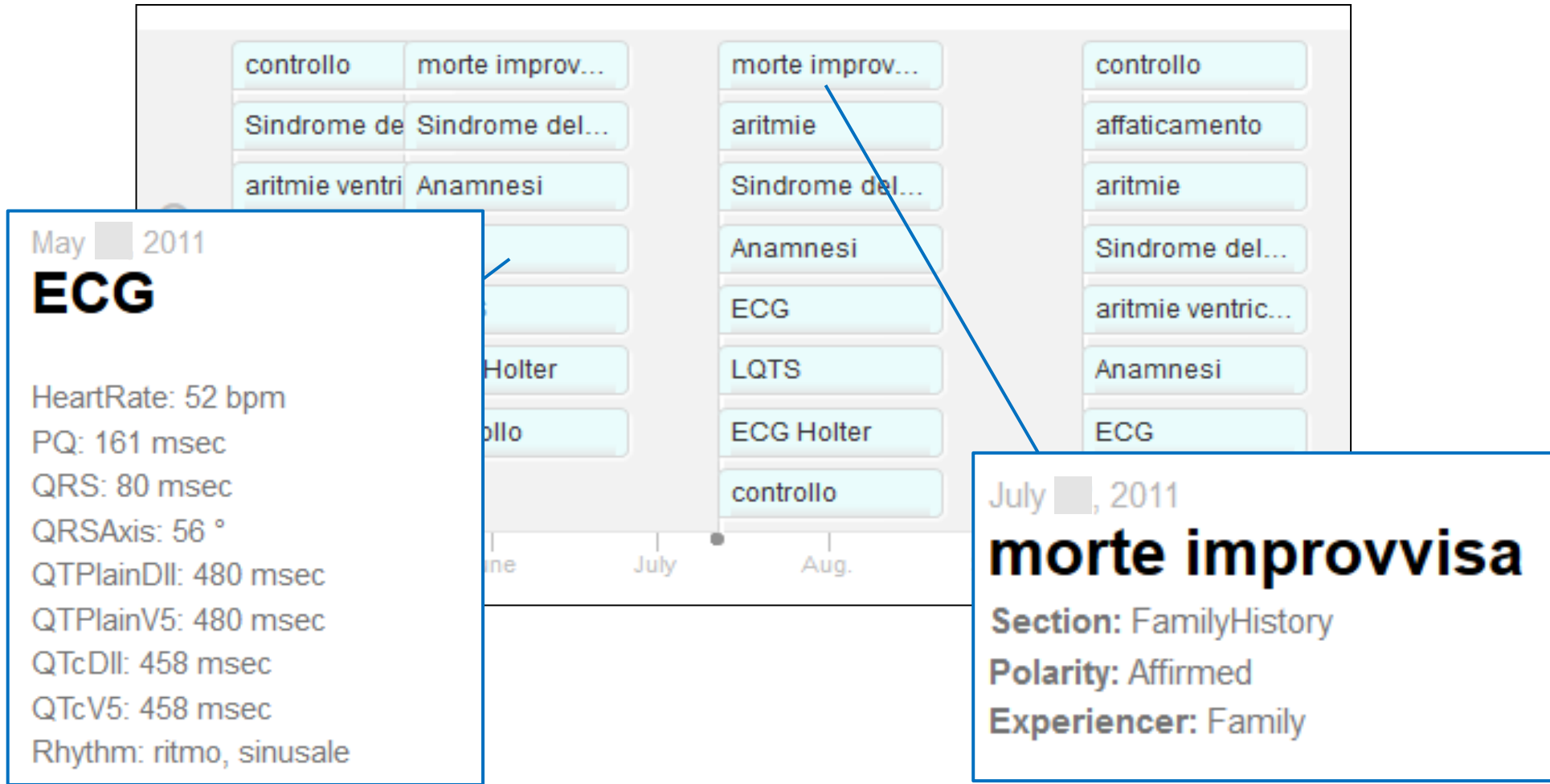
System	Set	TP	FP	FN	F1
HeidelTime original	Training	425	196	389	59.2%
HeidelTime updated	Training	760	47	54	93.8%
HeidelTime updated	Test	273	13	15	95.1%

System	Set	TP	Property	Accuracy
HT original	Training	425	value	91.5%
HT updated	Test	273	value	93.8%
TN original	Training	760	value	56.7%
TN updated	Test	273	value	89.0%

# Reconstructed patient timeline



# Reconstructed patient timeline





# Information extraction in a non-English language: Italian

## Extensions and Integrations

# Extension to a different domain (1)

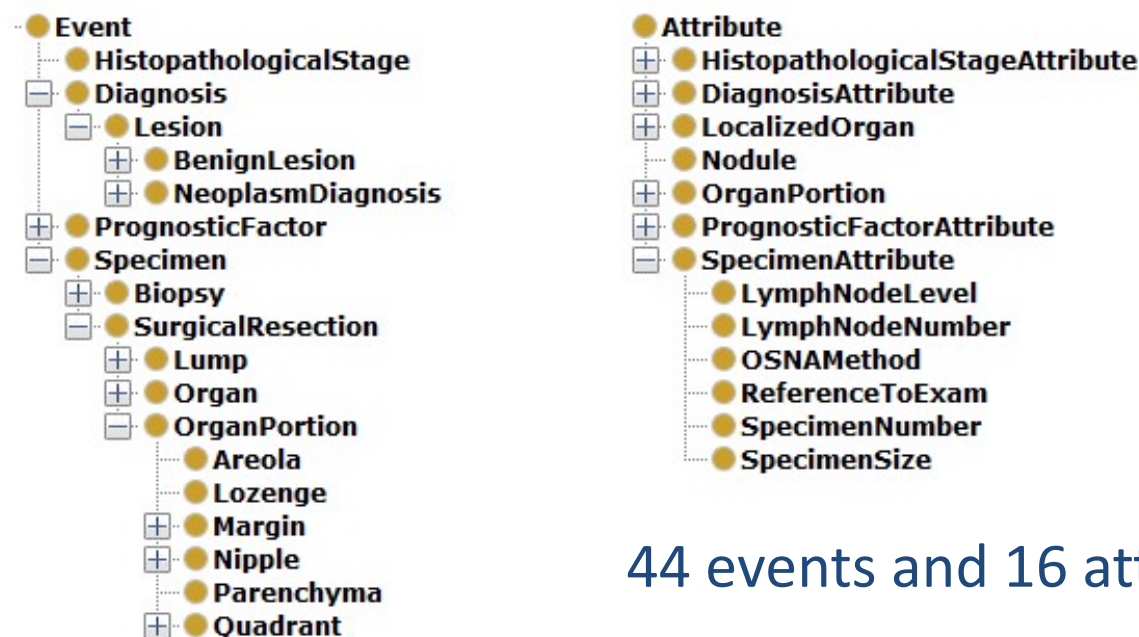
- 221 anatomic pathology reports
- Hospital Papa Giovanni XXIII in Bergamo, Italy
- 20 reports: ontology design set
- 34 reports: test set



SECTION:NOTIZIE_CLINICHE Vedi I17-xxx (core biopsy), T17-xxx (indagine FISH) e I17-xxx (linfonodo sentinella).	← Clinical information
SECTION:MATERIALE_INVIATO 1. Quadrante supero-interno della mammella destra. 2. Margine profondo. 3. Margine superiore. 4. Margine inferiore.	← Sent specimen
SECTION:TESTO_MACRO 1- Frammento di parenchima mammario di 6x6x2 cm con losanga di cute di 5x0,7 cm, pervenuto già sezionato in corrispondenza di una neoplasia di 0,9 cm di asse maggiore. 2- Frammento di parenchima mammario di 4x3,5x1 cm, orientabile. 3- Frammento di parenchima mammario di 7x2,5x1 cm, orientabile. 4- Frammento di parenchima mammario di 8x2,5x2 cm, orientabile.	← Specimen description
SECTION:TESTO_DIAGNOSI 1- Carcinoma duttale infiltrante a medio grado di differenziazione. [...] 2,3- Parenchima mammario esente da neoplasia. 4- Focolaio di carcinoma lobulare in situ di tipo classico (diametro istologico pari a 3 mm) distante 3 mm dal margine di resezione; si associa iperplasia lobulare atipica. [...] Stadiazione istopatologica sec. TNM VIII edizione: pT1b G2 Linfonodo sentinella esente da metastasi, esaminato con metodica molecolare O.S.N.A. (I17-xxx).	← Diagnosis

# Extension to a different domain (2)

- Events (with Attributes): specimen, diagnosis, histopathological stage, prognostic factor
- **New IE task:** specimen-diagnosis Event-Event links



44 events and 16 attributes

# Extension to a different domain (3)

- Validation with Expert
- 476 system items
- Three types of errors: missing items, FN, FP

Items	Raw count	Distinct count
Missing items	57	38
FN	15	11
FP	26	21

Missing items:  
Information to be  
added to the ontology

Precision: 94.5%  
Recall: 96.8%  
F1 score: 95.6%

# Information extraction in the mental health domain

My experience at BRC

# Mental health domain

## Challenges for NLP

- large proportion of free-text
- heterogeneity in self-reported experiences, circumstances, treatment and outcomes
- symptomology and health progression often described without relying on structured fields

**MeDESTO project:** Measuring Duration of Untreated Psychosis by Extraction of Symptom and Treatment Onset from mental health records using language technology.

Swedish Research Council (2015-00359), Marie Skłodowska Curie Actions, Cofund, Project INCA 600398.

# Introduction (1)

**Aim:** Identification of time expressions (TIMEXes) and symptom onset in mental health records for patients with a diagnosis of schizophrenia.

**Relevance:** For this disease, analysing symptom and treatment onset is essential to measure the duration of untreated psychosis (DUP).

*The patient's partner reports that the patient was diagnosed with **schizophrenia** in **1990**....*

***Past** medication trials that the patient reports include **haloperidol** and **lithium** (started in **1991**, on and off **for 2 years**), neither of which particularly helpful....*

# Introduction (2)

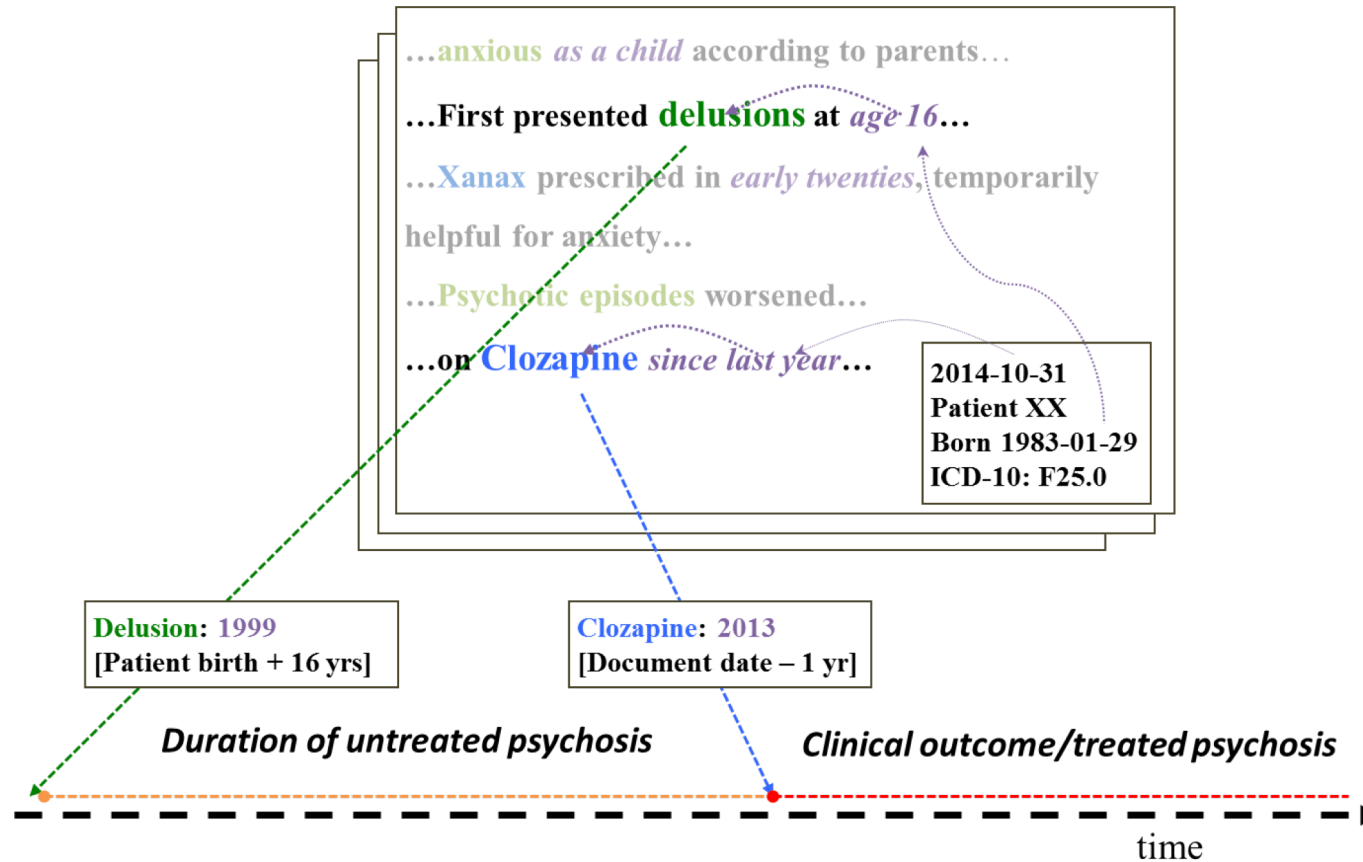


Image courtesy of Dr. Sumithra Velupillai, King's College



# Background

## Temporal link extraction from clinical narratives in English

### 2012 i2b2

- intensive care unit
- 310 discharge summaries
- events, temporal expressions, and 8 types of temporal relations (e.g., before, overlap)

>>> 2012 i2b2 NLP Challenge for Clinical Records

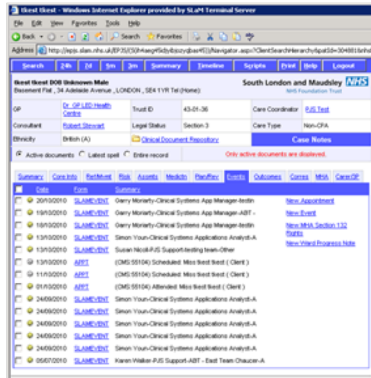
### THYME corpus

- breast cancer, colon cancer
- 1,254 records
- events, temporal expressions, and 2 types of temporal links: DocTimeRel, and relations to narrative containers

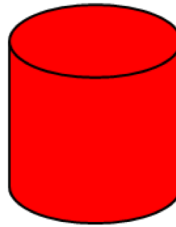
>>> 2015, 2016, and 2017 Clinical TempEval (440, 591, and 1186 docs)

- Sun W, Rumshisky A, Uzuner O. Annotating temporal information in clinical narratives. *Journal of biomedical informatics*. 2013;46:S5–S12.
- Styler IV WF, Bethard S, Finan S, Palmer M, Pradhan S, de Groen PC, et al. Temporal annotation in the clinical domain. *Transactions of the Association for Computational Linguistics*. 2014;2:143.

# CRIS – core functionality

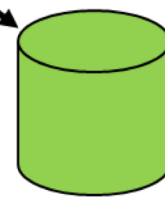


EHR Data Source



Processing pipeline

CRIS front end



CRIS SQL

>280,000 cases  
35,000 'active' cases  
125 tables  
6500 fields

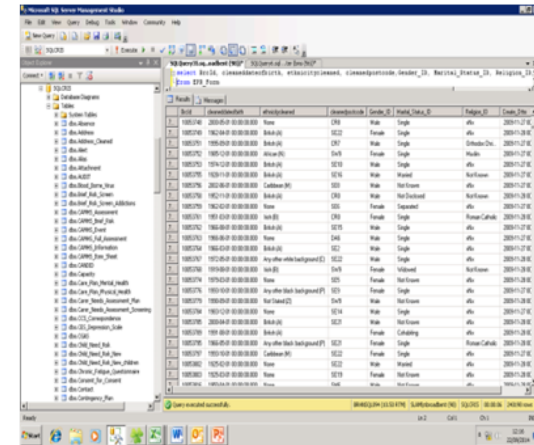
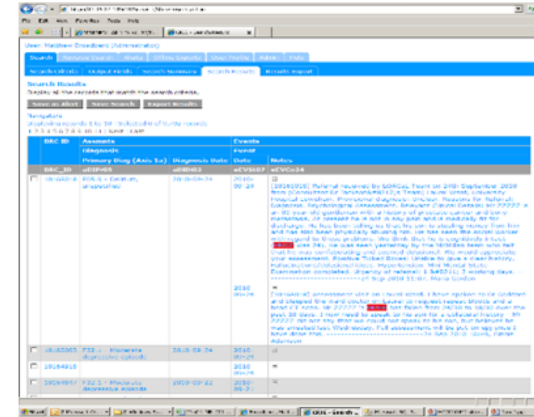
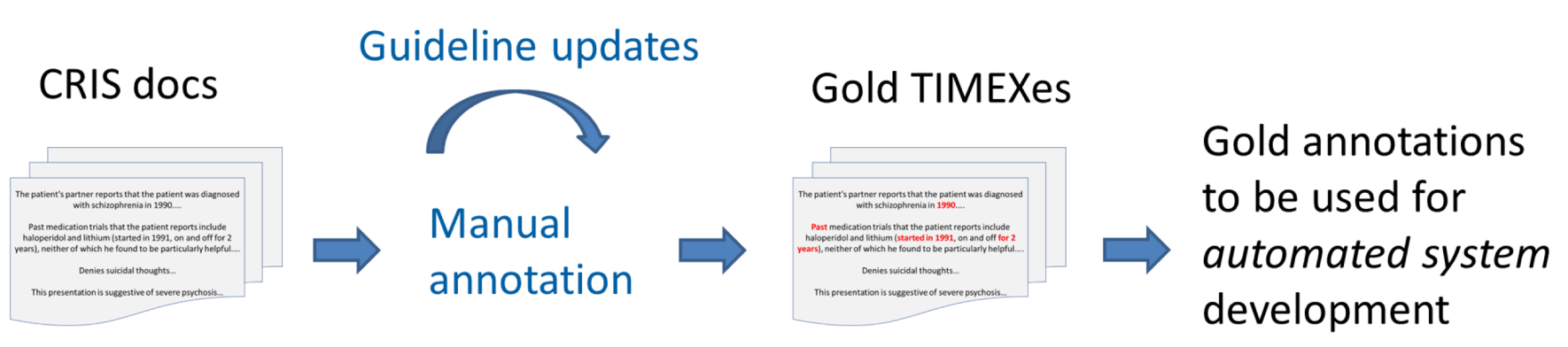


Image courtesy of Prof. Rob Stewart, King's College

# Temporal expression annotation

**Data:** Mental health records from the Clinical Record Interactive Search (CRIS) database were manually annotated for TIMEXes.



## Guidelines development

- annotation guidelines developed based on previous work.
- discussion stage for guideline updates.

Perera G, Broadbent M, Callard F, et al. Cohort profile of the South London and Maudsley NHS Foundation Trust Biomedical Research Centre (SLaM BRC) Case Register: current status and recent enhancement of an Electronic Mental Health Record-derived data resource. *BMJ Open*. 2016;6(3):e008721.

# First annotation process

## Document selection

- Documents written within three months from first referral
- Longest document per each patient

Three annotators independently annotated **20 documents**.

New TIMEX type referred to the patient's age: **Age-related**

- “*she first experienced hallucinations at the age of 18...*”
- “*he has been hearing voices since his teens...*”

# MeDESTO corpus

## Extension of annotations

- **52 documents** annotated for time expressions
- 65.6 annotations per document

# TIMEXes	3413 (65.6/doc)
Date	1903 (55.8%)
Duration	563 (16.5%)
Time	366 (10.7%)
Frequency	276 (8.1%)
Age-related	305 (8.9%)

# Automated system development

Annotated corpus used to adapt two rule-based TIMEX extraction systems:

- SUTime
- HeidelTime

Main adaptations:

- Added age-related TIMEXes and domain-specific expressions (e.g., OD for once daily)
- Post-processing for determining the age-related type

• Strötgen J, Gertz M. HeidelTime: High Quality Rule-based Extraction and Normalization of Temporal Expressions. Proceedings of the 5th International Workshop on Semantic Evaluation. 2010:321-324.

• Angel X Chang and Christopher D Manning. 2012. SUTime: A library for recognizing and normalizing time expressions. In Lrec, volume 2012, pages 3735–3740.

# Event annotation

MeDESTO corpus manually annotated with events

- **symptoms**
- **signs**
- **diagnoses**
- medications
- life events or social circumstances
- healthcare services
- patient behaviour
- other health problems

## **Guidelines development**

- discussion stage for guideline updates
- input by domain experts

# Onset information annotation

**Problem:** find documents that are likely to contain the onset information.

- Extract all documents related to early intervention services (services that support people who are experiencing the symptoms of psychosis for the first time)
- Filter documents according to:
  - Length
  - Average line length



# First document selection

1) extract all documents related to early intervention services

18281 documents  
3840 patients



2) Filter documents

- length > 50th percentile
- avg\_line\_length > 25th percentile

8496 documents  
3198 patients

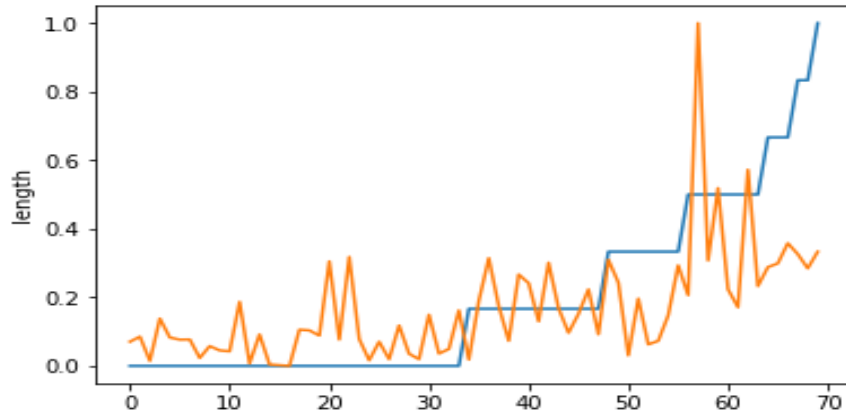


3) Randomly select 20 patients and save all their documents

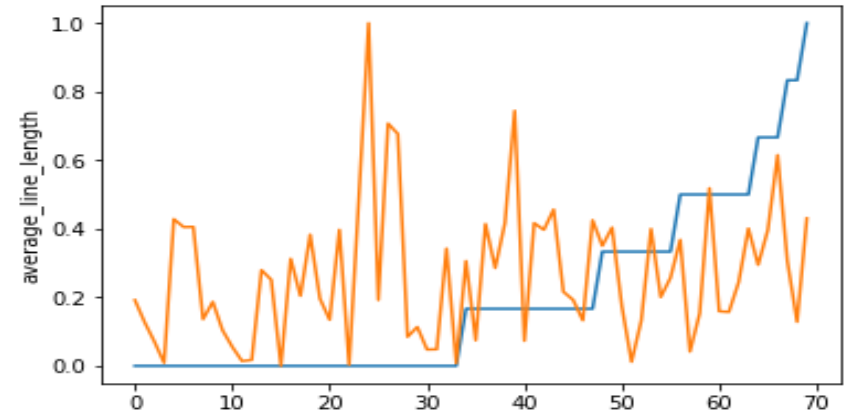
70 documents  
20 patients (1-8 docs each)

# Annotation results

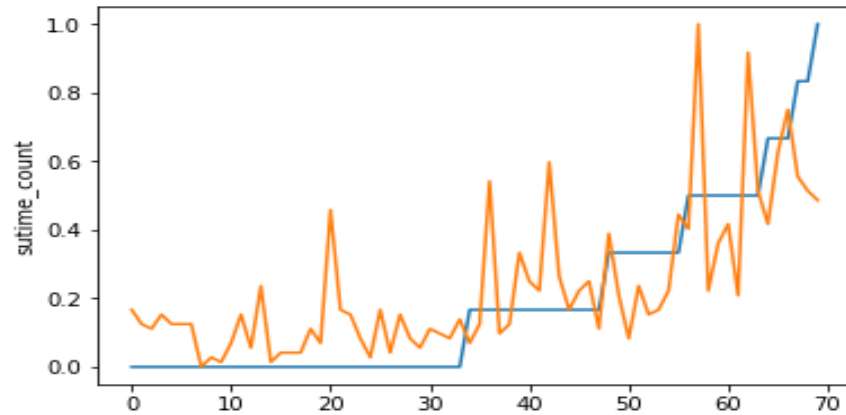
## Length



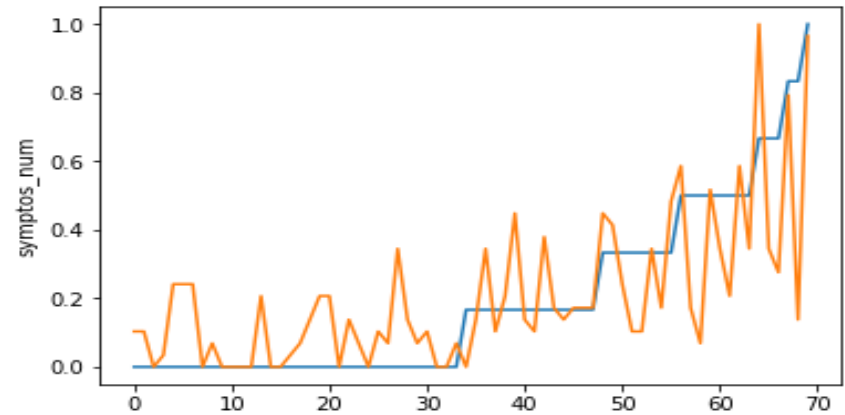
## Avg line length



## Num timexes (SUTime processing)

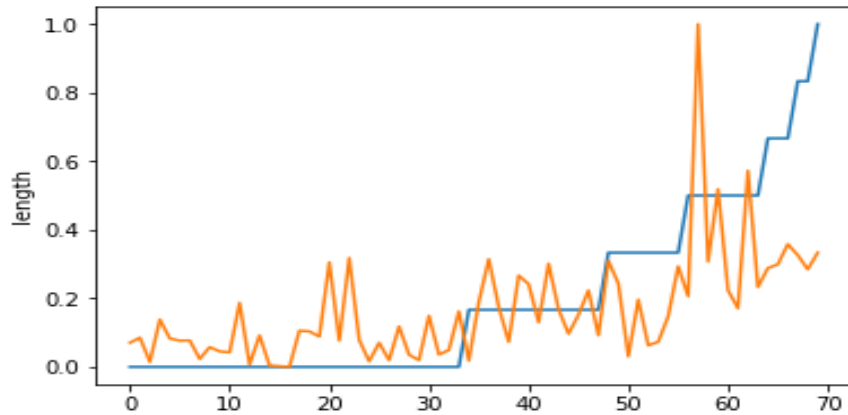


## Num symptoms (list of 598 keywords)

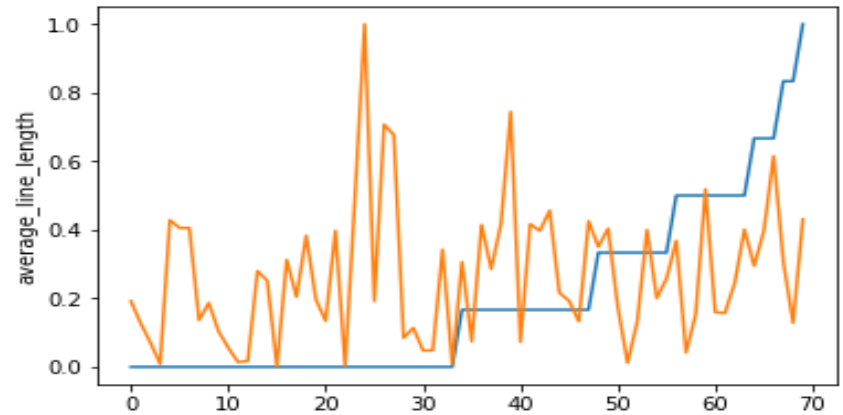


# Annotation results

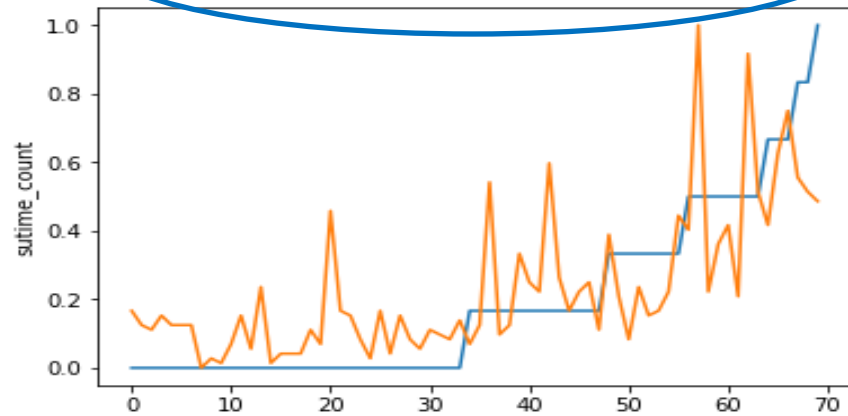
Length



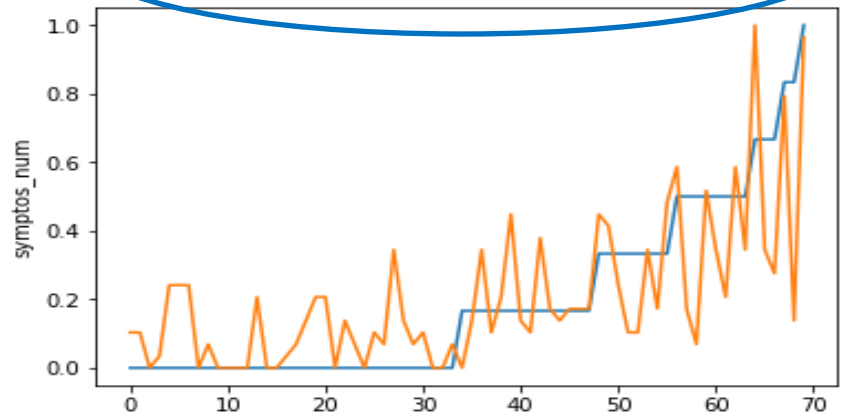
Avg line length



Num timexes (SUTime processing)



Num symptoms (list of 598 keywords)



# Second document selection

1) extract all documents related to early intervention services

36594 documents  
4166 patients



2) Filter documents

- length > 50th percentile
- avg\_line\_length > 25th percentile

16318 documents  
3819 patients



3) New filters:

- Num symptoms > 3
- Num timexes > 5

8842 documents  
3308 patients



4) Randomly select 20 patients and save all their documents

54 documents  
20 patients (1-6 docs each)

# Ongoing work

- Definition of additional symptom keywords
- Time expression normalization
- Temporal link annotation (just started)

Date: 2018-05-04

She reported she has been hearing voices since last year...”

hearing voices → last year (2017)

# Conclusions

- Extracting information from clinical text is essential to make unstructured data available for further research
- Developing NLP applications for a specific clinical use-case is challenging
  - domain-specific language
  - lack of annotated resources

Future directions

system adaptation

multilingual approaches

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Thank you!

Questions?