A statistical approach to utilizing electronic health records

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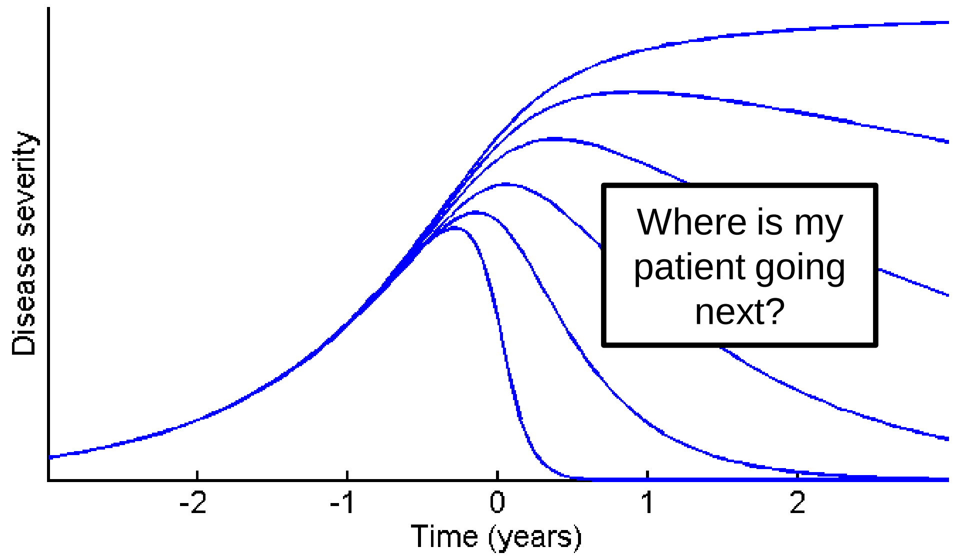
Know your Patients

- ❑ Can a health system make use of what it knows about patients to make informed decisions?
  - Lots of data.
  - What questions to ask?
  - How to generate answers?
- ❑ Where is my patient going next?
- ❑ What will help me know?
  - EHR data, labs, genetics, “quantified self” data, genomics?



Complicated Messy Data

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- ❑ Electronic Health Records data has
  - ▪ Continuous data (labs, age, vitals)
  - ▪ Categorical data (gender, race, family history)
  - ▪ Written text (nurses' and physicians' notes, radiology reports)
  - ▪ Images (x-ray, CT, EKG)
- ❑ Important information everywhere
  - ▪ Example: A diabetic might have any or all of the following
    - Synonym of "diabetes" in a note
    - High lab values (glucose, HbA1C)
    - Relevant medications
    - Billing codes related to treatment of diabetes
    - Predisposing demographics (weight, race, family history)
    - Genetic predisposition (TCF7L2, JAZF1, HHEX, etc)
- ❑ We want to incorporate all of this information
- ❑ Don't want to be fooled by mistakes

Approach

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- ❑ Automated “Patients like me”
- ❑ Create groups of homogeneous patients
- ❑ This allows:
  - Automated generation of differential diagnosis
  - Novel comparative effectiveness studies
  - Listing of treatment options
  - Identification of Adverse drug events
  - Estimation of disease progression and prognosis
  - Assessment clinical utility of novel lab tests
- ❑ Predict probable patient type from other data
- ❑ Group patients through time

Model

$$P(n_i = k|X) = f(m_k)\prod_l P_l(n_i = k|X)$$

- Product densities from each component
- Each data type is treated independently
- Doesn't explicitly model correlation across different data types

Topic Model for Text

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$$q_k \sim Dir(\beta)$$

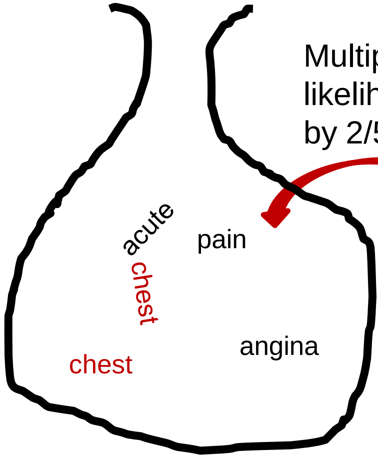
$$p(w_{i,j}|n_i = k) \sim MN(q_k)$$

$$P(w_i) \propto \sum_k f(m_k) \prod_j MN(w_{i,j}|q_k) Dir(q_k|\beta) I_{[n_i=k]}$$

Compute the likelihood that $n_i = k$:

1. Start with likelihood 1.
2. Pick a word from document i.
3. Multiply by the fraction of words in topic k that are equal to the chosen word.
4. Add the word to the topic and repeat until all words have been added.

i – index for document
j – index for word
k – index for cluster
n_i – topic for document i
q_k – latent word frequencies
m_k – # documents in cluster k
w_i – indicator vector



Multiply likelihood by 2/5.

chest pain with exercise

Topic Models, NLP, Mixed data

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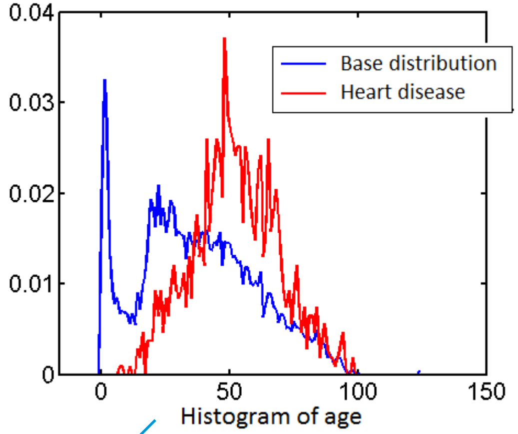
Clustering patient visits to identify features of disease processes

Medications
Asa/buffers
Aspirin
Hctz
Lantus
Lipitor
Lisinopril
Metoprolol
Metformin

Medical (NLP) Concepts
No trauma
No fever
No diarrhea
Aspirin
Back
Chest
Dyspnea
Exercise



Topic Model
$P(w_{i,j} \mid n_i = k) \sim MN(q_k)$
$q_k \sim Dir(\beta)$

Normal-Gamma Clustering
$P(r_i|n_i=k) \sim N(\mu_k, \sigma_k)$
$P(\mu_k, \sigma_k) \sim \text{NormGamma}$

Diagnoses
Angina pectoris
CAD
Chest pain acute
Chest pressure
MI
Palpitations
Chest tightness
Myocardial infarction
Pericarditis

Profile of a patient with heart disease
- Combined evidence from multiple sources
- Relationships between drugs and patient group
- Metformin is protective
- Lantus: heart failure is side effect

1. Henao, Murray, Ginsburg, Carin, Lucas (2013) "Patient clustering with uncoded text in electronic medical records", Proc Annual Symposium AMIA
2. Murray, Dunson, Carin, Lucas (2013) "Bayesian Gaussian copula factor models for mixed data", *JASA*, **108**(502) 656-665

Nice features

- Very fast mixing
- MCMC without ever having to sample parameters
- Can compute MAP
- Model knows when it doesn't know
- Use to identify trends in other data

Model fitted to clinical data

Assess ability of new data to predict clusters

New data type

Predict patient type based on new data

Example: Suppose a small percentage of your customers use your clinic. What do they purchase in the rest of the store? Does that inform on other potential clinic users? Can/should you market to them?

Case Study: Data

- 54,000 records from ED
- Contains
  - Vocabularies
    - Notes
    - Orders
    - Patient reported meds
    - Diagnoses
  - Categorical data
    - Chief complaint
    - Gender
    - Disposition
    - Zip code
  - Continuous data
    - Age
    - Priority
    - Vitals
    - Weight
- None is codified
- All data subject to parsing errors

Messy data

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weakness/aching/headaches
weakness/discomfort
weakness/dizziness
weakness/dizziness/recent
weakness/faintness/congestion
weakness/fatigue
weakness/flaccid
weakness/heaviness
weakness/numbness
weakness/pain
weakness/shaking
weakness/tingling
weakness;
weaknessambulatory
weaknesscoughfeverlwbswent
weaknesscoughing
weaknessdiahrrea
weaknessdizziness
weaknesses
weaknessfalling
weaknessfatigue
weaknessn\aloc
weaknessper
weaknesss
weaknesssob
weaknesssore
weaknessunstable
weaknessvison
weaknessx
weaknss

Over 50,000 unique “words” with no copy editing. How to clean up mistakes?

Unified Medical Language System (UMLS)

- Metathesaurus
  - 10.5 million atoms in thesaurus (1.2 in SNOMED)
- Semantic Network
  - 51.4 million relationships (2.9 in SNOMED)
- Lexicon
  - 3.3 million spellings, inflections, properties, modifiers, abbreviations
- Together: 23 gigabytes of plaintext
  - At 60 words per minute this is about 7 years of non-stop typing.

UMLS Challenges

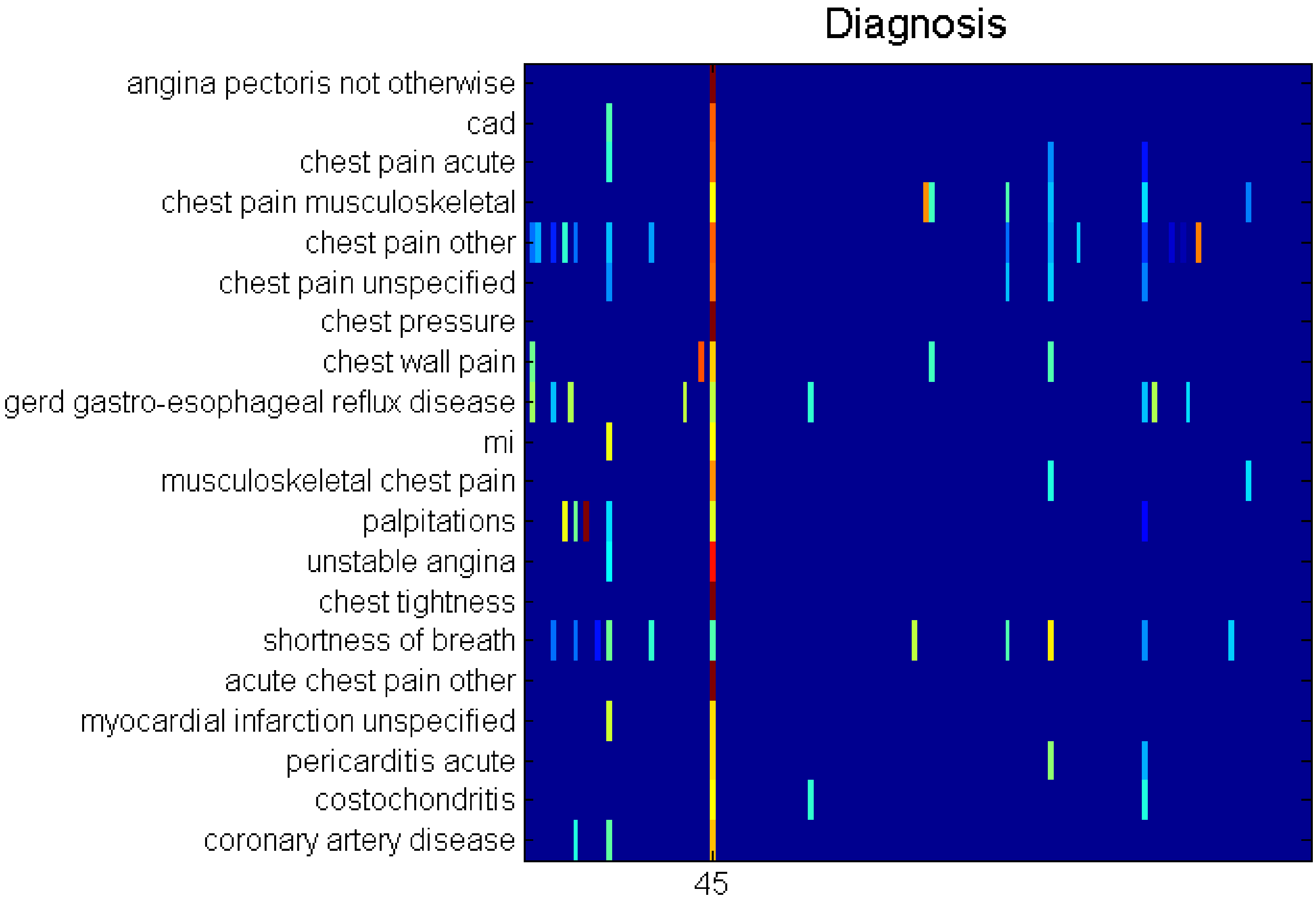
- Incredible number of arbitrary decisions
  - What should be the semantic types?
    - Why is Mammal a semantic type but not primate
  - What words to include?
  - What relationships?
- Overly inclusive
  - 10.5 million atoms in thesaurus(1.2 in SNOMED)
  - Orders of magnitude more words in the thesaurus than are unique words in the 50k records
  - How does one curate something this large?
- What do you do with it?

Metamap Results Example

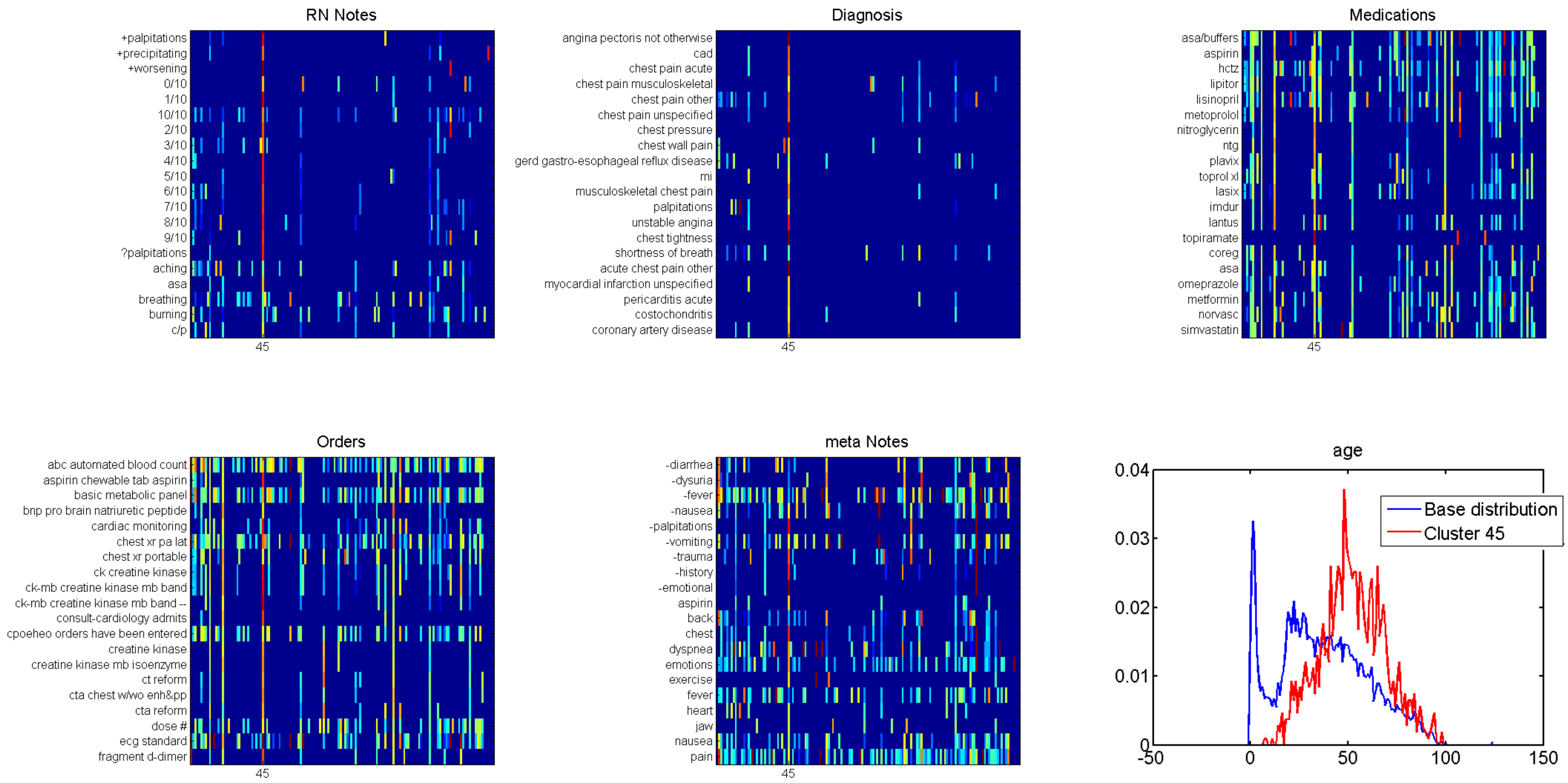
1. Pt here with c/o N/V and "shakes"
2. decreased po intake x 2 day
3. pt has pain pump which has been out of medication x 1 week
4. pt now taking PO narcotics
5. but presenting with N/V
6. pt with chronic back and neck pain

1. Tremor [Sign or Symptom]
2. Decreased [Quantitative Concept], Oral [Spatial Concept], /day [Temporal Concept]
3. Pain [Sign or Symptom], Pump, device [Medical Device], Drugs [Pharmacologic Substance], week [Temporal Concept]
4. Take [Health Care Activity], Oral [Spatial Concept]
5. Presentation [Idea or Concept], N+ (tumor staging) [Intellectual Product]
6. Chronic [Temporal Concept], Neck pain [Sign or Symptom]

Patients with Chest Pain

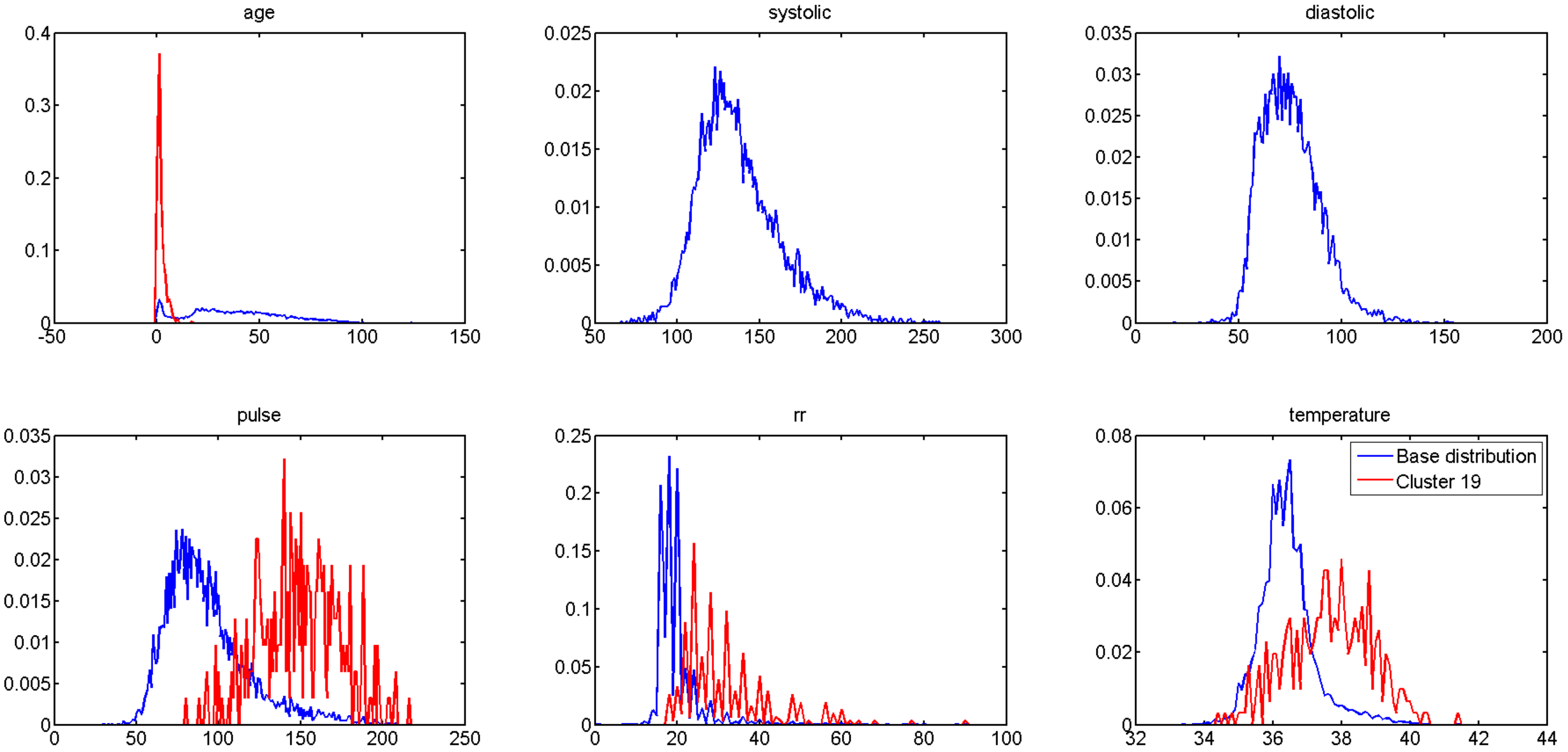


Chest Pain



RN Notes
+palpitations
+precipitating
+worsening
0/10
1/10
10/10
2/10
3/10
4/10
5/10
6/10
7/10
8/10
9/10
?palpitations
aching
asa
breathing
burning
c/p
45
Diagnosis
angina pectoris not otherwise
cad
chest pain acute
chest pain musculoskeletal
chest pain other
chest pain unspecified
chest pressure
chest wall pain
gerd gastro-esophageal reflux disease
mi
musculoskeletal chest pain
palpitations
unstable angina
chest tightness
shortness of breath
acute chest pain other
myocardial infarction unspecified
pericarditis acute
costochondritis
coronary artery disease
45
Medications
asa/buffers
aspirin
hctz
lipitor
lisinopril
metoprolol
nitroglycerin
ntg
plavix
toprol xl
lasix
imdur
lantus
topiramate
coreg
asa
omeprazole
metformin
norvasc
simvastatin
45
Orders
abc automated blood count
aspirin chewable tab aspirin
basic metabolic panel
bnp pro brain natriuretic peptide
cardiac monitoring
chest xr pa lat
chest xr portable
ck creatine kinase
ck-mb creatine kinase mb band
ck-mb creatine kinase mb band --
consult-cardiology admits
cpoeheo orders have been entered
creatine kinase
creatine kinase mb isoenzyme
ct reform
cta chest w/wo enh&pp
cta reform
dose #
ecg standard
fragment d-dimer
45
meta Notes
-diarrhea
-dysuria
-fever
-nausea
-palpitations
-vomiting
-trauma
-history
-emotional
aspirin
back
chest
dyspnea
emotions
exercise
fever
heart
jaw
nausea
pain
45
age
0.04
0.03
0.02
0.01
0
-50
0
50
100
150
Base distribution
Cluster 45

Fever / Febrile Seizure



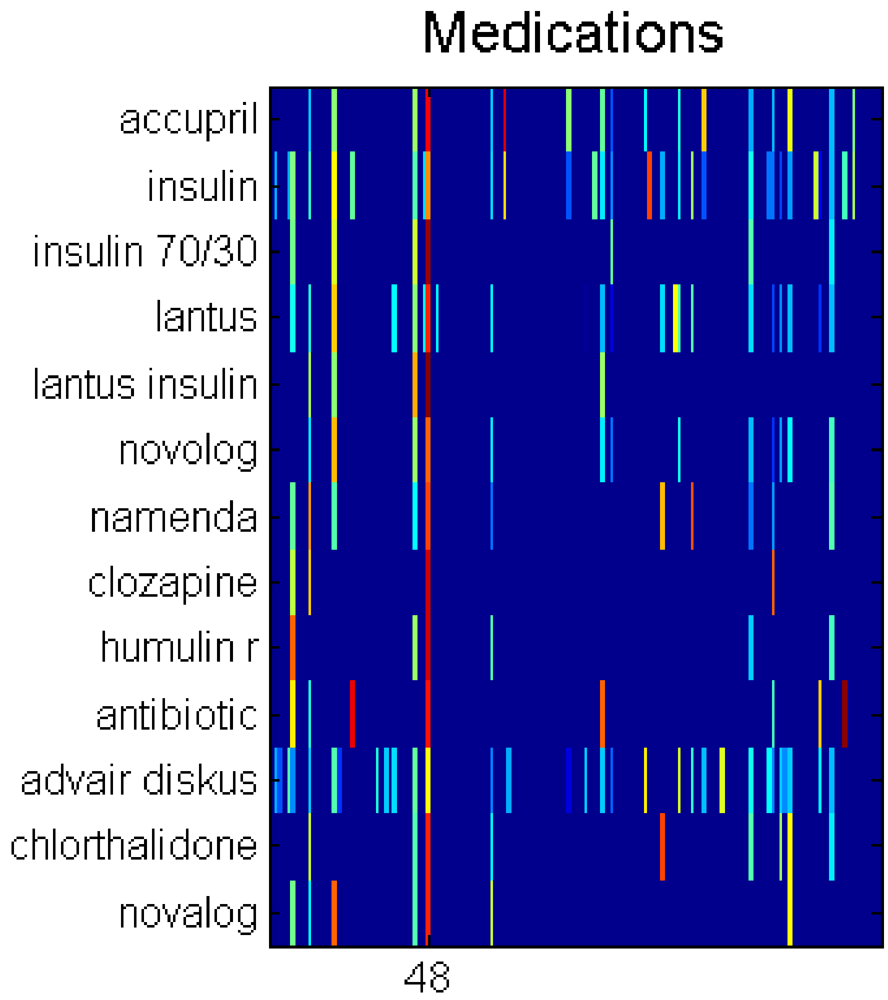
Pharmacovigilance: Patients with Diabetes

Blood pressure

Dementia

Schizophrenia

Diuretic



Some other associations

Drug	Indication	Patient cluster
Tussionex	Opioid	TIA
Altace	Blood pressure	Chest pain
Metformin	Blood sugar	Nose bleed
Tylenol	Analgesic	Rabies
Buspirone	Anxiolytic	Dog/cat bite
Cassodex	Chemo	Sickle cell
Vasotec	Blood pressure	Nose bleed
Prednisolone	Inflammation	Eye pain
Wellbutrin	Depression	Nose bleed
Zomig	Migraine	Chest pain

Models for comparison

- Use UMLS to process RN notes
- Ignore UMLS and just throw out rare “words” from the RN notes
- Cluster with chief complaint
- Cluster with MetaMAP only

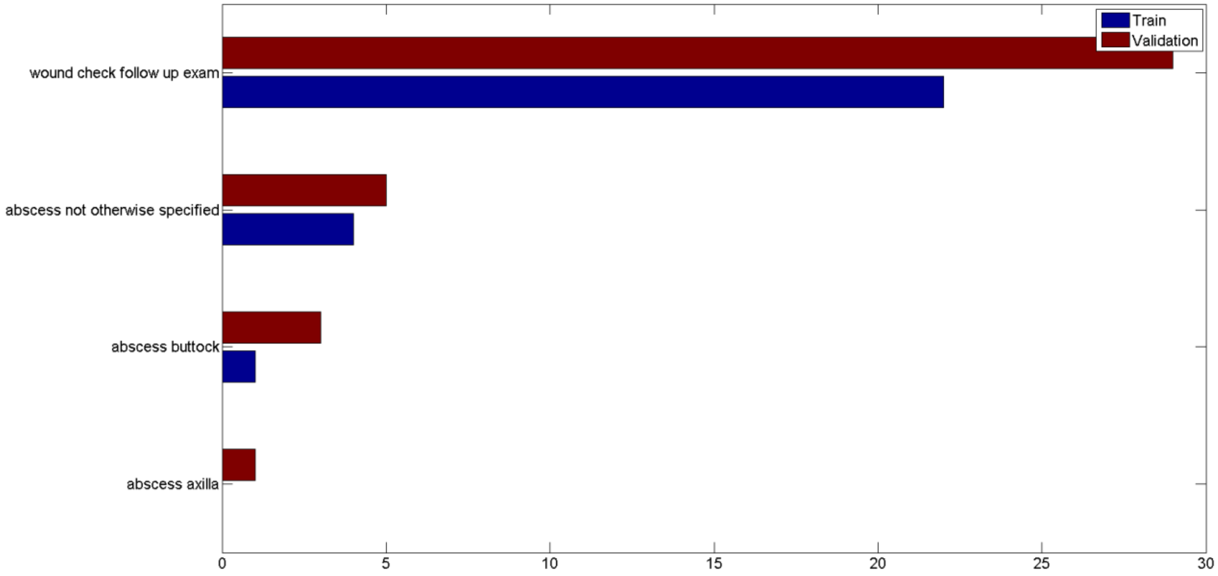
Validation of Associations

- ❑Train the model on 20,000 samples selected uniformly at random
  - Test for association between patient clusters and drugs
- ❑Fit the model to the test data
- ❑Model using MetaMap
  - 4% of drug – symptom association tests have p-value<.05 (3021)
  - 56% validate
- ❑Model using terms in RN notes
  - 2% of tests significant (2258)
  - 58% validate
- ❑Model using chief complaint
  - 3% of tests significant (9381)
  - 18% validate
- ❑Model using MetaMap concepts only
  - 3% of tests significant (9319)
  - 22% validate

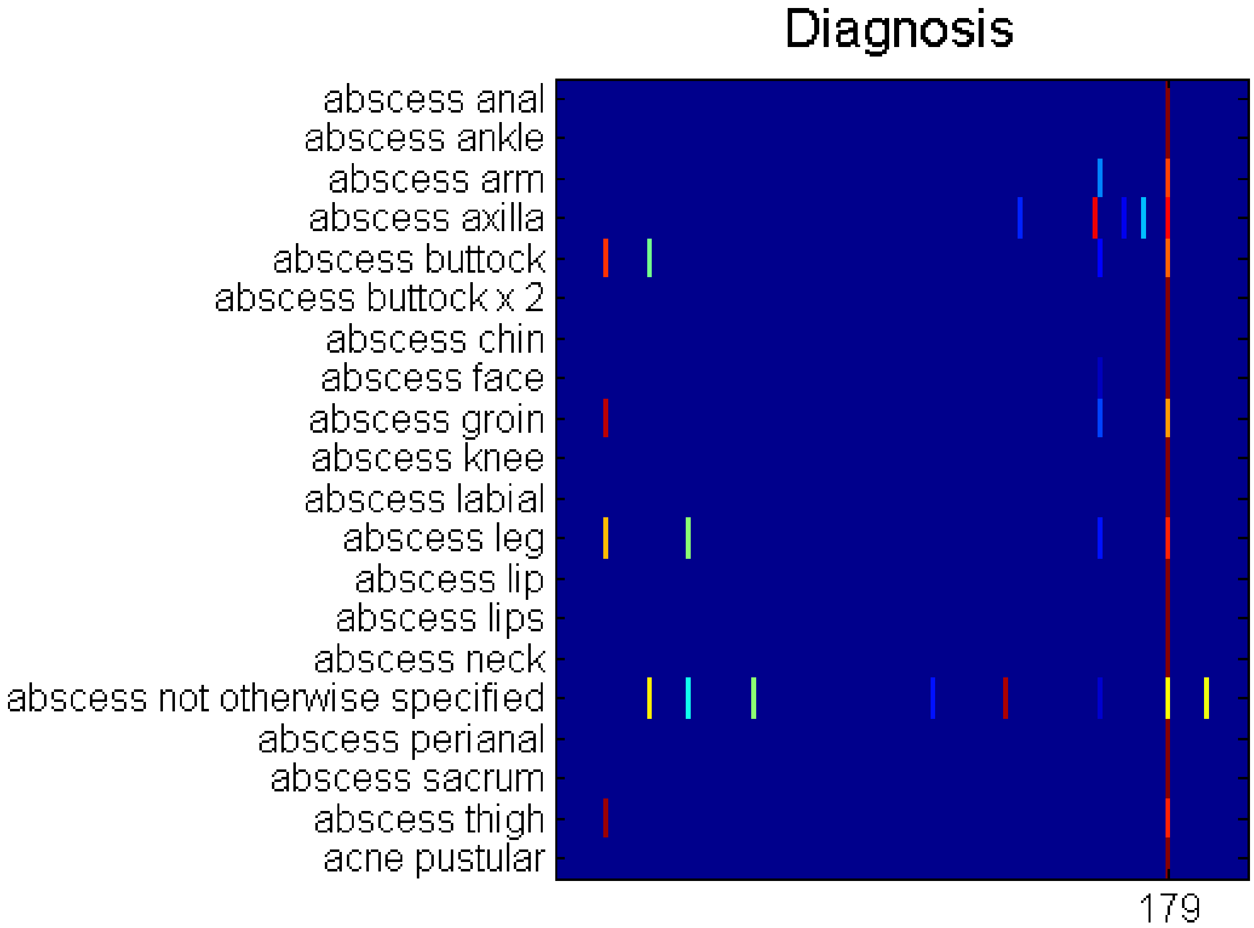
Differential Diagnosis

❑ Average correlation (nonparametric)

- Model with metamap, .61
- Model with RN notes, .62
- Chief complaint as classifier, .26



Identify New Patient Populations



1.3% of patients.

Other possible groups to add

- Minor trauma requiring x-ray, cast, splint
  - 13% of patients
- Chronic pain, headache, sickle cell crisis
  - 5.5%
- Cellulitis, local infection
  - 4%
- >50% of patients on either hydroxyurea or procrit presented with sickle cell crisis

ID Patients by Drug

Ritonavir	metabolic imbalance (kidney disease)
Hydroxyurea	sickle cell
Procrit	sickle cell
Levodopa	Altered mental status

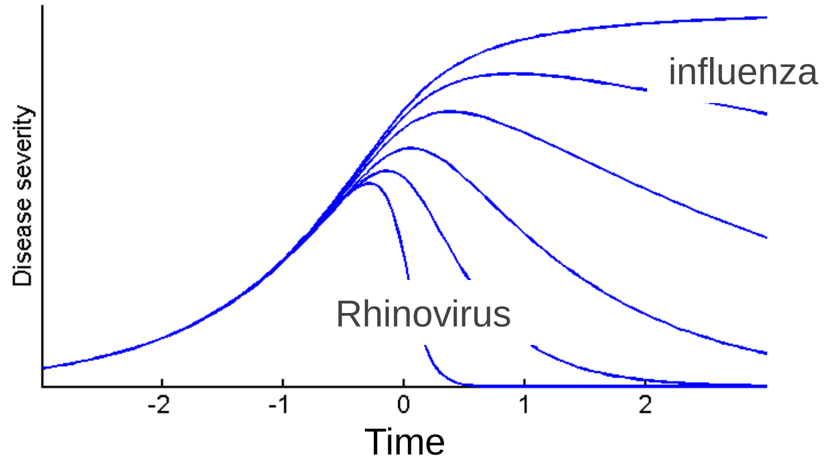
Disease Processes over Time

Learn a parametric model that describes the likelihood of observing particular diseases through time

- Probability of disease over time

y = disease severity
$\log(y) = -a(d^2+x^2)^{1/2}+bx$

- 'a' and 'b' give control of rate of change of disease severity
- 'd' gives control of peak width
- Additional parameters allow control of height and temporal shift



Combination of clustering model and temporal disease severity model allows identification and tracking of disease through time.

Disease Trajectory

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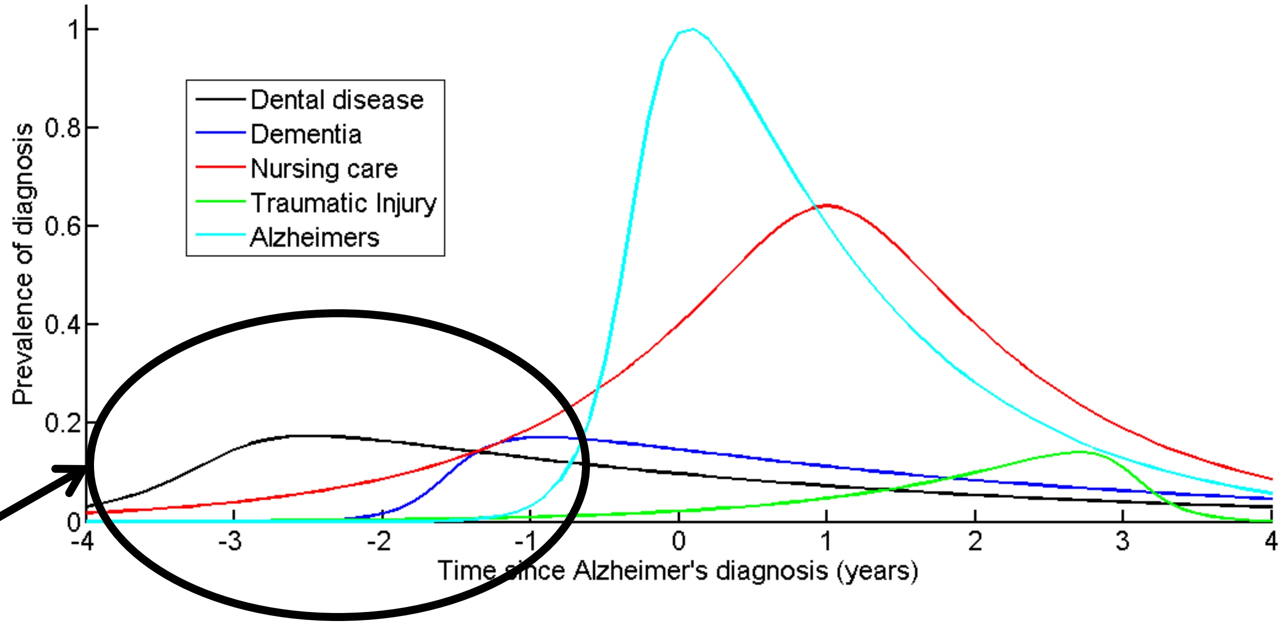
- ❑ New Data set: 3.5 million patients, 7 years
- ❑ Why is it important to predict future disease
  - Identification of high risk patients for early intervention
- ❑ Early intervention might be:
  - Standard therapy
  - Health coaching (telephone or in person)
  - Enrollment in clinical trial

Trajectory of a patient population with Alzheimer's



Early signs that patient is developing Alzheimer's disease

Utilize all types of data to track and predict important features in the evolution of a patient’s disease.

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