Natural language processing for (mostly population) health

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This talk

Illustrative applications of *NLP* and *Machine Learning* methods, aiming to improve healthcare in an era of information overload.

Figure from BMJ; 2014

Talk overview

- A tour of work in NLP + health, including:
  - Evidence-based medicine (EBM)
  - Modeling patient-doctor communication
  - Social media (surveillance)

- **Caveat**: This is **not** a general survey! NLP + health is a *huge* sub-area; this is an extremely biased sampling of work I've done or am familiar with.
  - No coverage of, e.g., EHR mining

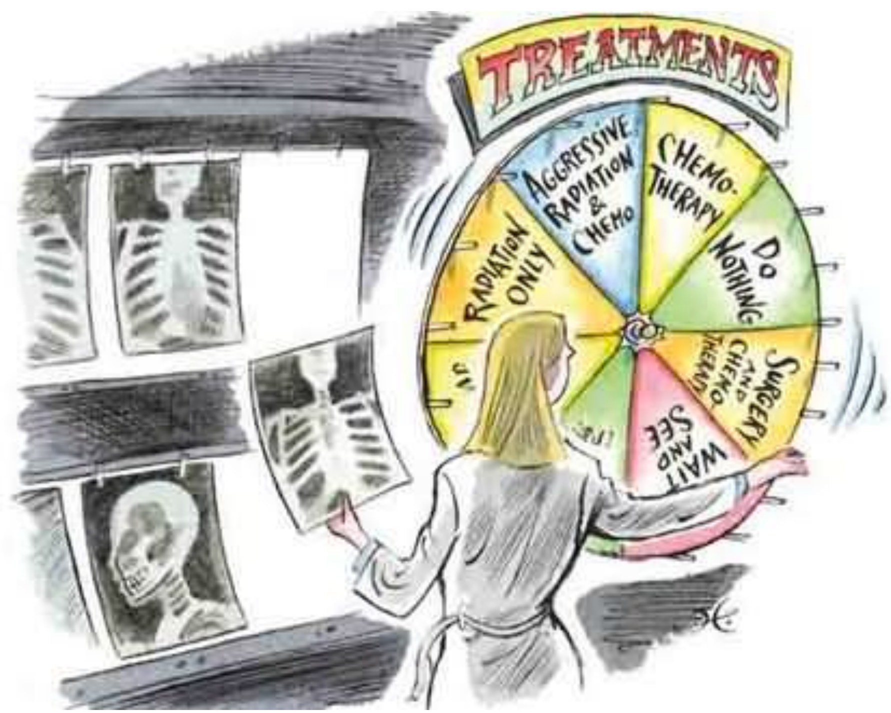
Evidence-based medicine + NLP/ML

Evidence-Based Medicine *n.*

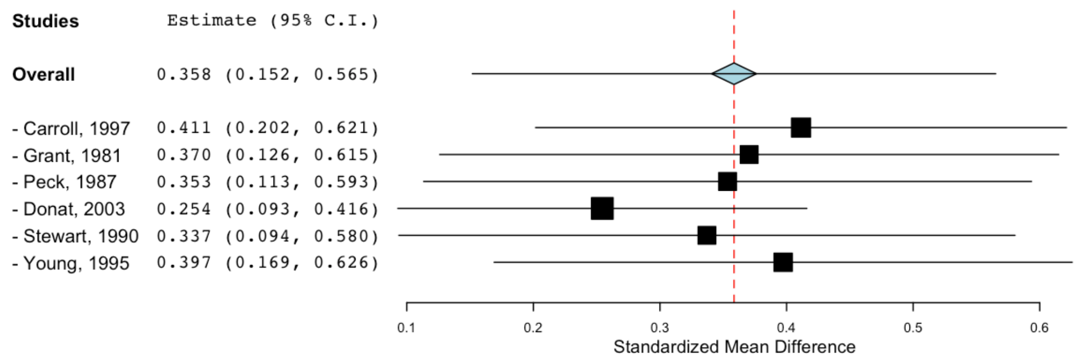
The conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients

The New York Times

“… only 20 percent of medical practices are based on rigorous research evidence … The rest are based on a kind of folklore.



From biomedical articles to actionable evidence



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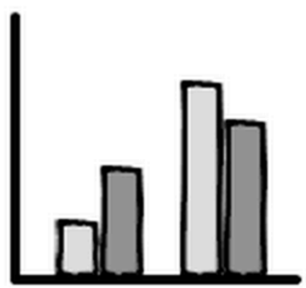

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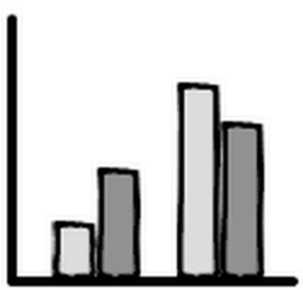

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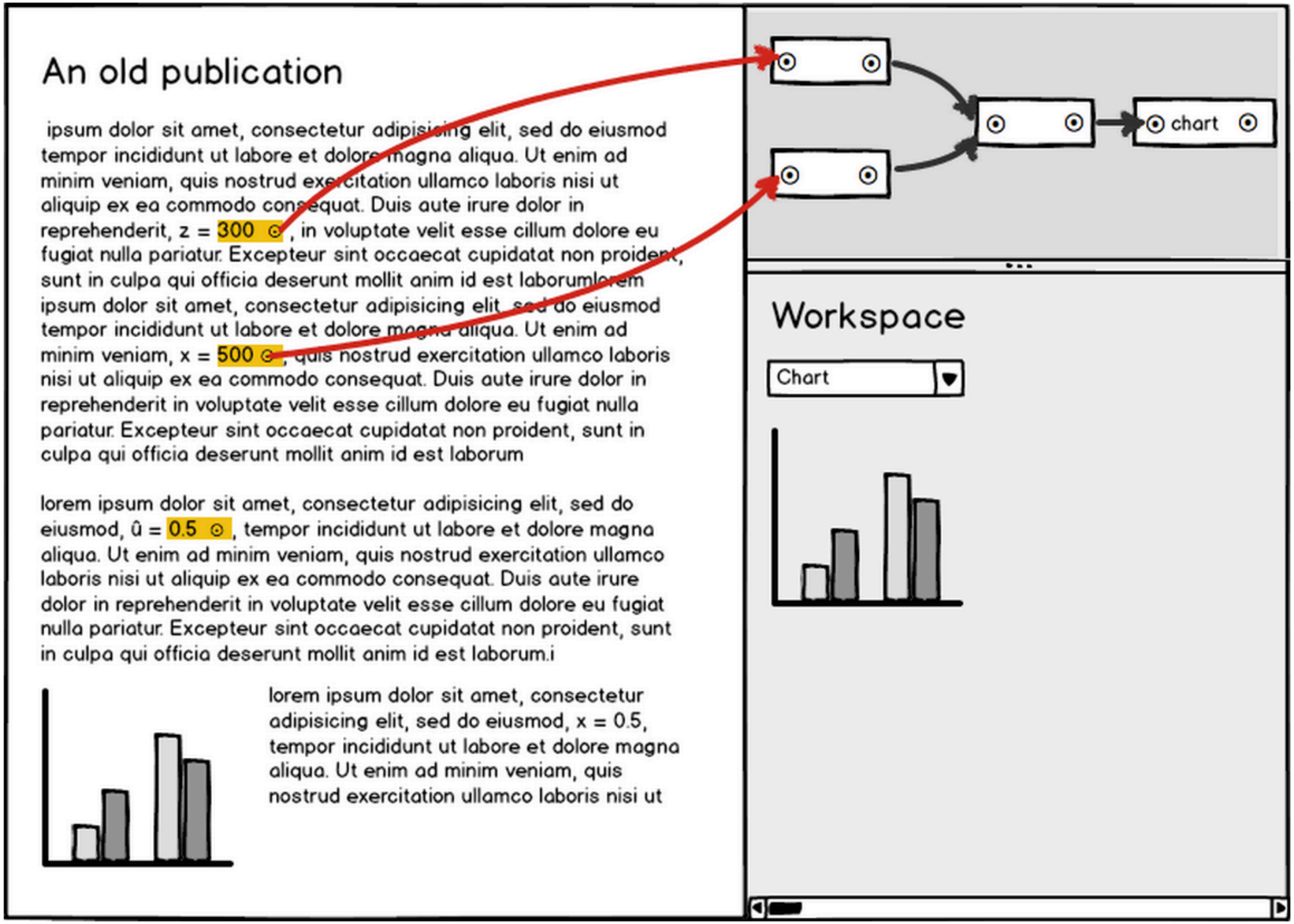
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chart
Workspace
Chart

The data deluge

On average, 75 articles describing results from clinical trials are published every day.

Bastian, PLoS Med, 2010


To Do
RCT
OLD
New

BMJ

BMJ 2013;346:f139 doi: 10.1136/bmj.f139 (Published 10 January 2013)

EDITORIALS

The automation of systematic reviews

Would lead to best currently available evidence at the push of a button

Lots of work in this space

- Two recent surveys:
  - O'Mara-Eves, Alison, et al. "Using text mining for study identification in systematic reviews: a systematic review of current approaches." Systematic reviews 4.1 (2015): 5.
  - Jonnalagadda, Siddhartha R., Pawan Goyal, and Mark D. Huffman. "Automating data extraction in systematic reviews: a systematic review." Systematic reviews 4.1 (2015): 78.
  - More resources at: https://github.com/bwallace/automating-ebm-resources/wiki/Papers

- I'll present just a specific piece of this work in class today

Semi-automating data extraction

this work supported by NIH grant ***R01LM012086***

Semi-automating Risk of Bias (RoB) assessment

Iain J. Marshall, Joël Kuiper, and Byron C. Wallace. RobotReviewer: Evaluation of a System for Automatically Assessing Bias in Clinical Trials. *Journal of the American Medical Informatics Association (JAMIA)*. 2015 (*in press*).

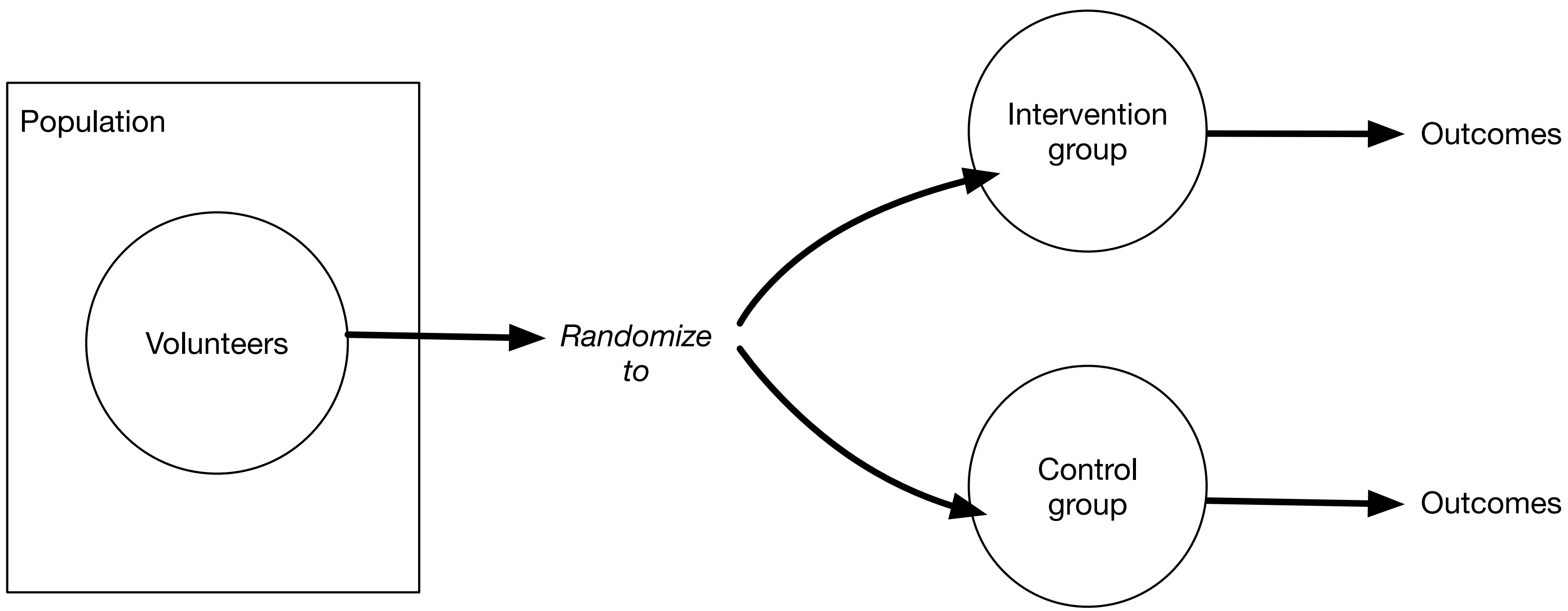
Joël Kuiper, Iain J. Marshall, Byron C. Wallace, and Morris A. Swertz. Spá: a web-based viewer for text mining in evidence based medicine. In Proceedings of the *European Conference on Machine Learning (ECML)*, pages 452–455. Springer, 2014.

Iain J. Marshall, Joël Kuiper, and Byron C. Wallace. Automating risk of bias assessment for clinical trials. In Proceedings of the *ACM Conference on Bioinformatics, Computational Biology and Health Informatics (BCB)*, pages 88–95. ACM, 2014. [*selected as the best paper on public heallth*]

Automating PICO extraction

Byron C. Wallace, Joël Kuiper, Aakash Sharma, Mingxi (Brian) Zhu and Iain J. Marshall. Extracting PICO Sentences from Clinical Trial Reports using *Supervised Distant Supervision. Under review at the Journal of Machine Learning Research (JMLR).*

Randomized Control Trials (RCTs)



Risk of Bias (RoB)

A key step in evidence synthesis: assessing the reliability of individual trials

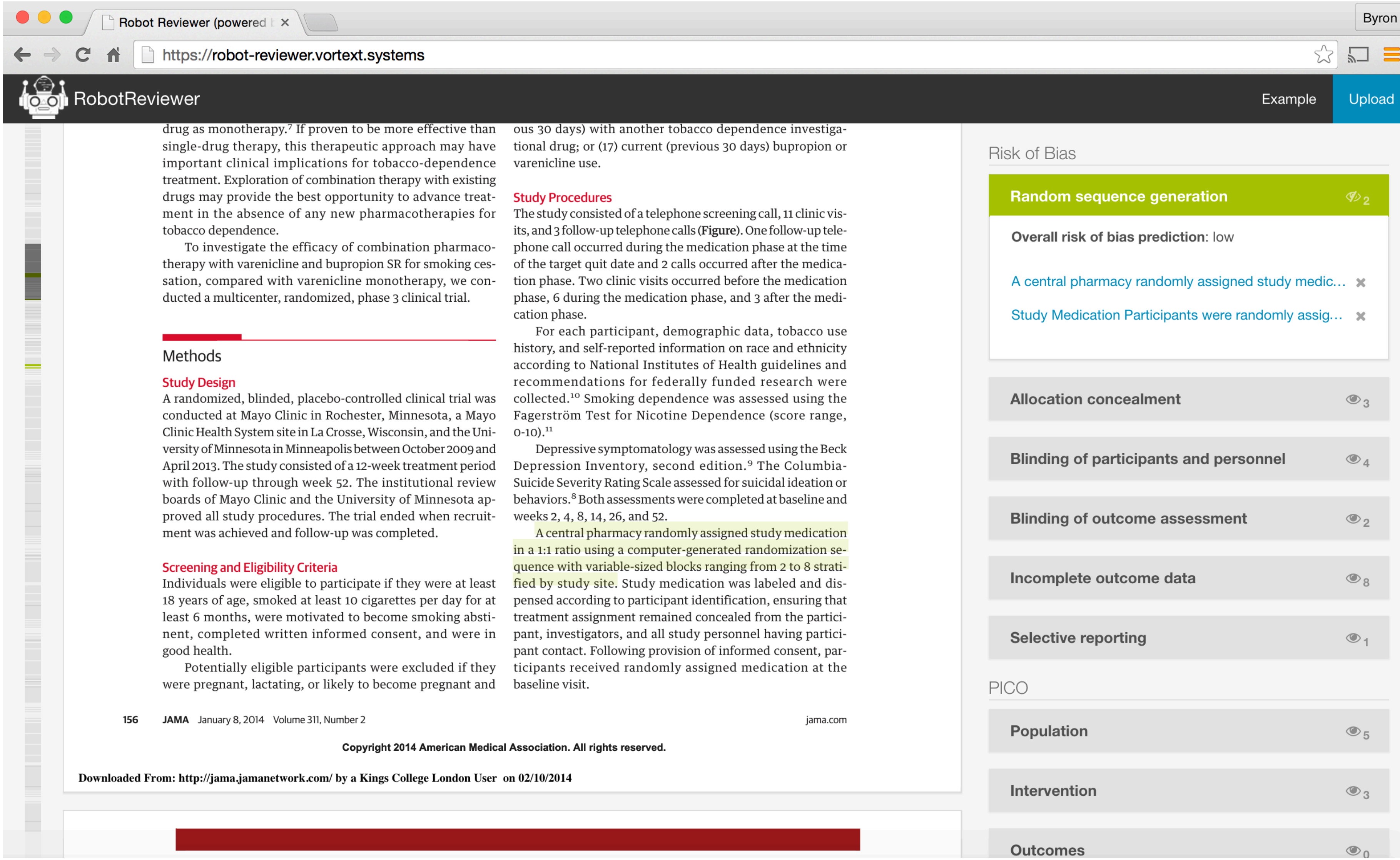
- Assess *risks of bias* across several ‘domains’

	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other sources of bias
Welschen 2012	+	-	-	-	+	?	+
Soureti 2011	+	+	-	-	+	+	+
Powers 2011	?	?	-	-	+	+	+
Benner 2008	+	-	-	+	+	+	-
Grover 2007	?	+	-	+	+	?	+
Maasland 2007	+	+	-	-	?	?	+
Steenkiste 2007	+	?	-	-	?	?	+
Sheridan 2006	+	+	+	-	+	+	+
McAlister 2006	+	+	-	+	+	+	+

Key

+	low risk of bias
-	high risk of bias
?	unclear risk of bias

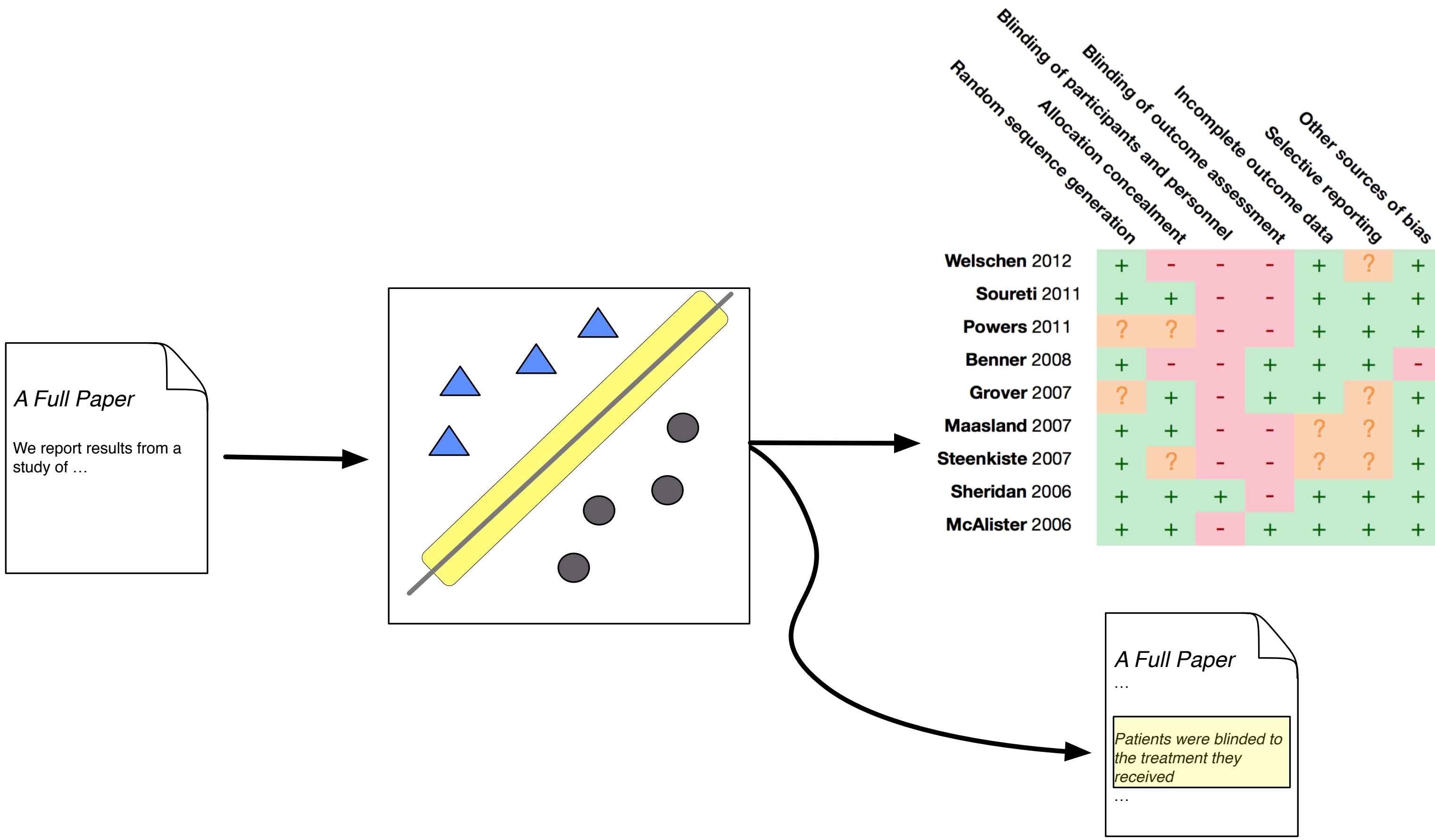
Bias	Allocation concealment
Authors judgement	Low risk
Support for judgement	Quote: "The Family Practice Research Coordinator at the University of British Columbia held this sequence independently and remotely"



https://robot-reviewer.vortext.systems/

https://github.com/ijmarshall/robotreviewer

The machine learning task



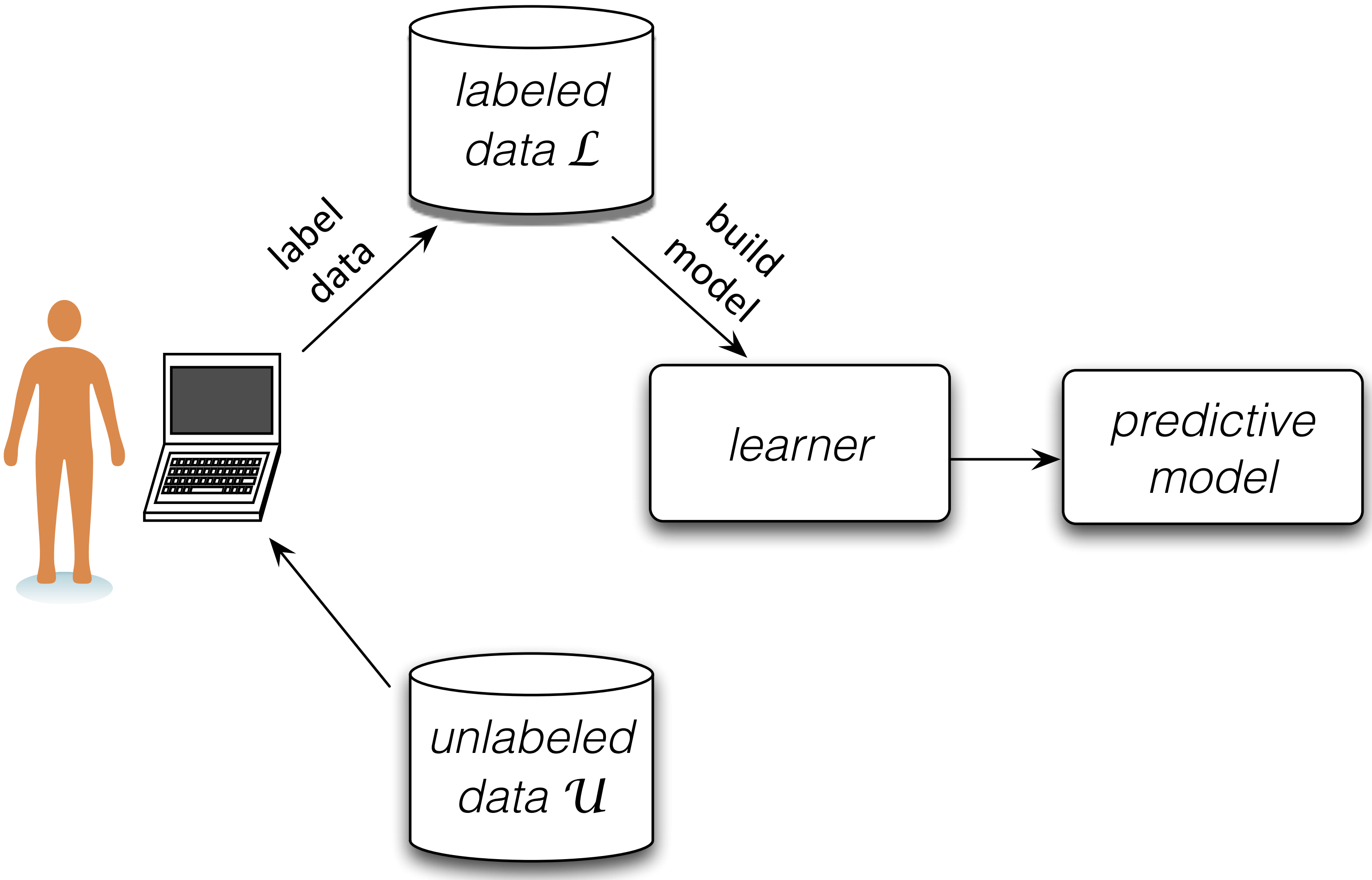
	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other sources of bias
Welschen 2012	+	-	-	-	+	?	+
Soureti 2011	+	+	-	-	+	+	+
Powers 2011	?	?	-	-	+	+	+
Benner 2008	+	-	-	+	+	+	-
Grover 2007	?	+	-	+	+	?	+
Maasland 2007	+	+	-	-	?	?	+
Steenkiste 2007	+	?	-	-	?	?	+
Sheridan 2006	+	+	+	-	+	+	+
McAlister 2006	+	+	-	+	+	+	+

Input: a full-text paper

Machine Learning

Output: RoB assessments and supporting quotes

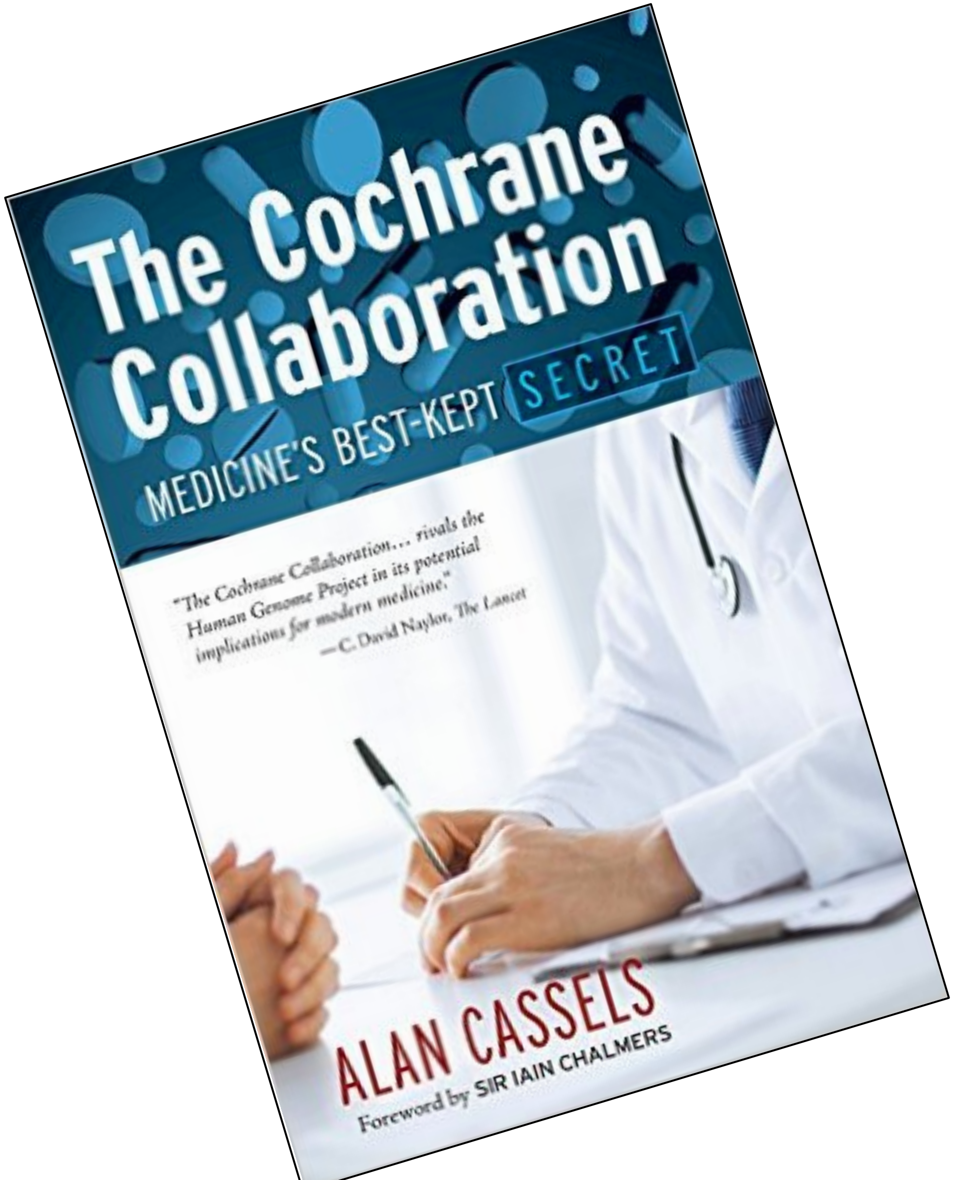
Traditional supervised learning



Training data

Collecting annotations is expensive and time-consuming.

Instead, **we will use previously conducted reviews** to train ML models.



THE COCHRANE COLLABORATION®

The Cochrane Database of Systematic Reviews (CDSR)

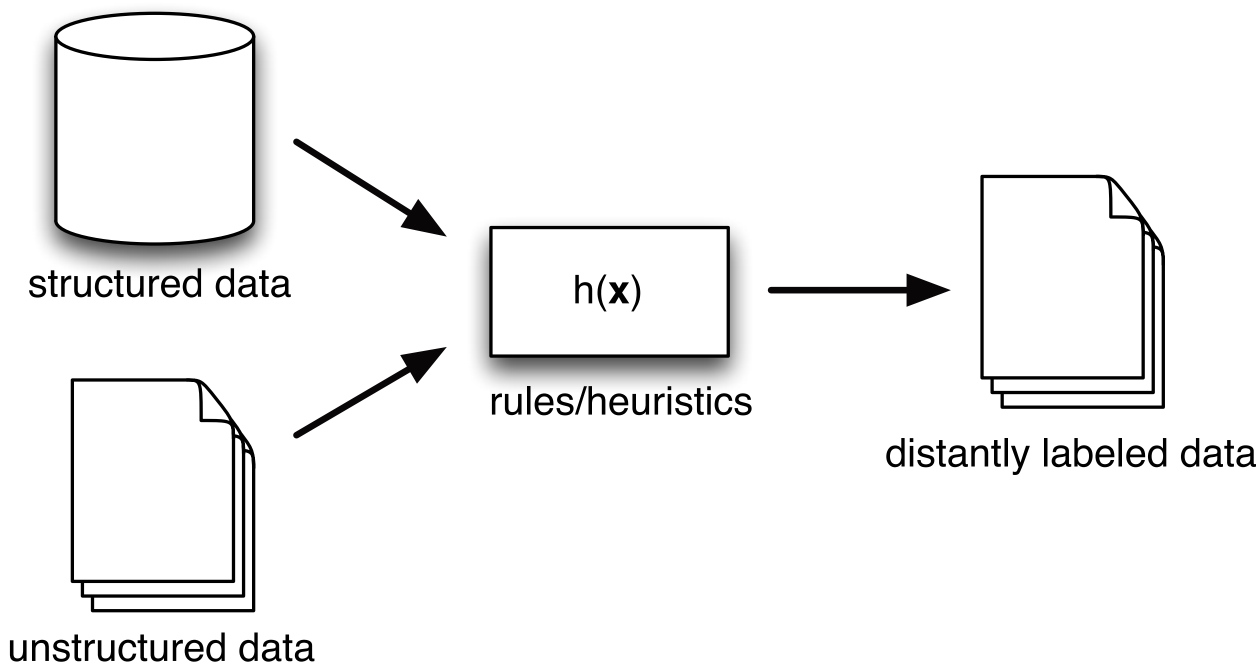
- We’ve linked 13,000 CDSR entries to published full-text PDFs describing trials

- We derive labels on articles and sentences from the CDSR

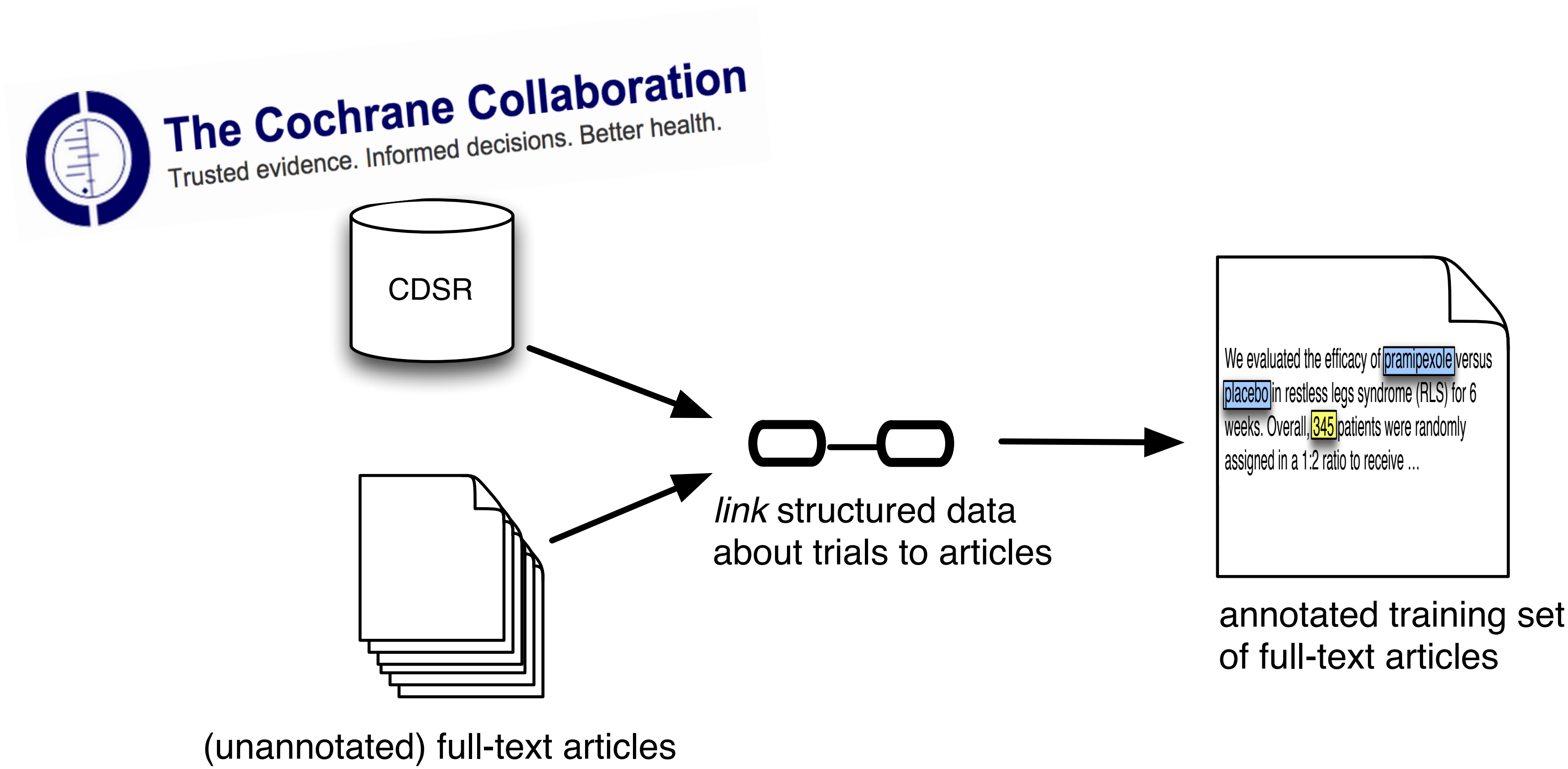
Distant supervision

alternatively, *supervision by database*

Craven & Kumlien, AAAI, 1999



Distant supervision via the CDSR



Machine learning approach overview

- Regularized linear models (parameterized by **w**)
- Very high-dimensional, sparse feature space
- Parameter estimation via stochastic gradient descent

Document-level objective

“low” or “high/unknown” risk of bias for domain *q*

$$\underset{\mathbf{w}_d^q}{\operatorname{argmin}}\, \alpha \|\mathbf{w}_d^q\|^2 + \sum_{i=1}^{n^q} \mathcal{L}\{\mathbf{w}_d^q \cdot \mathbf{x}_i, y_i^q\}$$

regularizer

empirical loss

… and basically the same for sentence model

$$\underset{\mathbf{w}_s^q}{\operatorname{argmin}}\, \alpha \|\mathbf{w}_s^q\|^2 + \sum_{i=1}^{n^q} \sum_{j=1}^{m_i} \mathcal{L}\{\mathbf{w}_s^q \cdot \mathbf{s}_{ij}, l_{ij}^q\}$$

s subscript for sentences

indicates whether sentence *j* in article *i* supports risk of bias judgement for domain *q*

But article level assessments are not independent of supporting sentences.

A simple joint model

as before: document level features

$$y_i^q = \mathrm{sign}\{\mathbf{w}_d^q \cdot \mathbf{x}_i + \mathbf{w}_{ds}^q \cdot s_{i*}^q\}$$

features that indicate tokens present in the supporting sentence for this domain

A simple joint model

$$y_i^q = \mathrm{sign}\{\mathbf{w}_d^q \cdot \mathbf{x}_i + \mathbf{w}_{ds}^q \cdot s_{i*}^q\}$$

e.g., *computer generated* indicates low risk for poor randomization; *double blind* does so for proper blinding

A simple joint model

At test time, we don't know which sentences support assessments for which domains, so we use the predictions.

prediction that sentence 0 supports judgment for domain *q*

$$y_i^q = \text{sign}\{\mathbf{w}_d^q \cdot \mathbf{x}_i + \hat{l}_{i0}^q \cdot (\mathbf{w}_{ds}^q \cdot \mathbf{s}_{i0}^q) + \ldots$$
$$\ldots + \hat{l}_{im_i}^q \cdot (\mathbf{w}_{ds}^q \cdot \mathbf{s}_{im_i}^q)\}$$

m_i sentences in document *i*

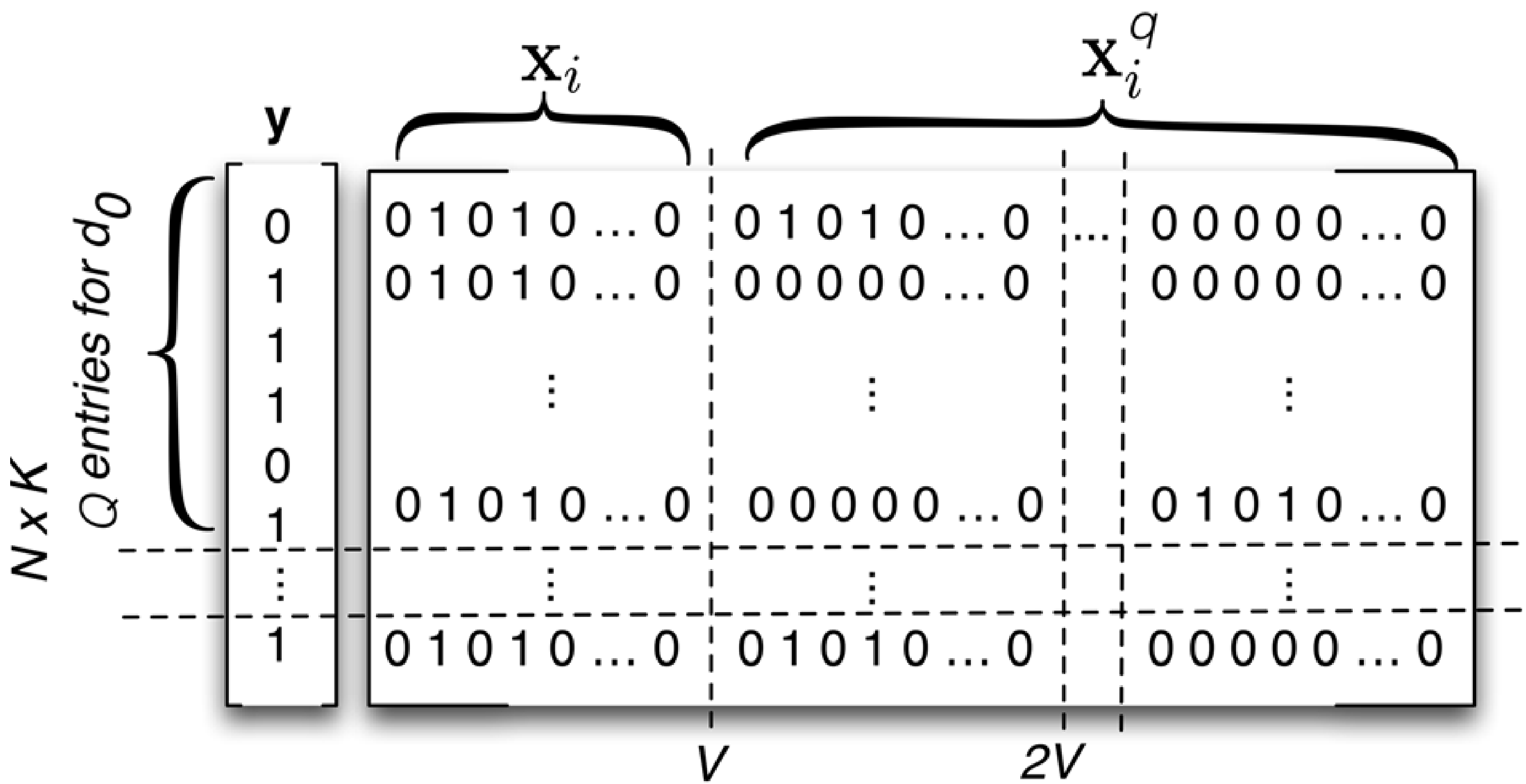
This model ignores correlations between domains.

We use a *multi-task* approach to tie weight vectors across domains in a joint model.

Multi-task learning

- Predict multiple outputs from a shared representation
- Allows ‘borrowing of strength’ across tasks

A ‘frustratingly easy’ approach



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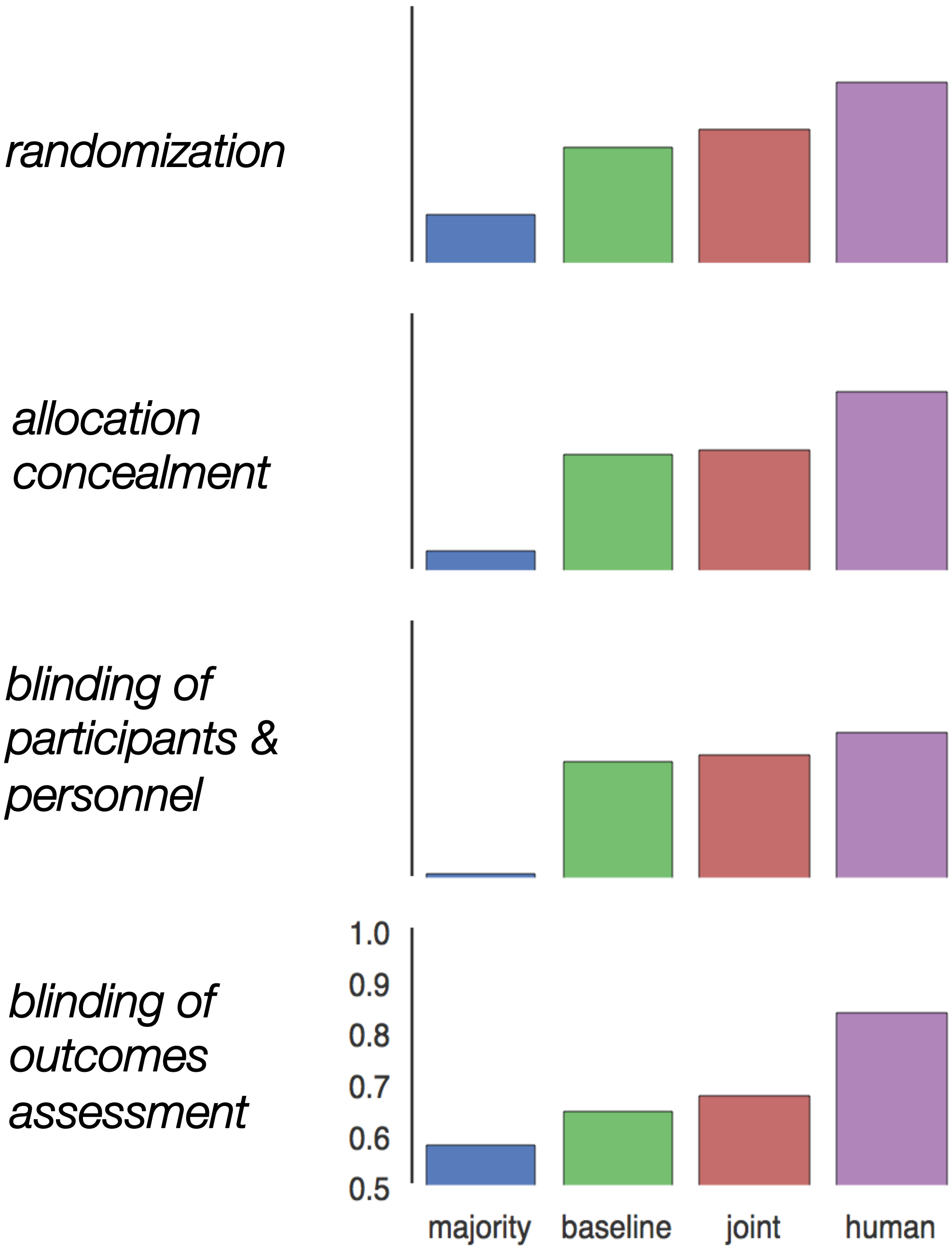


- **Joint** model achieves an average of 3+% absolute improvement in accuracy over **baseline** (mean 0.70 v 0.73)
- Still 5-10% behind humans (~80% accurate)

Sentence evaluation

- We showed domain experts sentences extracted for different domains by
  (1) random guessing (a baseline approach)
  (2) human reviewers (i.e., from the Cochrane database)
  (3) our model

- They didn’t know where these sentences came from.

- They rated sentences as *highly relevant, somewhat relevant*, or *not relevant*.

Sentence evaluation

Domain	Trials (n)	baseline	cochrane
Overall	378	0.50%	56.50%
1. Random sequence generation	81	0.00%	60.50%
2. Allocation concealment	75	0.00%	60.00%
3. Blinding of participants and personnel	76	0.00%	68.40%
4. Blinding of outcome assessment	56	0.00%	57.10%
5. Incomplete reporting of outcomes	67	3.00%	50.80%
6. Selective reporting	23	0.00%	4.60%

percent of sentences deemed ‘highly relevant’ by experts

Sentence evaluation

Domain	Trials (n)	baseline	top1	top3	cochrane	top1 v cochrane	top3 v cochrane
Overall	378	0.50%	45.00%	60.40%	56.50%	-11.6% (-18.5% to -4.4%); P<0.001	+3.9%, (-3.2% to +10.9%); P=0.141
1. Random sequence generation	81	0.00%	55.60%	65.40%	60.50%		
2. Allocation concealment	75	0.00%	44.00%	60.00%	60.00%		
3. Blinding of participants and personnel	76	0.00%	55.30%	72.40%	68.40%		
4. Blinding of outcome assessment	56	0.00%	39.30%	62.50%	57.10%		
5. Incomplete reporting of outcomes	67	3.00%	40.90%	57.60%	50.80%		
6. Selective reporting	23	0.00%	0.00%	4.60%	4.60%		

performance is actually **better,** and at least non-inferior, to human performance if we consider the top-3 sentences extracted by the model

Statistical models of patient-doctor communication

Wallace, Byron C., et al. "A Generative Joint, Additive, Sequential Model of Topics and Speech Acts in Patient-Doctor Communication." EMNLP, 2013.

Wallace, Byron C., et al. "Automatically annotating topics in transcripts of patient-provider interactions via machine learning." Medical Decision Making (2013): 0272989X13514777.

Wallace, Byron C., et al. "Identifying Differences in Physician Communication Styles with a Log-Linear Transition Component Model." AAAI, 2014.

Patient-doctor communication

- Patient-doctor communication is a critical part of quality care
- Especially for *patient-centered* care
  - Patients need to understand *what* is wrong with them, *steps* to fix it and *why* those steps will work
- There are significant correlations between verbal behaviors and health outcomes
- But it’s difficult to study

Patient-doctor communication

Role	Utterance
D	Let me just write down some of these issues here so I get them straight in my mind.
P	Doctor you ain't got to tell me nuttin'.
P	I'm in very good hands when I'm around you.
P	If push comes to a shove, you open the window and throw me out.
D	I wanted to ask you, too -
D	you know you had that colonic polyp -
D	- is it two years from now that they're going to be doing the repeat?
P	Yeah.
D	We'll do the repeat coloscopy in about two years.

Patient-doctor communication

Role	Utterance	Topic
D	Let me just write down some of these issues here so I get them straight in my mind.	*Logistics*
P	Doctor you ain't got to tell me nuttin'.	*Socializing*
P	I'm in very good hands when I'm around you.	*Socializing*
P	If push comes to a shove, you open the window and throw me out.	*Socializing*
D	I wanted to ask you, too -	*Biomedical*
D	you know you had that colonic polyp -	*Biomedical*
D	- is it two years from now that they're going to be doing the repeat?	*Biomedical*
P	Yeah.	*Biomedical*
D	We'll do the repeat coloscopy in about two years.	*Biomedical*

Topics

Topic Codes	*Description*
Biomedical	Patient health and treatment: “what medication do you take?”
ARV	Adherence barriers; "so you're taking your meds"
Psychosocial	Substance abuse, jobs, housing, etc.; "My job is really stressful right now."
Logistics	Appointments; "I need to get that script refilled"
Physical examination	“Take a deep breath”
Socializing	“Did you see the ball game?”

The utility of topic annotations

- Q*uantitatively* address questions about communication
- Consider an intervention intended to alter doctor communication around *ARV adherence*
  - How do we know if it worked?

Wilson *et al.*, 2010

- Administered an intervention to a bunch of doctors
- Counted *ARV adherence* utterances in conversations before and after intervention: is there a difference?
- 116 visits manually annotated (58 visits before/58 after)
  - Median *ARV* utterances in controls (no intervention): 49.5
  - And in *cases* (intervention): 76
  - *p*-value = 0.067
- But annotation is laborious. Can we automate it?

Predicting topics given utterances

Input		**Output**
"How do you feel?"	$\longrightarrow$	*Biomedical*
"My stomach hurts"	$\longrightarrow$	*Biomedical*

- Standard *structured learning problem*

- Standard structured learning approach (that you're now familiar with) *conditional random field*

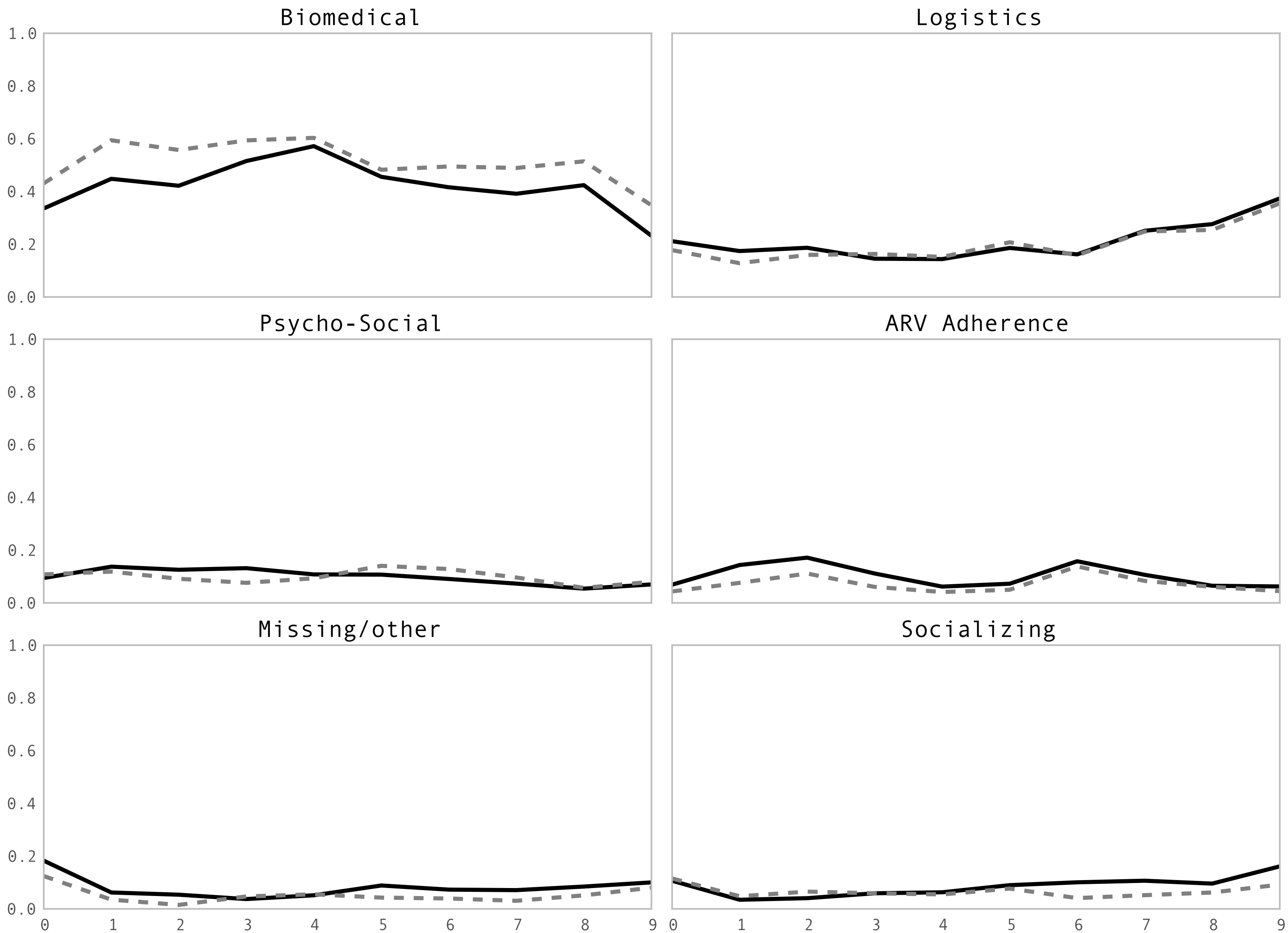
$$p_{\boldsymbol{\theta}}(\mathbf{y}|\mathbf{x}) = \frac{1}{Z_{\boldsymbol{\theta}}(\mathbf{x})} \exp\left\{ \sum_{t=1}^{T} \sum_{k=1}^{K} \theta_k f_k(y_{t-1}, y_t, x_t) \right\}$$

Topic Prediction Results

Average overall accuracy: about 64% (62% to 66%)

Average Kappa: .49 (.47 to .53)

Topic prediction results



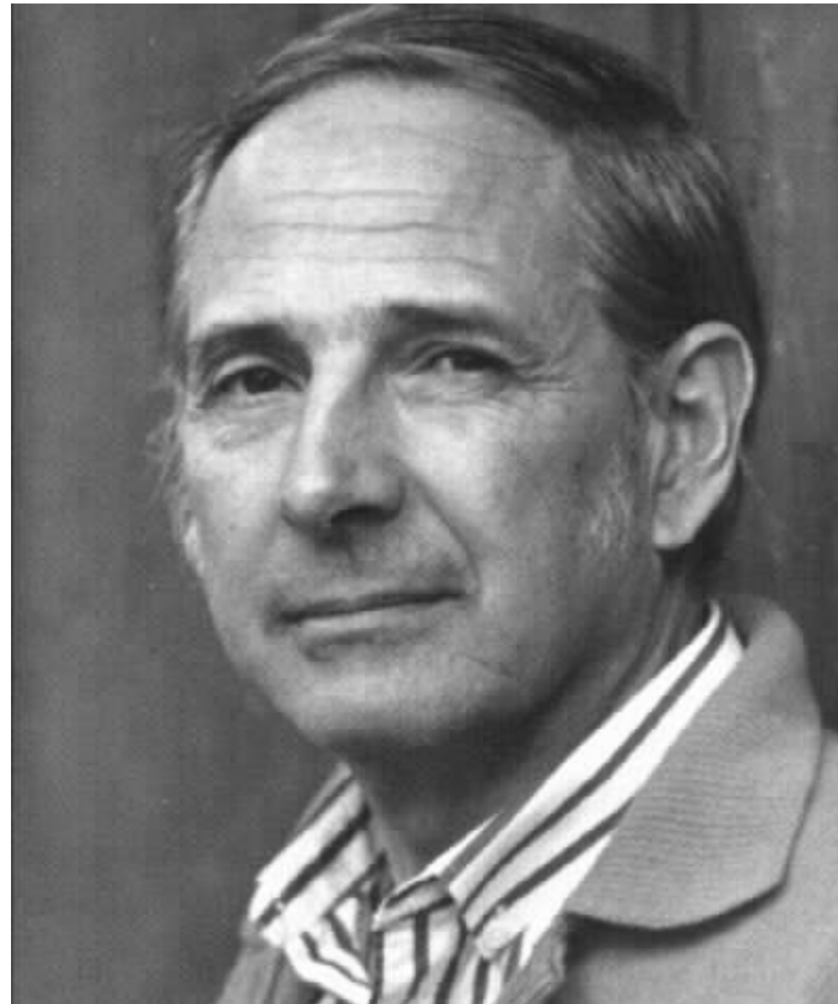
Reproducing the RCT analysis

- From manual codes: 49.5 median *ARV* utterances for control visits and 76 for cases (*p*-value .067)
- Using *predicted* codes: 39 for control visits; and 55 for cases (*p*-value .036)
- So predicted codes reveal the same trend at a comparable significance level

So we can predict topic codes, but is that enough?

- Tells us *what* is being discussed but not *how* it is
- "Would you please take your ARV meds?" vs. "You need to take your ARV meds!"
  - Both are *ARV adherence* utterances, but the communication styles are very different
- Enter *speech acts*

A bit of sociolinguistics



Speech acts in GMIAS

- GMIAS includes following speech act codes: *ask question, commissive, conversation management, directive, empathy, give information, humor/levity,* and *social-ritual.*

Patient-Doctor communication

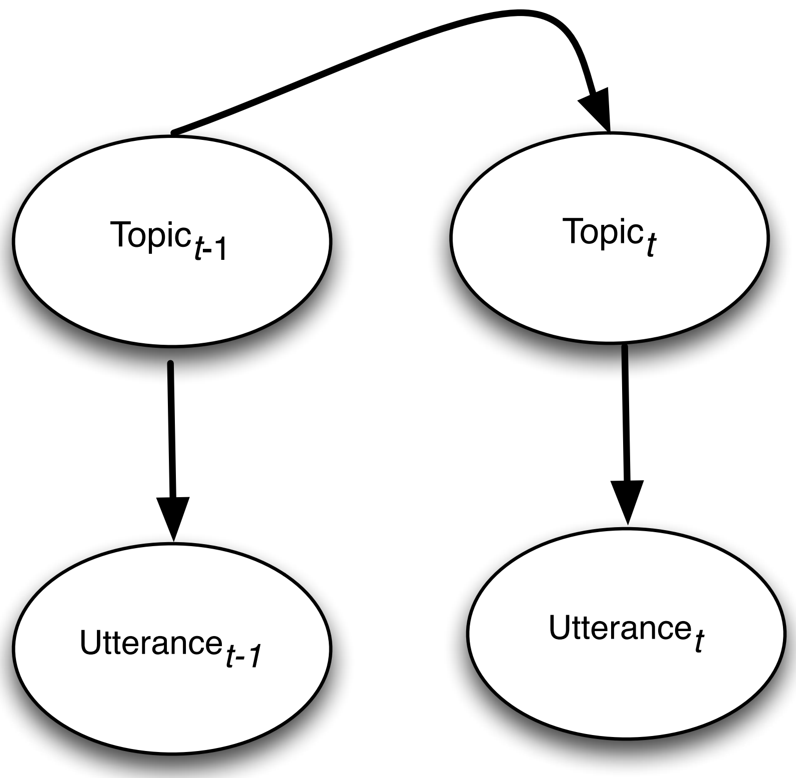
Role	Utterance	Topic	Speech act
D	Let me just write down some of these issues here so I get them straight in my mind.	*Logistics*	*Commissive*
P	Doctor you ain't got to tell me nuttin'.	*Socializing*	*Directive*
P	I'm in very good hands when I'm around you.	*Socializing*	*Give Info.*
P	If push comes to a shove, you open the window and throw me out.	*Socializing*	*Humor/Levity*
D	I wanted to ask you, too -	*Biomedical*	*Conv. Mgmt.*
D	you know you had that colonic polyp -	*Biomedical*	*Ask Q.*
D	- is it two years from now that they're going to be doing the repeat?	*Biomedical*	*Ask Q.*
P	Yeah.	*Biomedical*	*Conv. Mgmt.*
D	We'll do the repeat coloscopy in about two years.	*Biomedical*	*Give Info.*

Jointly modeling topics *and* speech acts

- Want an interpretable *generative* model to analyze interactions (not just predictions)

- But standard structural generative models only handle univariate case

Markov-Multinomial model



Markov-Multinomial model

- Decompose sequence into *transitions* and *emissions*

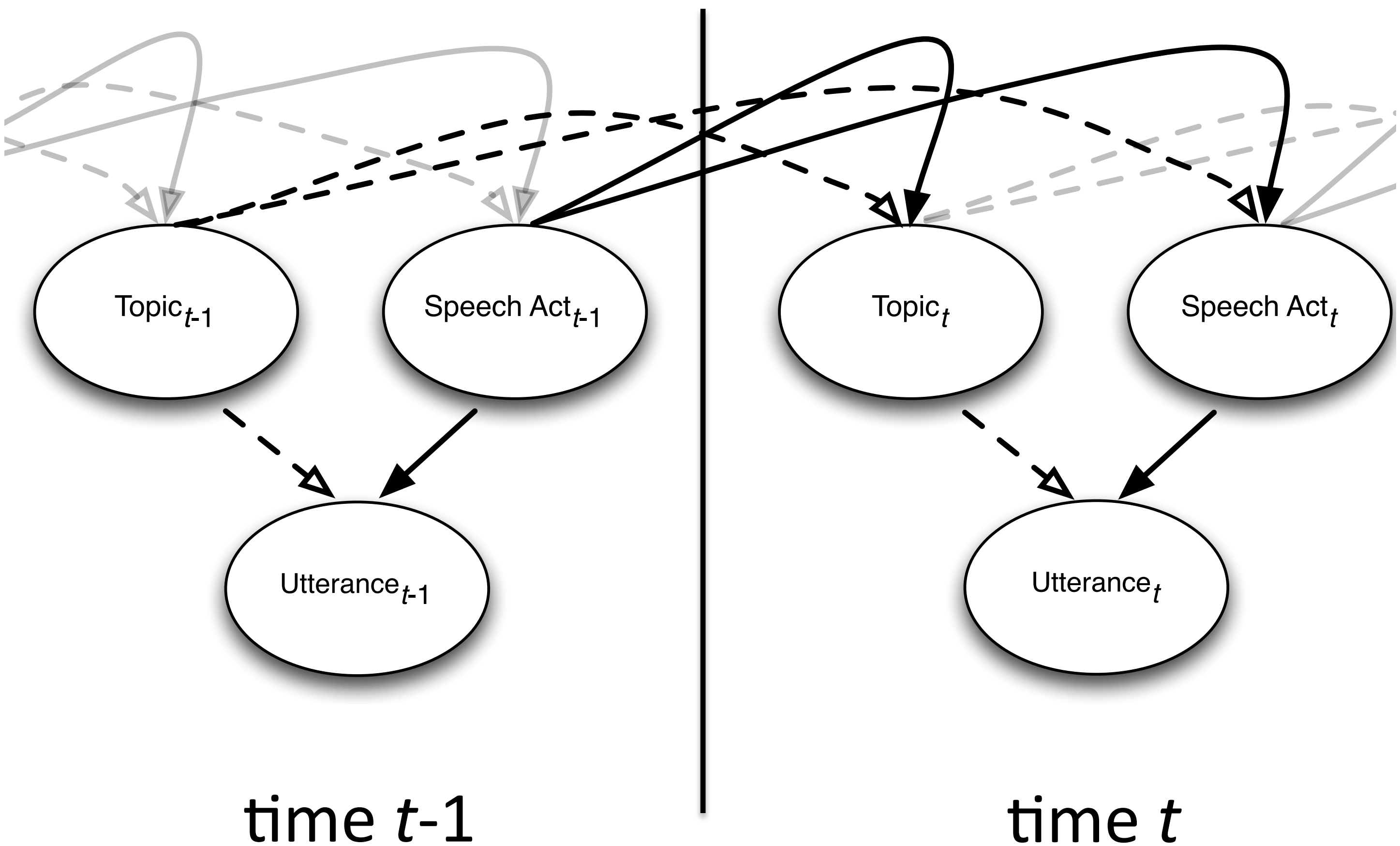
- Transitions:

$$P(y_t|y_0, ..., y_{t-1}) = P(y_t|y_{t-1}) = \lambda_{y_{t-1},y_t}$$

- Emissions:

$$P(u_t|y_t) = \prod_{w \in u_t} P(w|y_t) = \prod_{w \in u_t} \tau_{y_t,w}$$

Jointly modeling topics *and* speech acts



An additive component sequential model: transitions

component corresponding to previous *topic*

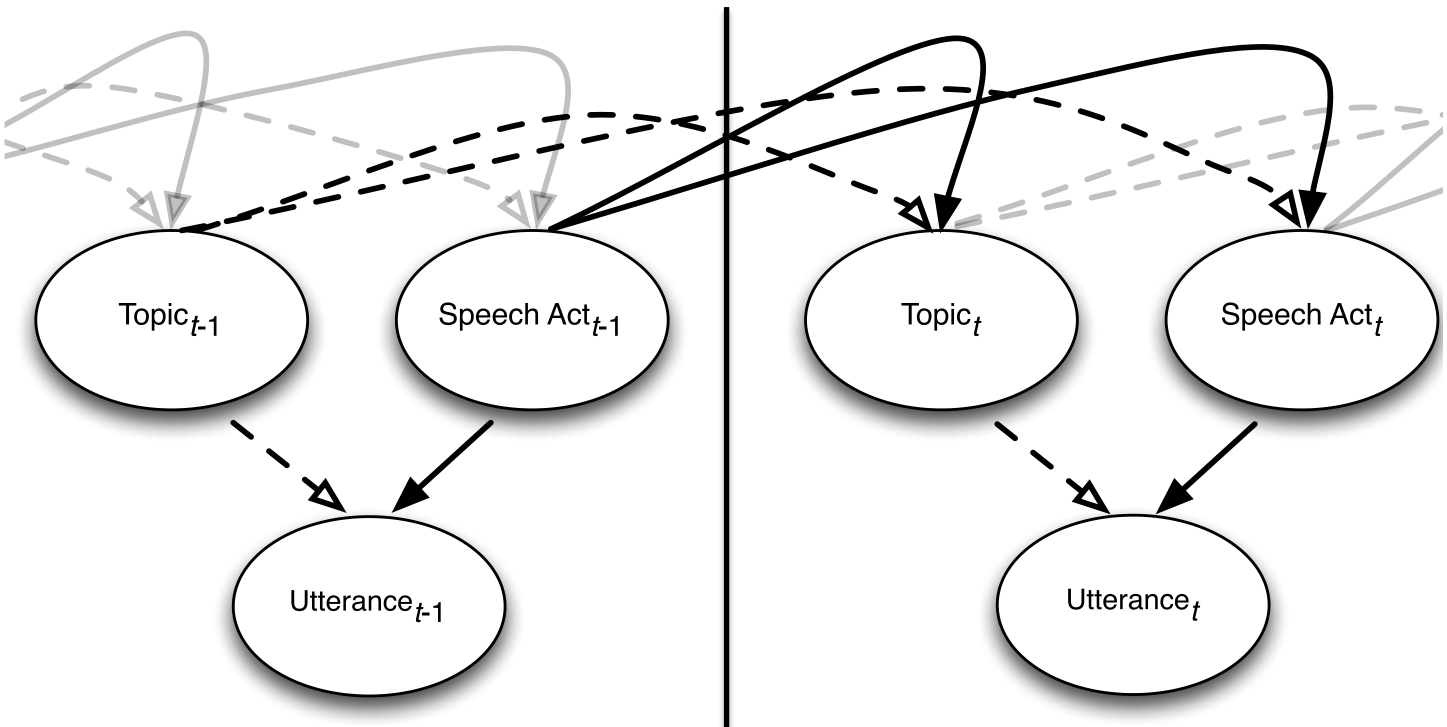
$$P(s_t|s_{t-1}, y_{t-1}) =$$
$$\frac{1}{Z_s} exp\{\pi^{\mathcal{S}}_{s_t} + \sigma_{s_{t-1},s_t} + \sigma_{y_{t-1},s_t} + \sigma_{(y_{t-1},s_{t-1}),s_t}\}$$

baseline probability of s_t

component corresponding to previous *speech act*

interaction component for *topic/speech act* interactions

Jointly modeling topics *and* speech acts



P(y_t) is independent of P(s_t) given y_{t-1} and s_{t-1} because time is a *blocking* agent

An Additive Component Sequential Model: Emissions

component corresponding to
current *topic*

$$P(w|y_t, s_t) = \frac{1}{Z_w} exp\{\theta_w + \eta_w^{y_t} + \eta_w^{s_t} + \eta_w^{s_t, y_t}\}$$

baseline probability of *w*

topic / speech act
interaction component

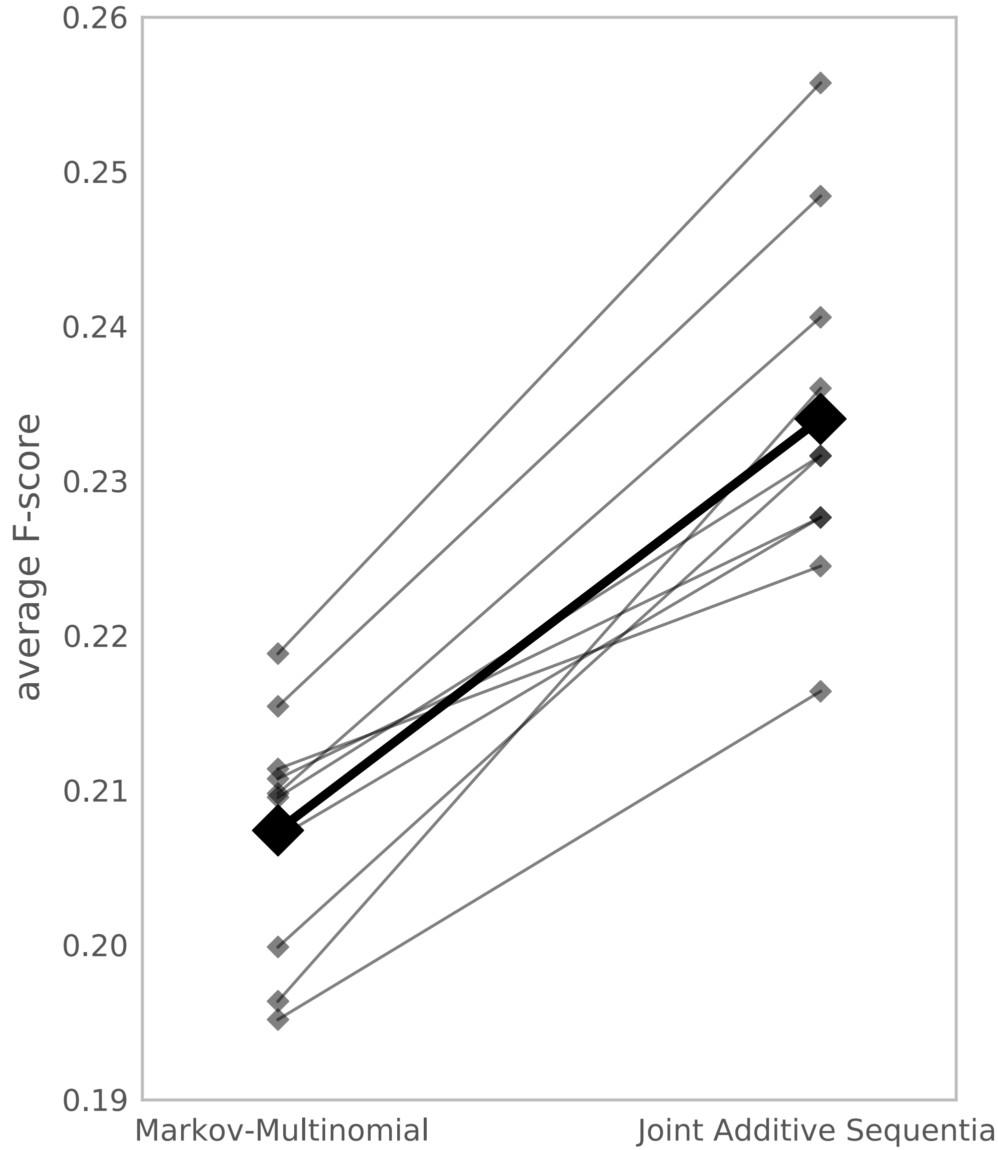
component corresponding to
speech act

Putting it all Together

$$P(y_t, s_t | s_{t-1}, y_{t-1}, u_t) =$$
$$P(u_t | y_t, s_t) \cdot P(y_t | y_{t-1}, s_{t-1}) \cdot P(s_t | s_{t-1}, y_{t-1})$$

- Optimization via gradient descent
- Prediction via Viterbi decoding

Results (Macro-averaged)



Revisiting the ARV Study

- Median (lower, upper) counts of utterances that have topic *ARV* and speech act *give information* over control (no intervention before visit) and intervention visits

True		MM		JAS	
control	intervention	control	intervention	control	intervention
10 (4, 28)	23 (11, 39)	13 (5, 33)	27 (16, 44)	12 (5, 28)	23 (14, 40)

Physician-specific parameters

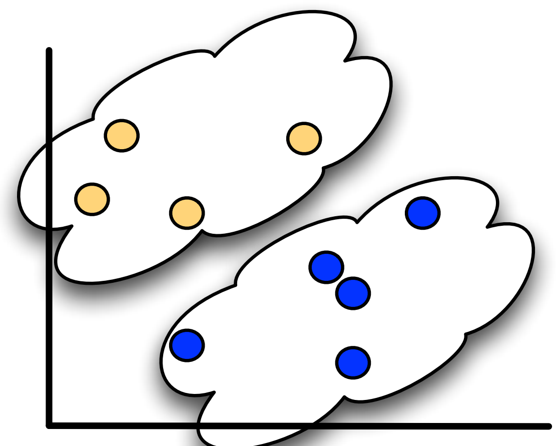
$$P(s_t|s_{t-1}, d) \propto exp\{\pi_{s_t} + \sigma_{s_{t-1},s_t} + \sigma^d_{s_{t-1},s_t}\}$$

doctor *d's* specific tendency to transition from speech act s_{t-1} to s_t

Physician-specific parameters

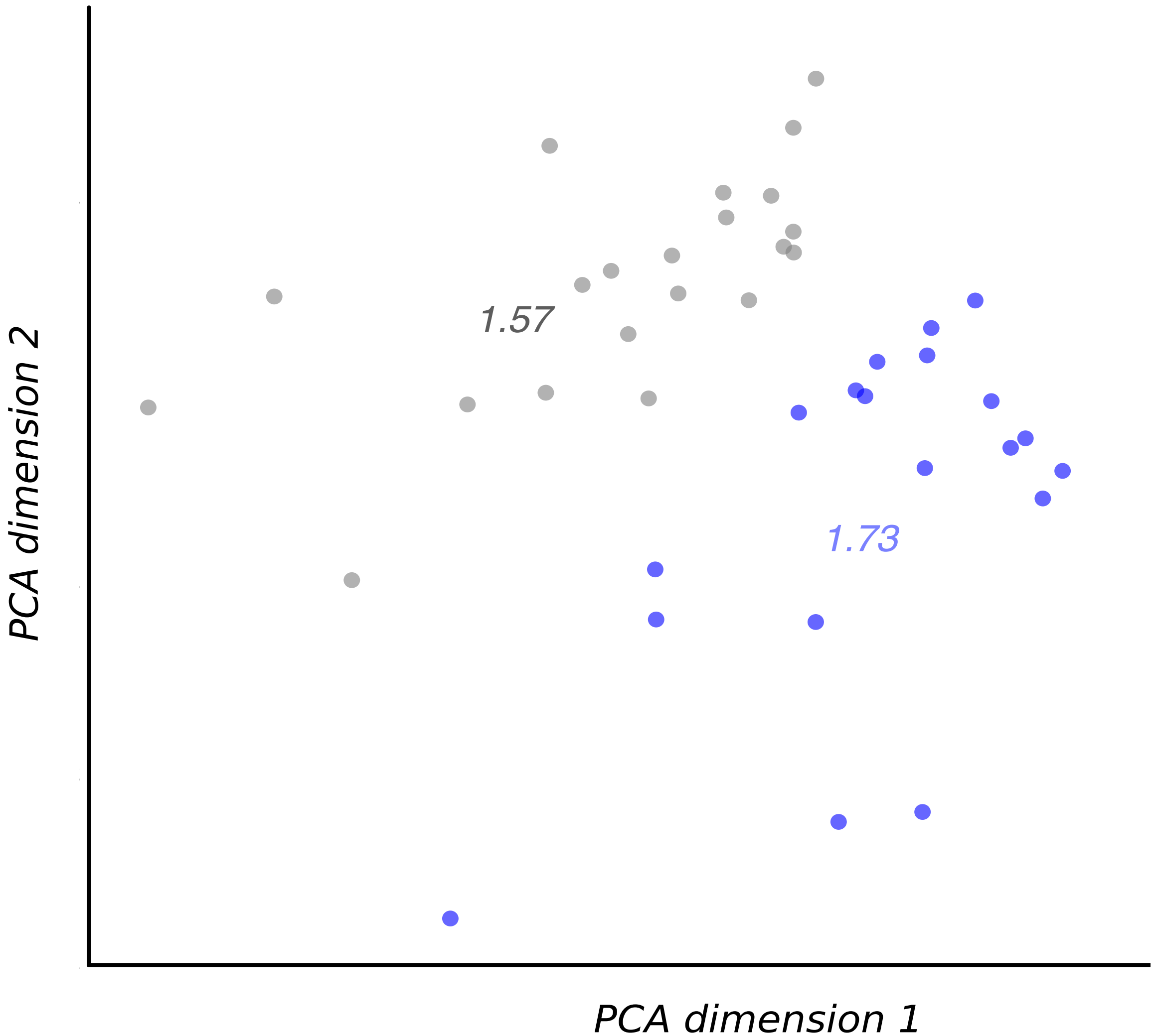
$$
\begin{array}{c c}
\text{Doctors} & \begin{bmatrix}
\hat{\theta}_{0,0} & \hat{\theta}_{0,1} & \cdots & \hat{\theta}_{0,|\mathcal{S}|\times|\mathcal{S}|} \\
\hat{\theta}_{1,0} & \hat{\theta}_{1,1} & \cdots & \hat{\theta}_{1,|\mathcal{S}|\times|\mathcal{S}|} \\
\vdots & \vdots & \ddots & \vdots \\
\hat{\theta}_{|\mathcal{D}|,0} & \hat{\theta}_{|\mathcal{D}|,1} & \cdots & \hat{\theta}_{|\mathcal{D}|,|\mathcal{S}|x|\mathcal{S}|}
\end{bmatrix}
\end{array}
\xrightarrow{\textit{PCA reduce}}
$$

Speech act to speech act transition parameters



Identify clusters (communication styles)

Clustering Physicians



Are the Clusters Meaningful?

How is the provider who takes care of your HIV at ...
Overall
Q1 ... explaining the results of tests in a way that you understand?
Q2 ... giving you facts about the benefits and risks of treatment?
Q3 ... telling you what to do if certain problems or symptoms occur?
Q4 ... demonstrating caring, compassion, and understanding?
Q5 ... understanding your health worries and concerns?
HIV-specific
Q6 ... talking with you about your sex life?
Q7 ... asking you about stresses in your life that may affect your health?
Q8 ... asking about problems with alcohol?
Q9 ... asking about problems with street drugs like heroin and cocaine?
Adherence
Q10 ... giving you information about the right way to take your antiretroviral medicines?
Q11 ... understanding the problems you have taking your antiretroviral medicines?
Q12 ... helping you solve problems you have taking your antiretroviral medicines the right way?

Clustering Physicians