Welcome to the Sentinel Innovation and Methods Seminar Series

The webinar will begin momentarily

Please visit www.sentinelinitiative.org for recordings of past sessions and details on upcoming webinars.

Note: closed-captioning for today's webinar will be available on the recording posted at the link above.

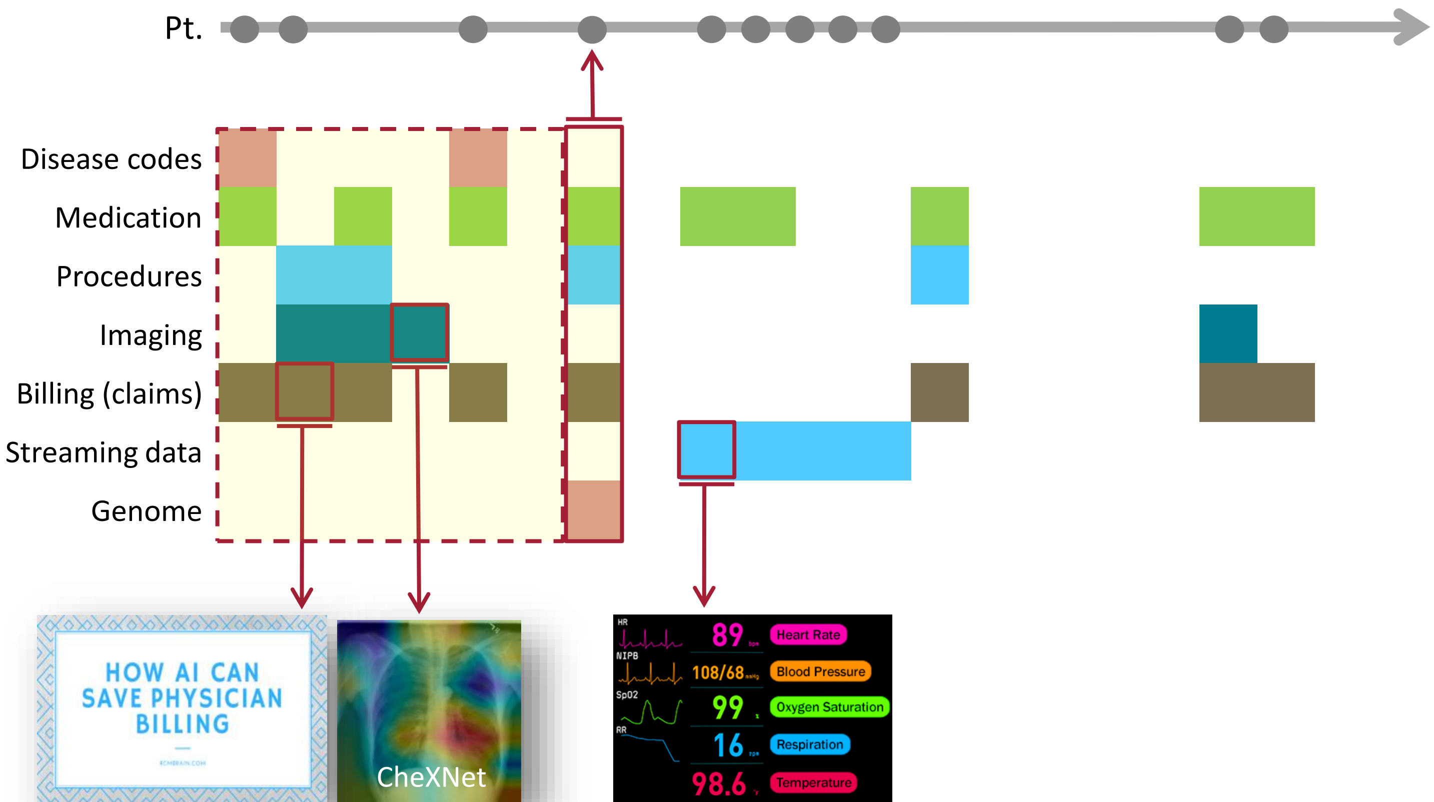
Sentinel

Ontology-driven weak supervision for clinical entity classification in electronic health records

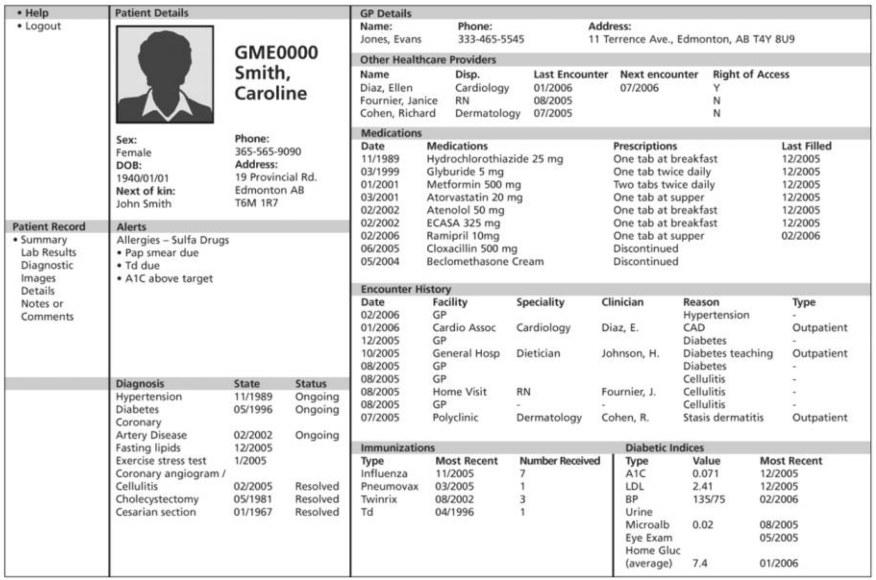
Nigam Shah

Stanford MEDICINE | Technology & Digital Solutions
Stanford Health Care and School of Medicine

A patient timeline view of the data



Converting patient timelines to datasets



- Help
- Logout

Patient Details

GME0000
Smith,
Caroline

Sex: Female
DOB: 1940/01/01
Next of kin: John Smith
Phone: 365-565-9090
Address: 19 Provincial Rd. Edmonton AB T6M 1R7

Patient Record

- Summary
  Lab Results
  Diagnostic
  Images
  Details
  Notes or
  Comments

Alerts

Allergies – Sulfa Drugs
- Pap smear due
- Td due
- A1C above target

Diagnosis	State	Status
Hypertension	11/1989	Ongoing
Diabetes	05/1996	Ongoing
Coronary Artery Disease	02/2002	Ongoing
Fasting lipids	12/2005	
Exercise stress test	1/2005	
Coronary angiogram / Cellulitis	02/2005	Resolved
Cholecystectomy	05/1981	Resolved
Cesarian section	01/1967	Resolved

GP Details

Name:	Phone:	Address:
Jones, Evans	333-465-5545	11 Terrence Ave., Edmonton, AB T4Y 8U9

Other Healthcare Providers

Name	Disp.	Last Encounter	Next encounter	Right of Access
Diaz, Ellen	Cardiology	01/2006	07/2006	Y
Fournier, Janice	RN	08/2005		N
Cohen, Richard	Dermatology	07/2005		N

Medications

Date	Medications	Prescriptions	Last Filled
11/1989	Hydrochlorothiazide 25 mg	One tab at breakfast	12/2005
03/1999	Glyburide 5 mg	One tab twice daily	12/2005
01/2001	Metformin 500 mg	Two tabs twice daily	12/2005
03/2001	Atorvastatin 20 mg	One tab at supper	12/2005
02/2002	Atenolol 50 mg	One tab at breakfast	12/2005
02/2002	ECASA 325 mg	One tab at breakfast	12/2005
02/2006	Ramipril 10mg	One tab at supper	02/2006
06/2005	Cloxacillin 500 mg	Discontinued	
05/2004	Beclomethasone Cream	Discontinued	

Encounter History

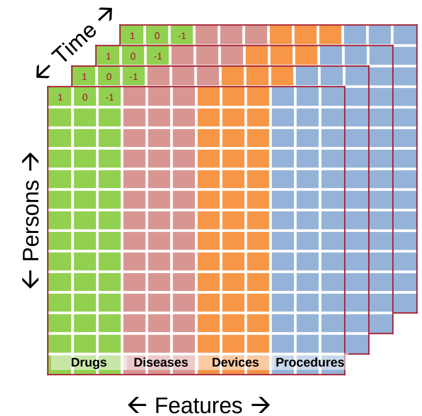
Date	Facility	Speciality	Clinician	Reason	Type
02/2006	GP			Hypertension	-
01/2006	Cardio Assoc	Cardiology	Diaz, E.	CAD	Outpatient
12/2005	GP			Diabetes	-
10/2005	General Hosp	Dietician	Johnson, H.	Diabetes teaching	Outpatient
08/2005	GP			Diabetes	-
08/2005	GP			Cellulitis	-
08/2005	Home Visit	RN	Fournier, J.	Cellulitis	-
08/2005	GP	-	-	Cellulitis	-
07/2005	Polyclinic	Dermatology	Cohen, R.	Stasis dermatitis	Outpatient

Immunizations

Type	Most Recent	Number Received
Influenza	11/2005	7
Pneumovax	03/2005	1
Twinrix	08/2002	3
Td	04/1996	1

Diabetic Indices

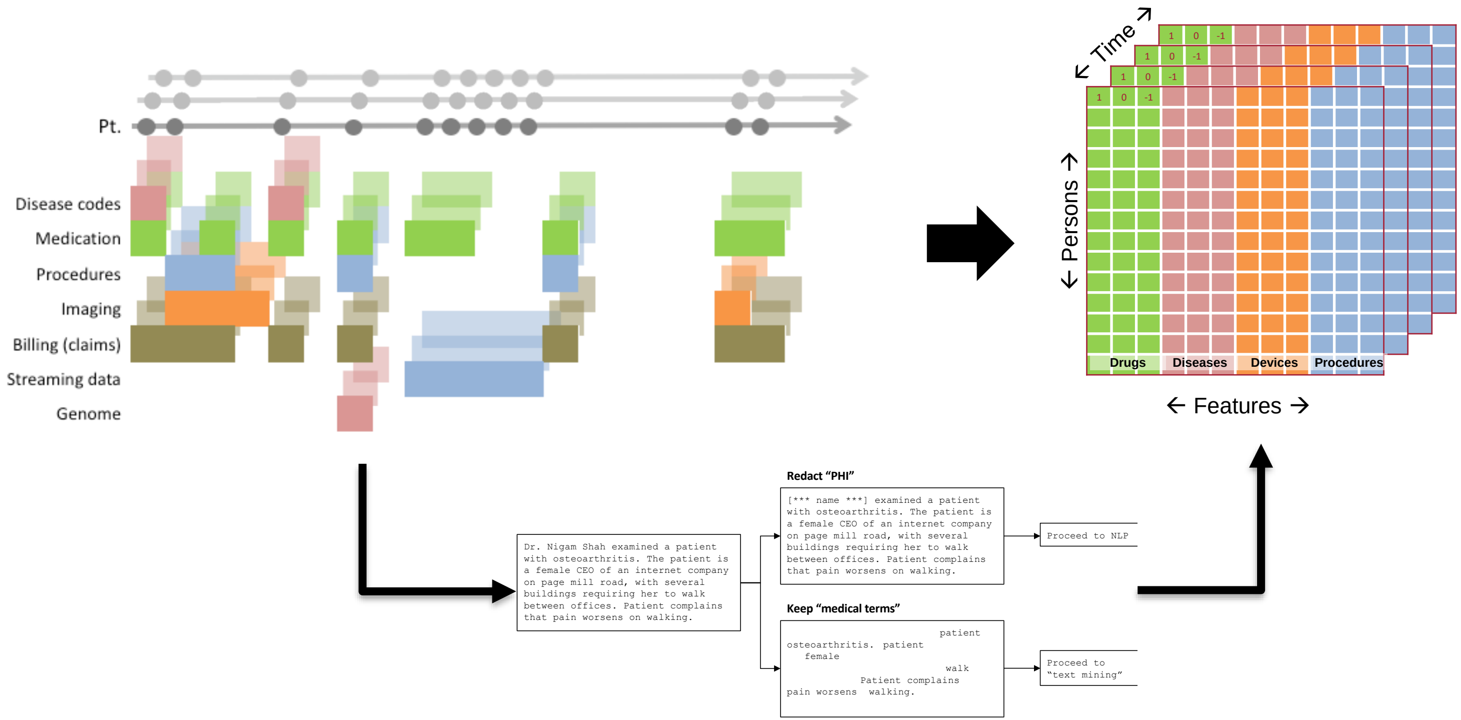
Type	Value	Most Recent
A1C	0.071	12/2005
LDL	2.41	12/2005
BP	135/75	02/2006
Urine Microalb	0.02	08/2005
Eye Exam		05/2005
Home Gluc (average)	7.4	01/2006



Decisions to make:

- About source and choice of features, including text
- About handling of time
- About defining an electronic phenotype
- About building a cohort

Text is <u>one source</u> to use [be careful how deep you go!]



Core concepts

- Processing of Text vs. Natural Language Processing
- Handling of knowledge graphs
- Ascertaining whether the patient had an “event” or not (and when)
  - We can choose to do this task just using a textual document
  - We can do this task as a classification problem, where text-extracted content is just one element on a patient timeline.

Handling of text – two world-views

```
Dr. Nigam Shah examined a patient
with osteoarthritis. The patient is
a female CEO of an internet company
on page mill road, with several
buildings requiring her to walk
between offices. Patient complains
that pain worsens on walking.
```

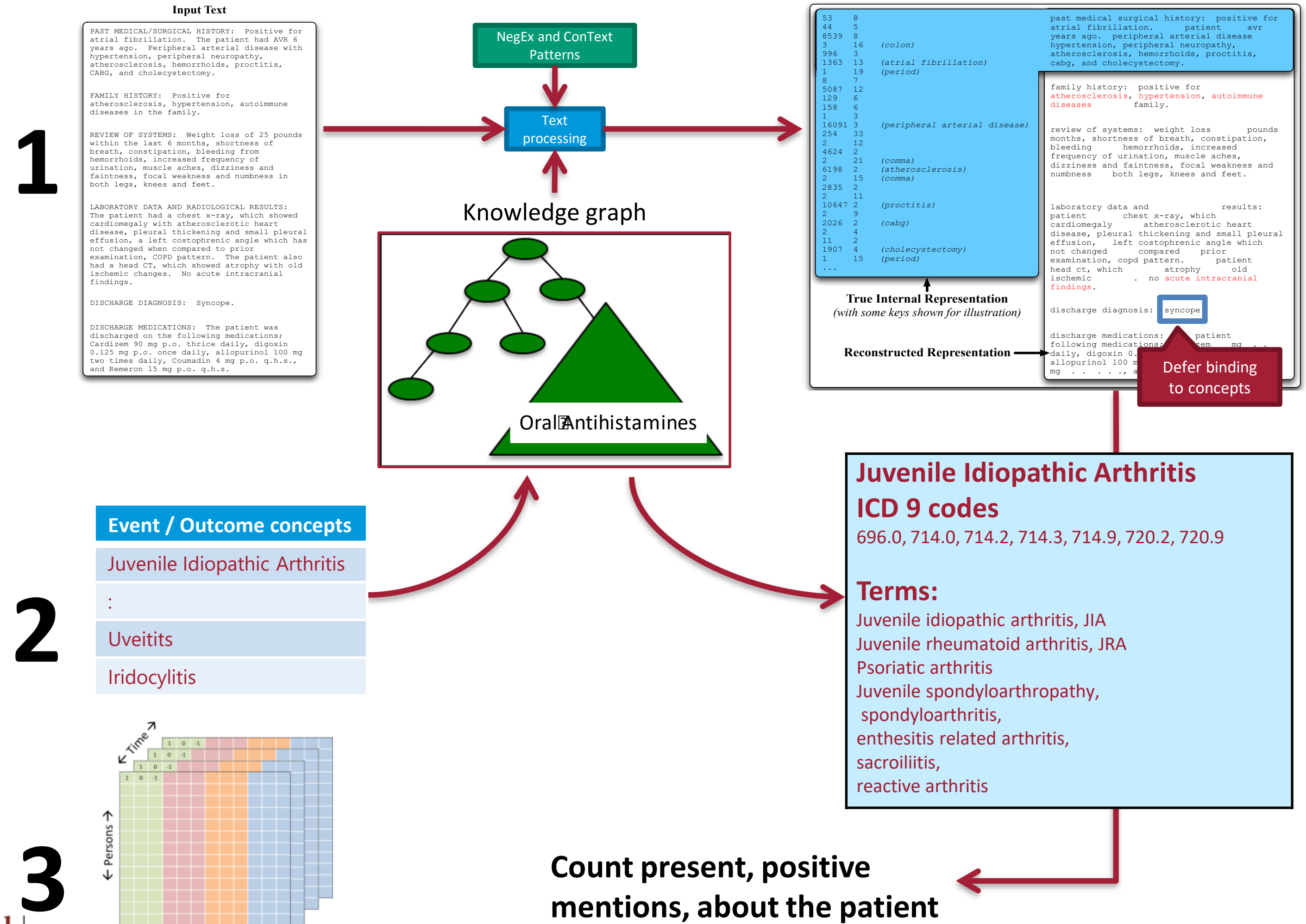
```
[*** name ***] examined a patient
with osteoarthritis. The patient is
a female CEO of an internet company
on page mill road, with several
buildings requiring her to walk
between offices. Patient complains
that pain worsens on walking.
```

Redacting "PHI"

```
                          patient
osteoarthritis.       patient
   female
                           walk
                  Patient complains
pain worsens  walking.
```

Keeping "medical terms"

Simple text processing



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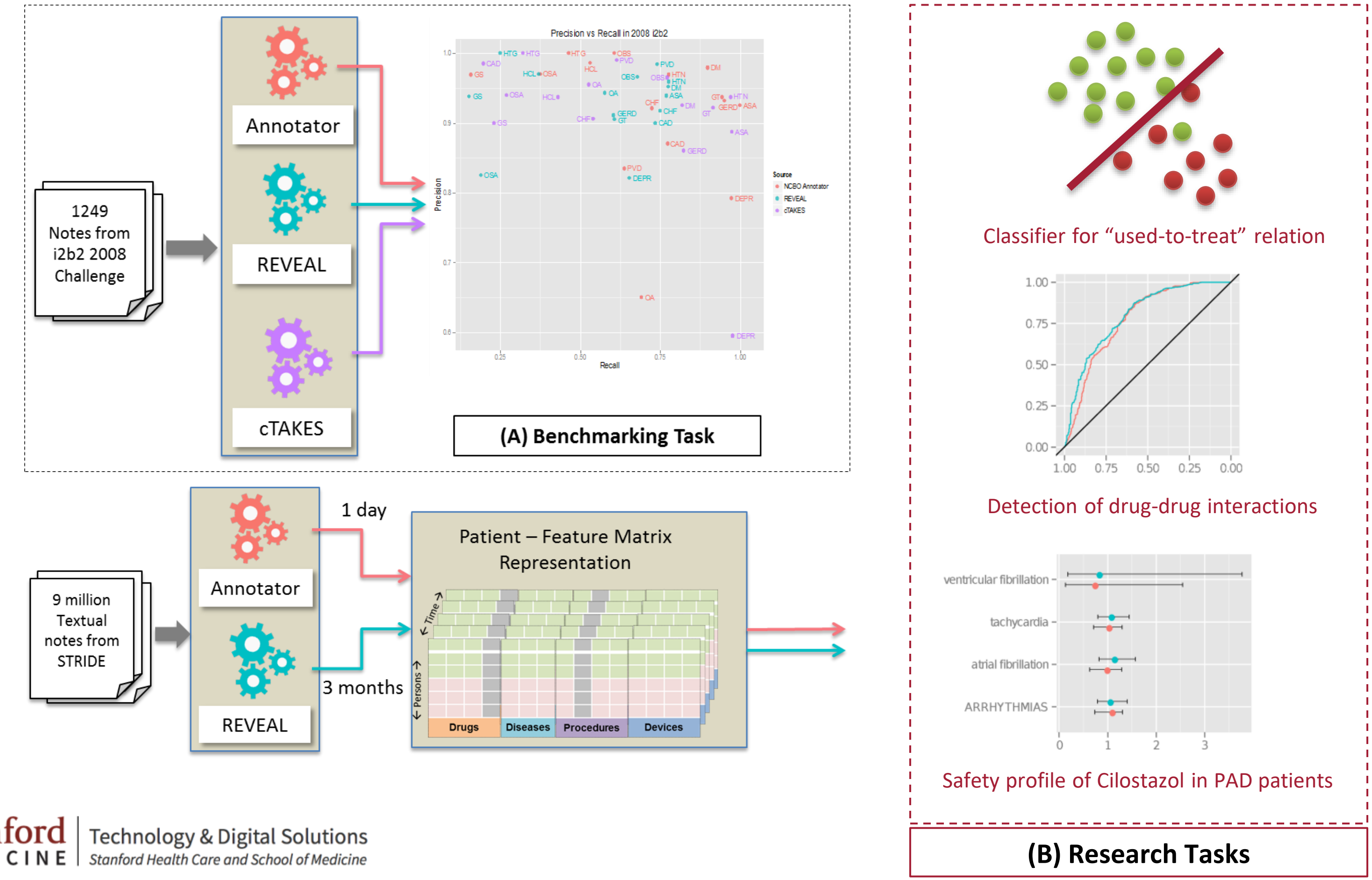
LePendu et al, Pharmacovigilance using clinical notes. Clin Pharmacol Ther. 2013 Jun;93(6):547-55. doi: 10.1038/clpt.2013.47

Trade-off: simple or advanced [text-processing]

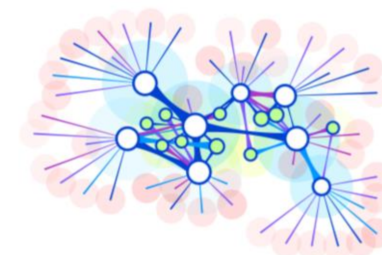


Weak supervision

The State of Clinical Concept Extraction in 2020

- Largely rule-based + manual feature engineering
- Many clinical entity types do not have expert labeled training sets available
- For existing labeled datasets we're locked into their annotation choices
- PHI / Privacy considerations when sharing labeled data

not many hand-labeled datasets



but many ontologies!

Fu et al. 2020 *Journal of Biomedical Informatics.*
"Clinical concept extraction: A methodology review"

Ontology-based Labeling

Semantic Labeling

Term mapped to entity type probability

```
aortic stenosis -> [0.0, 1.0]
        present -> [1.0, 0.0]
         aortic -> [1.0, 0.0]
```

Synonym Labeling

Use entire document context to tag **synonymous** entities

```
    {aortic stenosis, AS} -> [0.0, 1.0]
{mitral regurgitation, MR} -> [0.0, 1.0]
```

```
AORTIC VALVE: Mildly thickened aortic valve leaflets (3). No AS.
MITRAL VALVE: Normal mitral valve leaflets with trivial MR.

CONCLUSIONS
The aortic valve leaflets (3) are mildly thickened but aortic
stenosis is not present. Trace aortic regurgitation may be
present. The mitral valve appears structurally normal with
trivial mitral regurgitation.
```

Ontologies —> **Type** and **Synonymy** Information

Weakly Supervised: Ontologies + Task Rules

Task	+Task-specific rules				Hand-labeled	
	LFs	MV	LM	WS	FS	SOTA
Chemical	+9	81.1	89.2 ± 0.2†	**91.1 ± 0.1***	92.4 ± 0.2	93.5[24]
Disease	+6	76.4	79.8 ± 0.3†	**79.9 ± 0.2**	84.5 ± 0.2	87.2[24]
Disorder	+11	71.2	75.0 ± 0.2†	**76.3 ± 0.1***	79.6 ± 0.3	80.1[65]
Drug	+11	82.2	85.8 ± 0.4†	**88.3 ± 0.3***	93.2 ± 0.3	91.4[66]
Negation	17	92.5	**93.0 ± 0.0†**	92.7 ± 0.6*	96.1 ± 0.2	~
DocTimeRel	27	67.8	69.2 ± 0.0†	**72.9 ± 0.5***	86.2 ± 0.1	83.4[67]

NER performance within 4.1% F1 of models trained with hand-labeled data

Stanford MEDICINE

Fries et al, Ontology-driven weak supervision for clinical entity classification in electronic health records.
Nat Commun. 2021 Apr 1;12(1):2017. doi: 10.1038/s41467-021-22328-4.

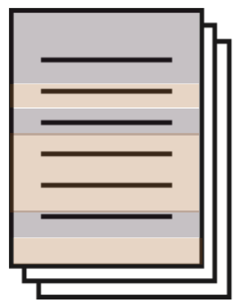
Continuous Symptom Monitoring for COVID-19

Could we use presenting symptoms to prioritize who should be tested for COVID-19?

Stanford HEALTH CARE

Emergency Department

Daily feed of all notes + timestamped edit deltas



Use first 30 minutes of note edits

Virus	AUROC
Adenovirus	0.68 (0.60–0.76)
Influenza virus A	0.73 (0.68–0.77)
Metapneumovirus	0.64 (0.57–0.71)
Parainfluenza virus	0.60 (0.53–0.68)
RSV	0.77 (0.73–0.80)
Rhinovirus	0.62 (0.58–0.66)
SARS-CoV-2	0.64 (0.49–0.79)

Limited ability to discriminate respiratory viruses from symptoms alone (Callahan et al. 2020)

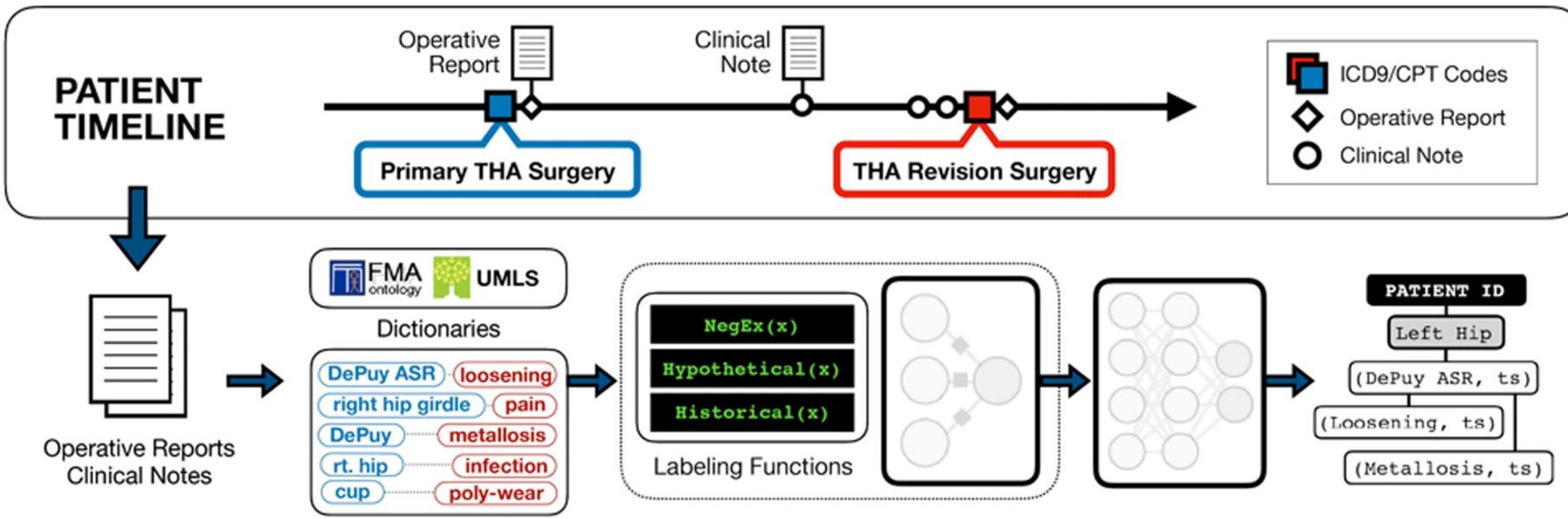
Weakly supervised symptom tagger
+2.3 F1 points over baseline

Enabled Symptom Data Sharing

Bill & Melinda Gates Foundation

CMU Delphi Group's COVIDCAST

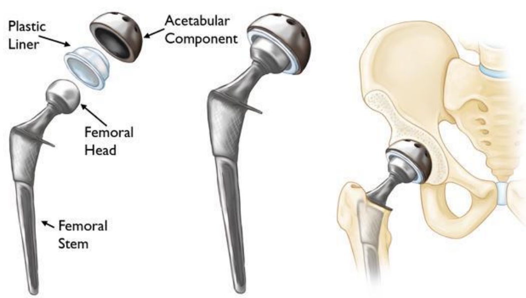
Medical device surveillance with EHRs



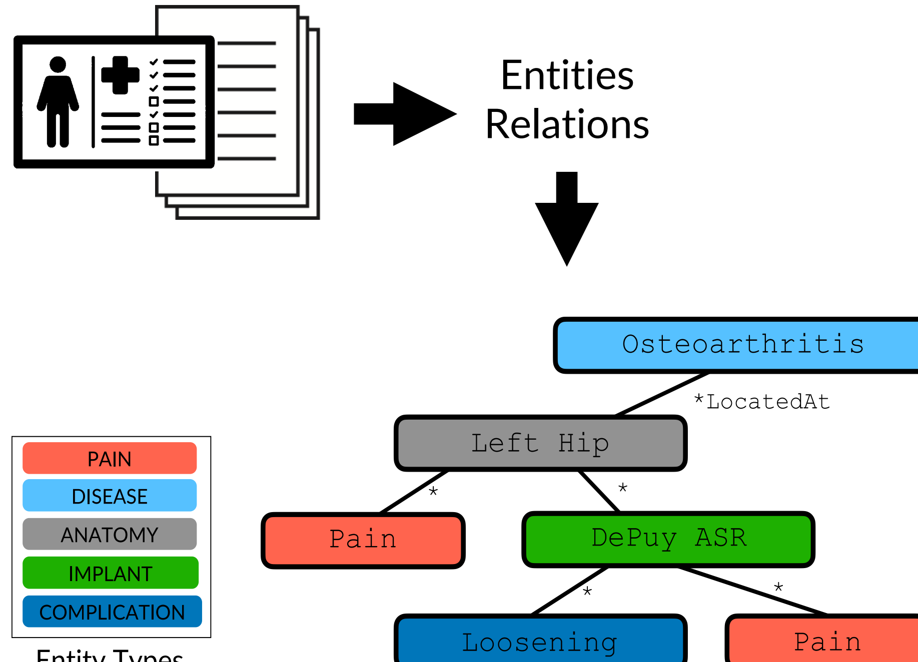
Callahan and Fries et al, npj Digital Medicine **volume 2**, Article number: 94 (2019)

Extracting Structured Information from Notes

Medical Device Surveillance



2018 global investigation on the medical device industry



Entity Types

Goal: Automatically supplement joint implant registry information

Implant Outcomes as Relation Extraction

`ComplicationAt(Implant, Event)` IMPLANT ↔ INFECTION | REVISION | COMPONENT WEAR | R. ABNORMALITY | PARTICLE DISEASE | MECHANICAL FAILURE

`PainAt(Anatomy, Pain)` ANATOMY ↔ PAIN

ComplicationAt

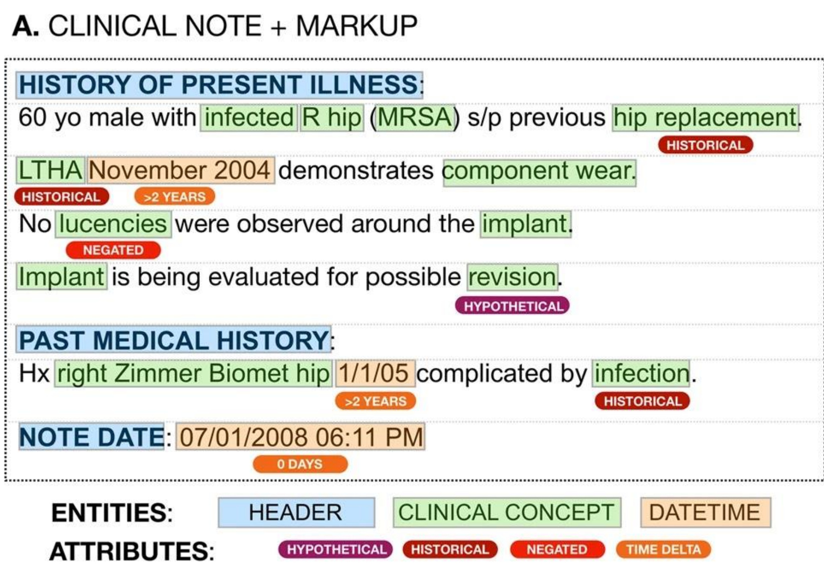
THE ACETABULAR COMPONENT HAS BEEN REPLACED, AND THE FEMORAL HEAD APPEARS WELL CENTERED.

Complication relations identified over sentences

Label Small Gold Standard
Dev & Test Sets

Programmatically label the training set

Example labeling function



Output from text-processor

B. LABELING FUNCTION DEFINITIONS

```
def LF1_contiguous_entities(c):
    v = len(between_words(c)) == 0
    return TRUE if v else ABSTAIN
```

```
def LF2_historical(c):
    v = has_historical_attrib(c)
    return FALSE if v else ABSTAIN
```

```
def LF3_reject_section(c):
    h1 = get_section_header(c)
    v = h1 in reject_headers
    return FALSE if v else ABSTAIN
```

```
def LF4_negated(c):
    v = NegEx.is_negated(c)
    return FALSE if v else ABSTAIN
```

```
FALSE: -1   ABSTAIN: 0   TRUE: 1
```

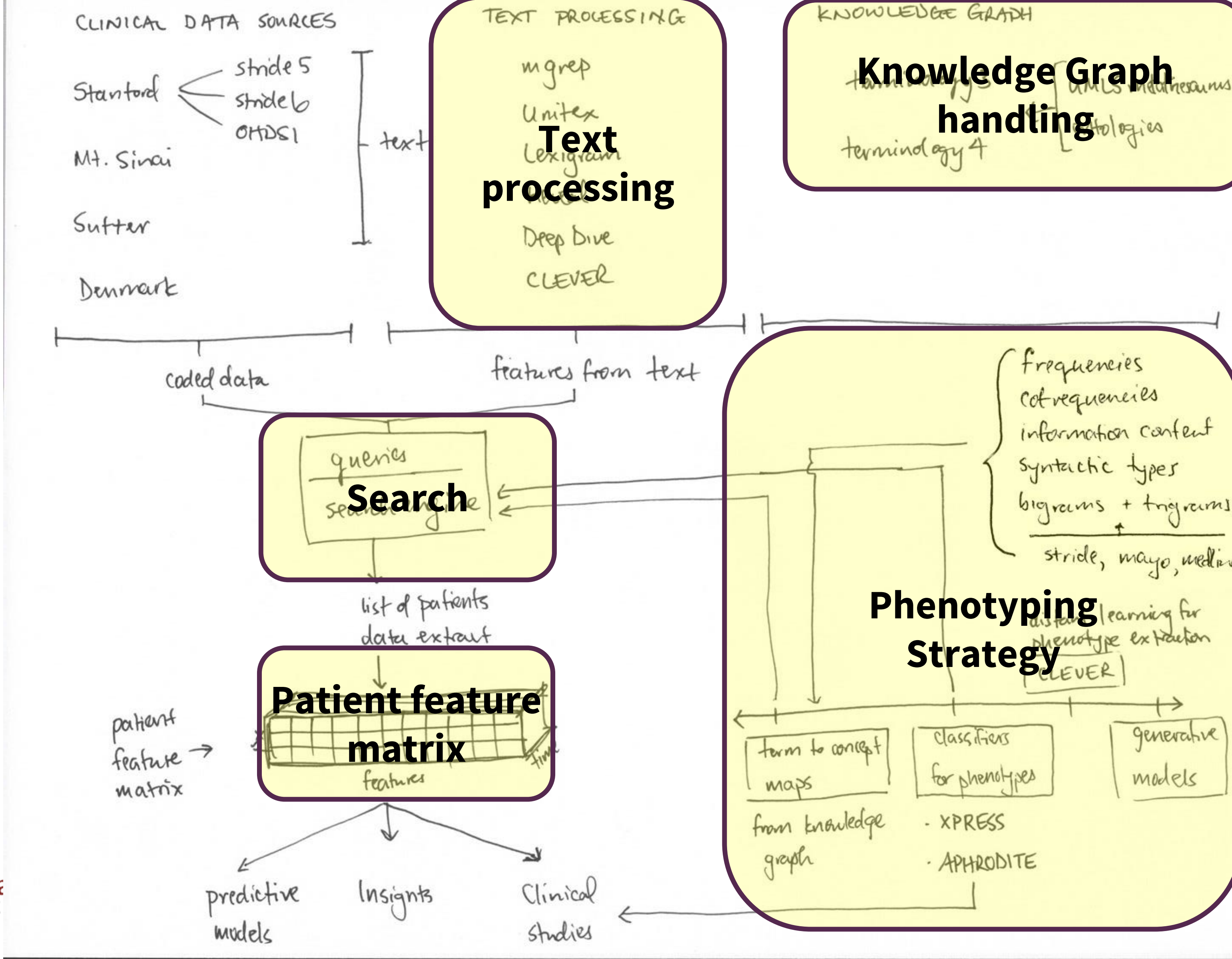
Labeling function

CATEGORY	# INSTANCES	PRECISION	RECALL	F1	+/- F1
Revision	63	75.5	58.7	**66.1**	+16.2%
Component Wear	48	72.9	72.9	**72.9**	+38.6%
Mechanical Failure	25	91.7	44.0	**59.5**	+40.3%
Particle Disease	65	97.1	52.3	**68.0**	+496.5%
Radiographic Abnormality	17	60.0	25.3	44.4	-18.5%
Infection	58	90.7	84.5	**87.5**	+54.0%
Implant-Complications	276	82.7	62.3	**71.1**	+53.2%
Pain-Anatomy	236	80.2	82.6	**81.4**	+12.7%

Big Boost in Recall

6x More complication events than with coded data alone

Closing thoughts


CLINICAL DATA SOURCES
Stanford
stride 5
stride 6
OHDSI
Mt. Sinai
Sutter
Denmark
text
TEXT PROCESSING
mgrep
Unitex
Deep Dive
CLEVER
Text processing
KNOWLEDGE GRAPH
Knowledge Graph handling
terminology 4
coded data
features from text
queries
Search
list of patients
data extract
Patient feature matrix
patient feature matrix
features
frequencies
cofrequencies
information content
syntactic types
bigrams + trigrams
stride, mayo, medline
Phenotyping Strategy
phenotype extraction
CLEVER
term to concept maps
from knowledge graph
classifiers for phenotypes
· XPRESS
· APHRODITE
generative models
predictive models
Insights
Clinical studies

Acknowledgements and Contact Information

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