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Transfer Learning using Electronic Health Record data

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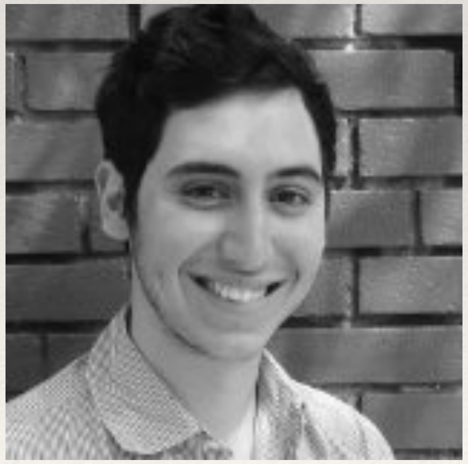
Thanks Sebastien & Nathanael!

- Sebastien Dubois (ICME)

- Nathanael Romano (MS&E)



Familial Hypercholesterolemia

- Genetic disorder causing very high LDL (“bad” cholesterol)
- 1/250 - 1/400 prevalence
- 90% undiagnosed
- Treatment by latest generation of statins can help (PCSK9 inhibitors)

Cost structure

- Assume 1/100 patients in a lipid clinic are undiagnosed cases
- $300 for genetic test
- $10,000 for PCSK9 inhibitor, 1 year
- Net $40,000 to find and treat one patient, *75% to find*

How can we bring cost down?

- Target genetic testing to enrich cases
- Assume a classifier with 50% PPV
- 1/2 tested patients are cases
- Net cost to find and treat one patient: $10,600

Electronic health records

- Where would the data come from?
  - Electronic Health Records (EHRs) have been in use at Stanford Hospital for many years
  - Increasing adoption in US (75%)

Data from Stanford Hospital’s EHR

- > 2 million patients
- Structured data (diagnosis, procedure, and medication codes) - 43 million records
- Unstructured data (free text clinical notes) - 42 million notes

But…

- 93 confirmed cases

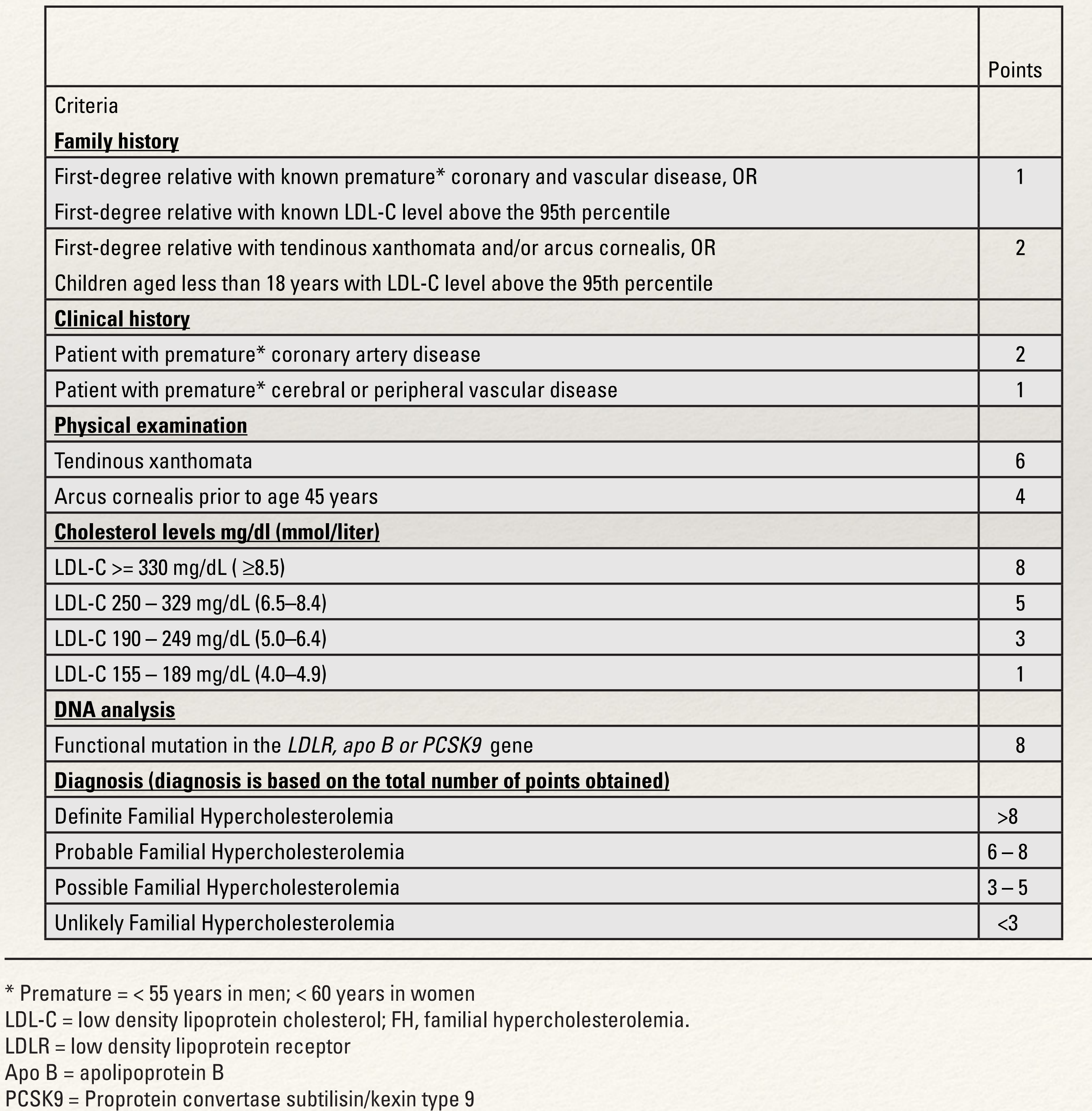
Does this seem right?

- “Fruit” appearing in the clinical notes is a significant predictor…

Explicit incorporation of domain knowledge

- "automate" existing diagnosis guideline
- Extract features from EHR that approximate guideline inputs
- Fit a linear model on ~20 features

Table 4. Dutch Lipid Clinic Network diagnostic criteria for Familial Hypercholesterolemia[1-3]



	Points
Criteria **Family history**	
First-degree relative with known premature* coronary and vascular disease, OR First-degree relative with known LDL-C level above the 95th percentile	1
First-degree relative with tendinous xanthomata and/or arcus cornealis, OR Children aged less than 18 years with LDL-C level above the 95th percentile	2
Clinical history	
Patient with premature* coronary artery disease	2
Patient with premature* cerebral or peripheral vascular disease	1
Physical examination	
Tendinous xanthomata	6
Arcus cornealis prior to age 45 years	4
Cholesterol levels mg/dl (mmol/liter)	
LDL-C >= 330 mg/dL (≥8.5)	8
LDL-C 250 – 329 mg/dL (6.5–8.4)	5
LDL-C 190 – 249 mg/dL (5.0–6.4)	3
LDL-C 155 – 189 mg/dL (4.0–4.9)	1
DNA analysis	
Functional mutation in the *LDLR, apo B or PCSK9* gene	8
Diagnosis (diagnosis is based on the total number of points obtained)	
Definite Familial Hypercholesterolemia	>8
Probable Familial Hypercholesterolemia	6 – 8
Possible Familial Hypercholesterolemia	3 – 5
Unlikely Familial Hypercholesterolemia	<3

* Premature = < 55 years in men; < 60 years in women
LDL-C = low density lipoprotein cholesterol; FH, familial hypercholesterolemia.
LDLR = low density lipoprotein receptor
Apo B = apolipoprotein B
PCSK9 = Proprotein convertase subtilisin/kexin type 9

Transfer learning using EHR data

- Despite “millions of patients”, very few labels of things we care about.
- Opportunity for transfer learning?

Transfer Learning

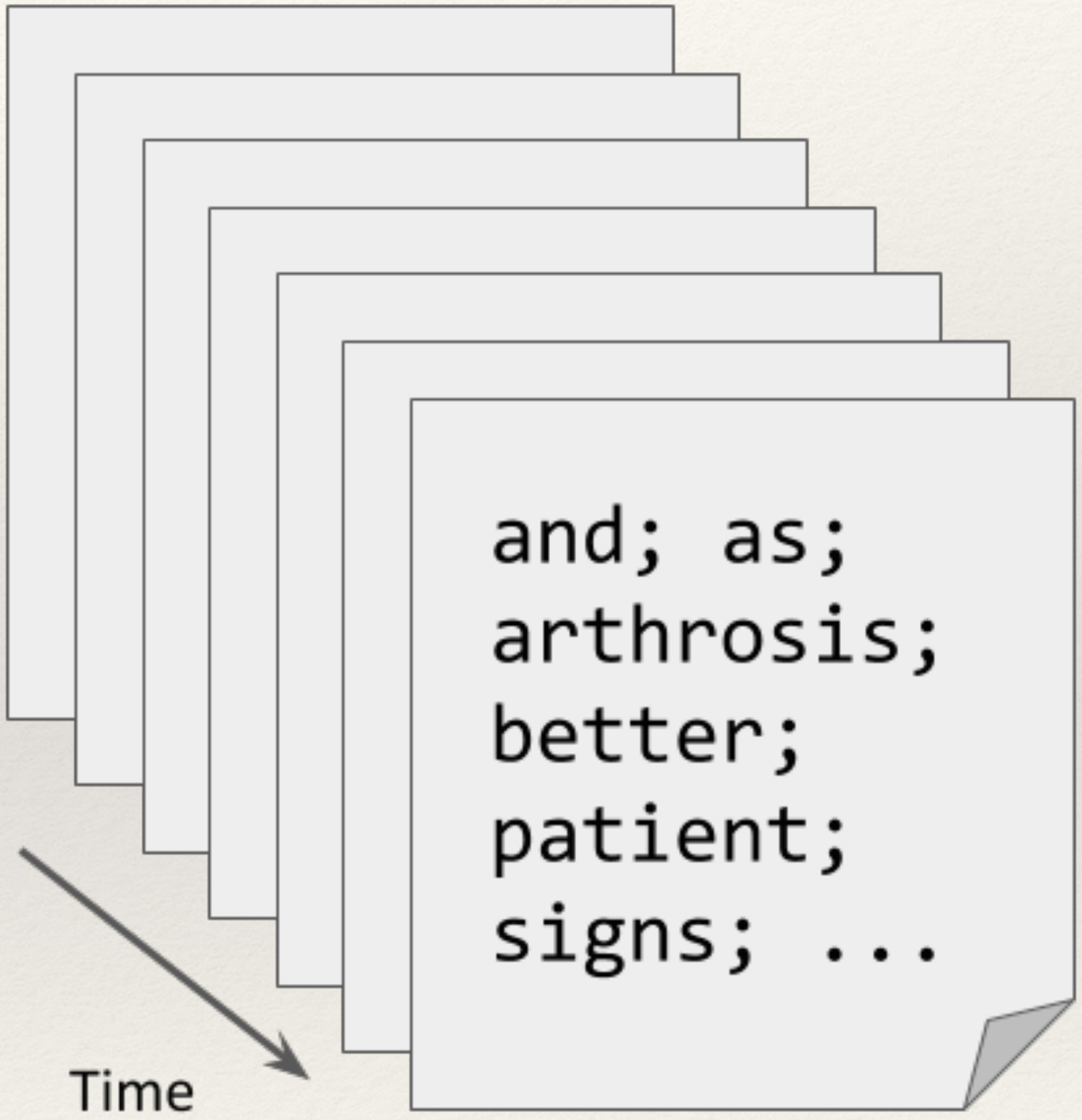
- Models trained on ImageNet ILSVRC are very useful for other tasks with less data.
- Learn a model on a source task with lots of labels
- Use for a target task with few labels

Clinical text

- Focus on transfer learning using clinical text
- Clinical notes are most complete source of information
  - but harder to use than medical codes
  - Most applications of ML to EHR data uses structured data

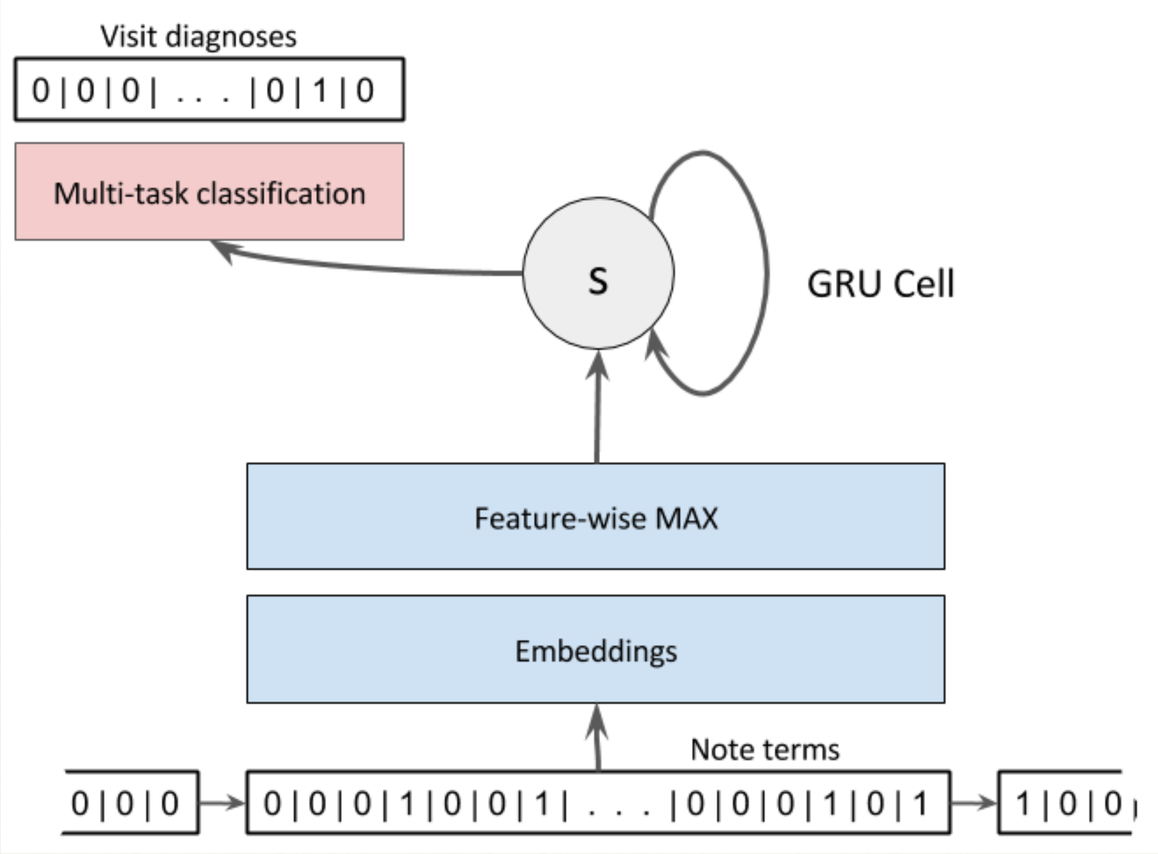
Representing clinical notes

- Each patient has a sequence of notes
- Sebastien & Nathanael explored ways of summarizing this sequence

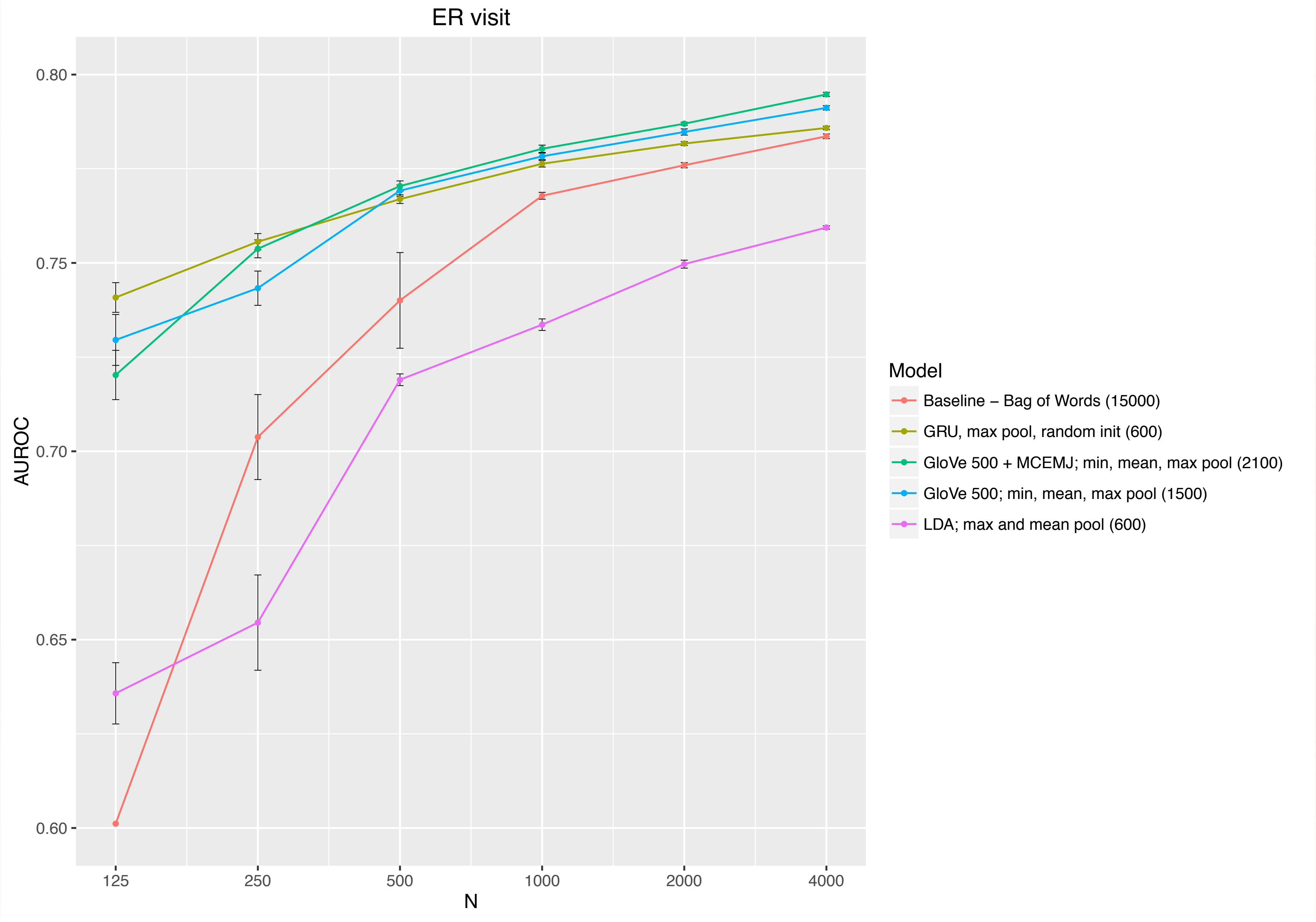


Representing clinical notes

- Baselines: bag of words, LDA
- Compare against:
  - Embed and aggregate
  - RNN Sequence models



Predicting complex clinical events



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FH FOUNDATION

Raising Awareness. Saving Lives.