Machine Learning for Population Health and Disease Surveillance

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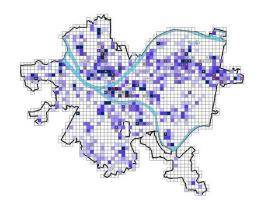
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Population Health:
Very early and
accurate detection of
emerging outbreaks.



Individual Health: Discovering novel "best practices" for patient care, to improve outcomes and reduce costs.



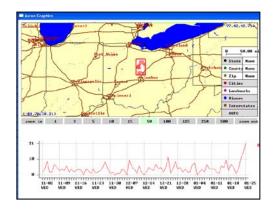
Community Health:
Detection, prediction,
and prevention of "hotspots" of violent crime.

My research is focused at the intersection of **machine learning (ML)** and **public policy**, with two main goals:

- Develop new ML methods for better (more scalable and accurate)
 detection and prediction of events and other patterns in massive datasets.
- 2) Apply these methods for the public good, particularly, to improve the quality of **individual**, **population**, and **community health**.



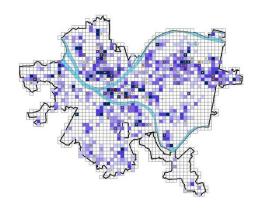
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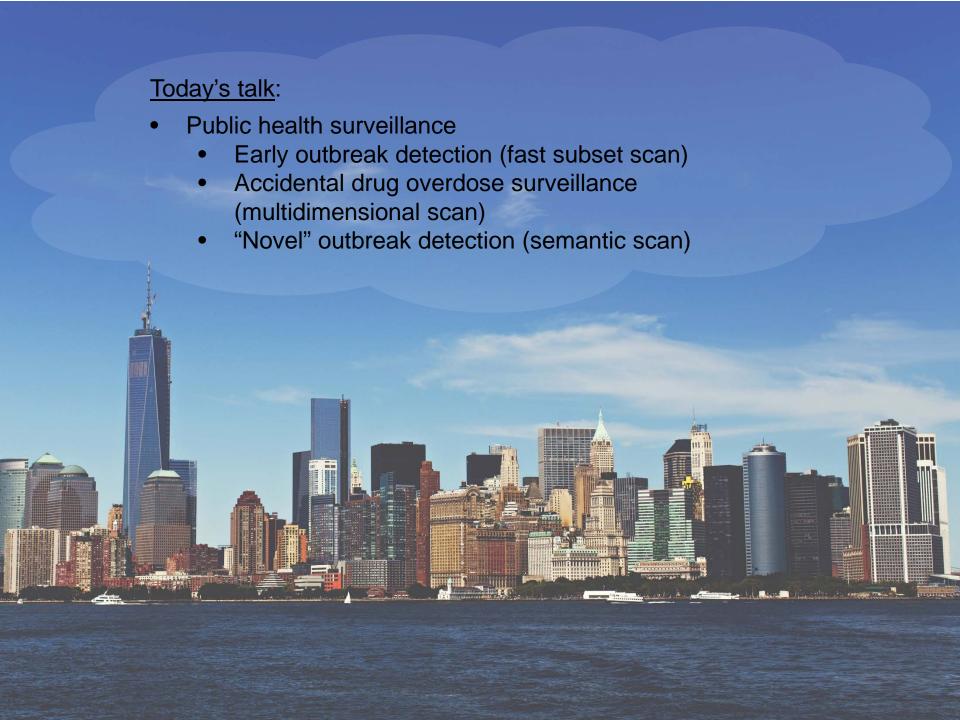
Individual Health: Discovering novel "best practices" for patient care, to improve outcomes and reduce costs.



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Detection, prediction,
and prevention of "hotspots" of violent crime.

Our disease surveillance methods are in use for deployed systems in the U.S., Canada, India, and Sri Lanka; currently working with NYC DOHMH. Our "CrimeScan" software has been in day-to-day operational use for predictive policing by the Chicago Police Dept.

"CityScan" has been used by Chicago city leaders for prediction and prevention of rodent infestations using 311 call data.



Why worry about disease outbreaks?

- Bioterrorist attacks are a very real, and scary, possibility
 Large anthrax release over a major city could kill 1-3 million and hospitalize millions more.
- Emerging infectious diseases "Conservative estimate" of 2-7 million deaths from pandemic avian influenza.
- Better response to common outbreaks and emerging public health trends.

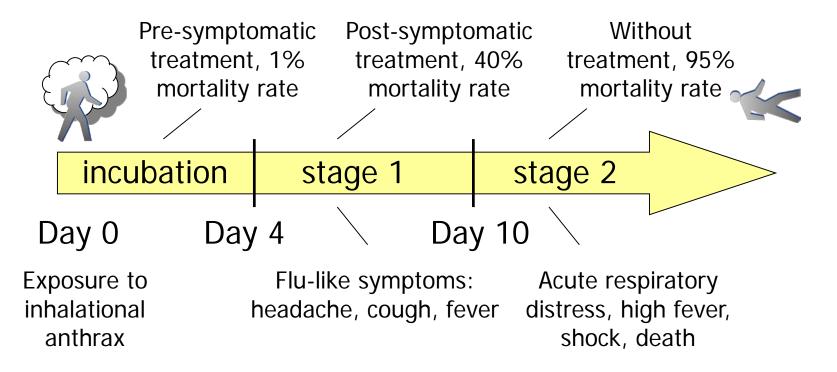






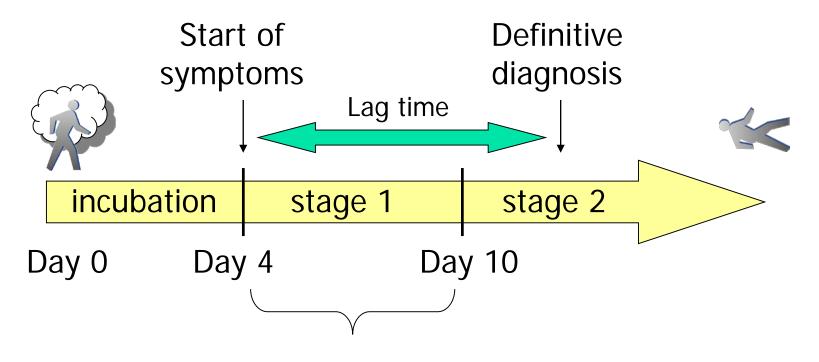
Benefits of early detection

Reduces cost to society, both in lives and in dollars!



DARPA estimate: a two-day gain in detection time and public health response could reduce fatalities by a factor of six.

Early detection is hard



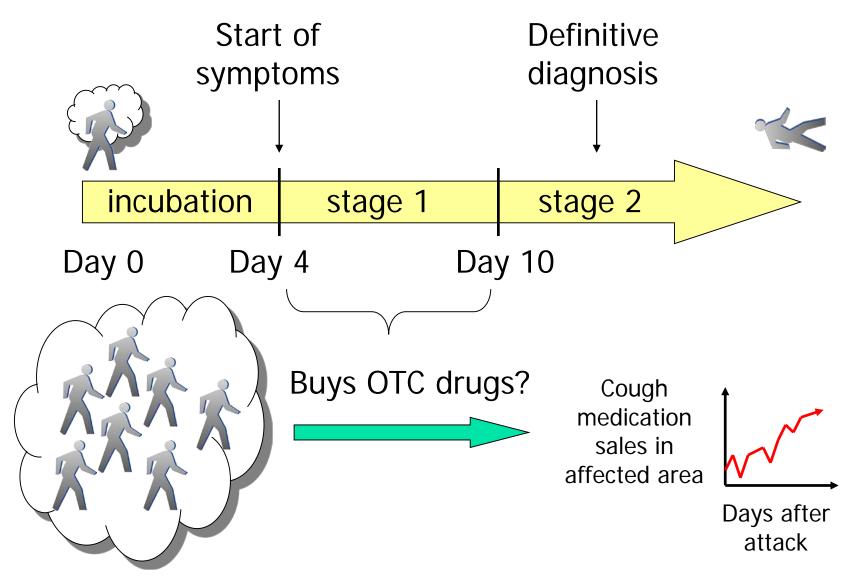
Buys OTC drugs

Skips work/school

Uses Google, Facebook, Twitter

Visits doctor/hospital/ED

Syndromic surveillance



Syndromic surveillance

Start of

Definitive diagnosis

We can achieve very early detection of outbreaks by gathering <u>syndromic</u> data, and identifying emerging <u>spatial clusters</u> of symptoms.



Buys OTC drugs?



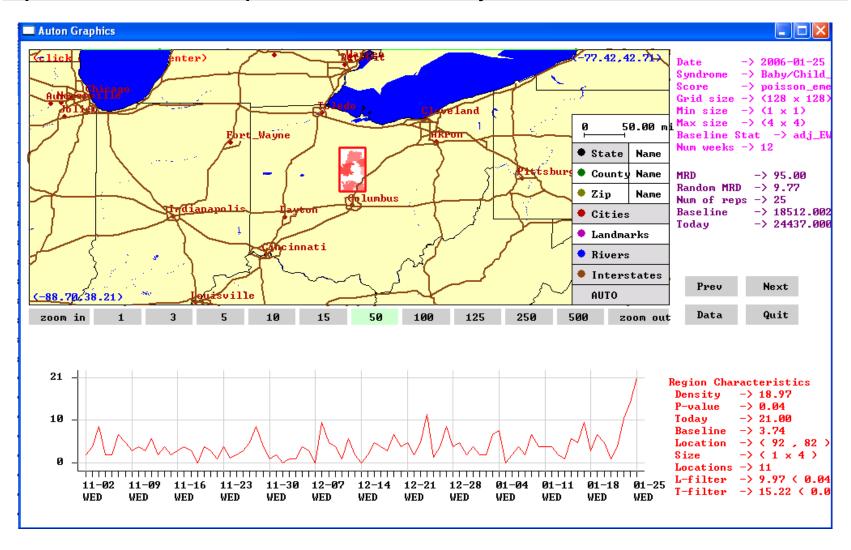
Cough
medication
sales in
affected area



Days after attack

Outbreak detection example

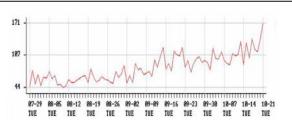
Spike in sales of pediatric electrolytes near Columbus, Ohio



Multivariate event detection



Spatial time series data from spatial locations s_i (e.g. zip codes)



Time series of counts $c_{i,m}^{t}$ for each zip code s_{i} for each data stream d_{m} .

Outbreak detection

 d_1 = respiratory ED d_2 = constitutional ED d_3 = OTC cough/cold d_4 = OTC anti-fever (etc.)

Main goals:

Detect any emerging events.

Pinpoint the affected subset of locations and time duration.

Characterize the event, e.g., by identifying the affected streams.

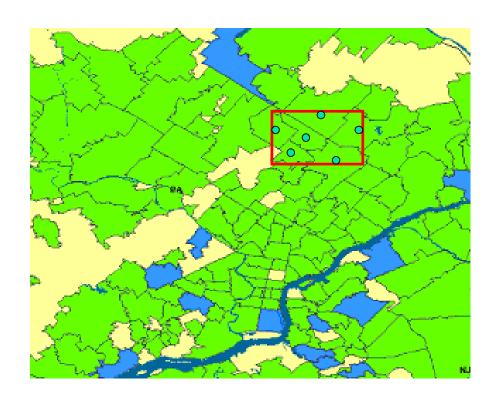
Compare hypotheses:

 $H_1(D, S, W)$

D = subset of streams
S = subset of locations
W = time duration

vs. H₀: no events occurring

Expectation-based scan statistics

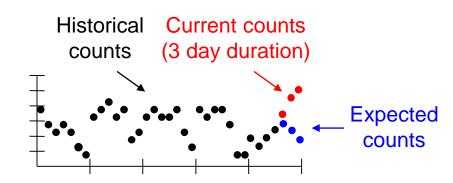


We then compare the actual and expected counts for each subset (D, S, W) under consideration.

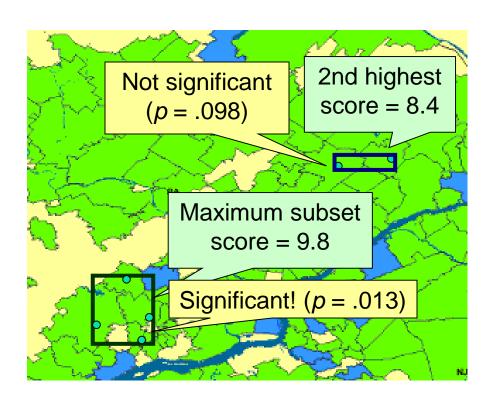
(Kulldorff, 1997; Neill and Moore, 2005)

We search for spatial regions (subsets of locations) where the recently observed counts for some subset of streams are significantly higher than expected.

We perform **time series analysis** to compute expected counts ("baselines") for each location and stream for each recent day.



Expectation-based scan statistics



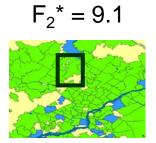
(Kulldorff, 1997; Neill and Moore, 2005)

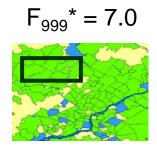
We find the subsets with highest values of a likelihood ratio statistic, and compute the *p*-value of each subset by randomization testing.

$$F(D, S, W) = \frac{\Pr(\text{Data} \mid H_1(D, S, W))}{\Pr(\text{Data} \mid H_0)}$$

To compute p-value
Compare subset score
to maximum subset
scores of simulated
datasets under H₀.







Likelihood ratio statistics

For our expectation-based scan statistics, the null hypothesis H_0 assumes "business as usual": each count $c_{i,m}{}^t$ is drawn from some parametric distribution with mean $b_{i,m}{}^t$. $H_1(S)$ assumes a multiplicative increase for the affected subset S.

Expectation-based Poisson

$$H_0$$
: $c_{i,m}^t \sim Poisson(b_{i,m}^t)$

$$H_1(S)$$
: $c_{i,m}^t \sim Poisson(qb_{i,m}^t)$

Let C =
$$\sum_{S} c_{i,m}^{t}$$
 and B = $\sum_{S} b_{i,m}^{t}$.

Maximum likelihood: q = C / B.

$$F(S) = C \log (C/B) + B - C$$

Expectation-based Gaussian

$$H_0$$
: $c_{i,m}^t \sim Gaussian(b_{i,m}^t, \sigma_{i,m}^t)$

$$H_1(S)$$
: $c_{i,m}^t \sim Gaussian(qb_{i,m}^t, \sigma_{i,m}^t)$

Let C' =
$$\sum_{S} c_{i,m}^{t} b_{i,m}^{t} / (\sigma_{i,m}^{t})^{2}$$

and B' = $\sum_{S} (b_{i,m}^{t})^{2} / (\sigma_{i,m}^{t})^{2}$.

Maximum likelihood: q = C' / B'.

$$F(S) = (C')^2 / 2B' + B'/2 - C'$$

Many possibilities: exponential family, nonparametric, Bayesian...

Which regions to search?

Typical approach: "spatial scan" (Kulldorff, 1997)

Each search region S is a **sub-region** of space.

- Choose some region shape (e.g. circles, rectangles) and consider all regions of that shape and varying size.
- Low power for true events that do not correspond well to the chosen set of search regions (e.g. irregular shapes).

Our approach: "subset scan" (Neill, 2012) Each search region S is a **subset** of locations.

- Find the highest scoring subset, subject to some constraints (e.g. spatial proximity, connectivity).
- For multivariate, also optimize over subsets of streams.
- Exponentially many possible subsets, O(2^N x 2^M): computationally infeasible for naïve search.

Fast subset scan

(Neill, 2012)

- In certain cases, we can optimize F(S) over the exponentially many subsets of the data, while evaluating only O(N) rather than O(2^N) subsets.
- Many commonly used scan statistics have the property of <u>linear-time subset scanning</u>:
 - Just sort the data records (or spatial locations, etc.) from highest to lowest priority according to some function...
 - ... then search over groups consisting of the top-k highest priority records, for k = 1..N.

The highest scoring subset is guaranteed to be one of these!

Sample result: we can find the **most anomalous** subset of Allegheny County zip codes in 0.03 sec vs. 10²⁴ years.

Linear-time subset scanning

- Example: Expectation-Based Poisson statistic
 - Sort data locations s_i by the ratio of observed to expected count, c_i / b_i.
 - Given the ordering $s_{(1)} \dots s_{(N)}$, we can **prove** that the top-scoring subset F(S) consists of the locations $s_{(1)} \dots s_{(k)}$ for some $k, 1 \le k \le N$.
 - <u>Key step</u>: if there exists some location s_{out} ∉ S with higher priority than some location s_{in} ∈ S, then we can show that F(S) ≤ max(F(S U {s_{out}}), F(S \ {s_{in}})).
- Theorem: LTSS holds for expectation-based scan statistics in any exponential family. (Speakman et al., 2015)

$$F(S) = \max_{q>1} \log \frac{P(Data \mid H_1(S))}{P(Data \mid H_0)} \qquad H_0: x_i \sim Dist(\mu_i)$$

$$H_1: x_i \sim Dist(q\mu_i)$$

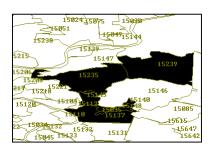
Constrained fast subset scanning

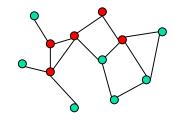
LTSS is a new and powerful tool for **exact** combinatorial optimization (as opposed to approximate techniques such as submodular function optimization). But it only solves the "best unconstrained subset" problem, and cannot be used directly for <u>constrained</u> optimization.

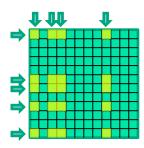
Many of our recent papers have focused on how LTSS can be extended to the many real-world problems with (hard or soft) constraints on our search.

- + Proximity constraints
- + Multiple data streams
- + Connectivity constraints
- + Group self-similarity

- → Fast spatial scan (irregular regions)
- → Fast multivariate scan
- → Fast graph scan
- → Fast generalized subset scan







(Neill, *JRSS-B*, 2012) (Neill et al., *Stat. Med.*, 2013)

(Speakman et al., JCGS, 2015)

(McFowland et al., JMLR, 2013)

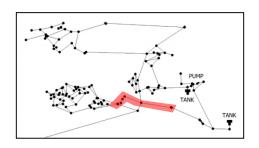
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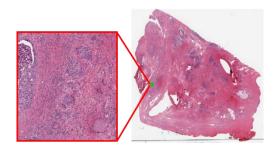
Many of our recent papers have focused on how LTSS can be extended to the many real-world problems with (hard or soft) constraints on our search.

 \rightarrow

- + Temporal dynamics
- + Hierarchical scanning
- + Scalable GP regression
- → Spreading contamination in water supply
- → Prostate cancer in digital pathology slides
 - Predicting and preventing rat infestations



(Speakman et al., ICDM 2013)



(Somanchi & Neill, DMHI 2013)



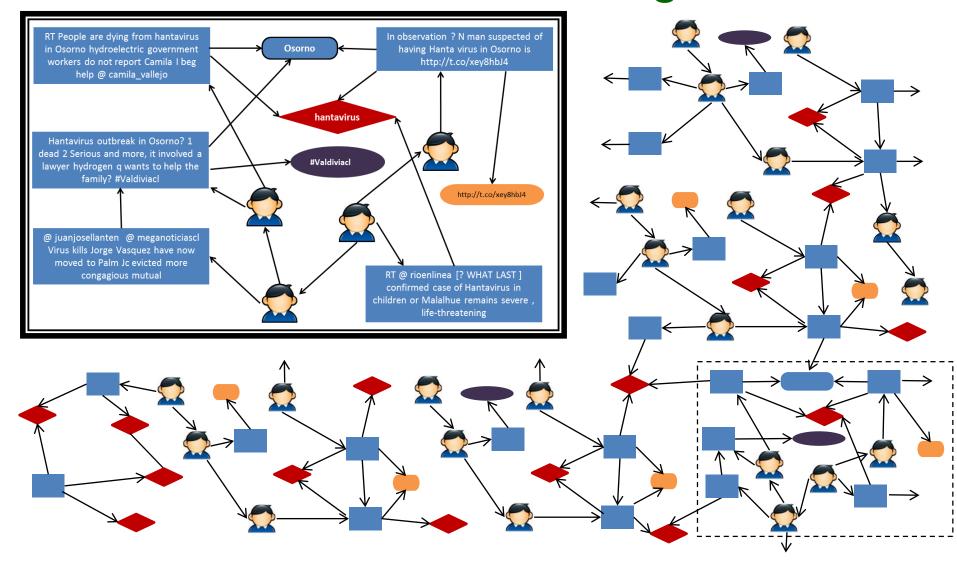
(Flaxman et al., 2015; Neill et al., in preparation)

Fast subset scan with spatial proximity constraints

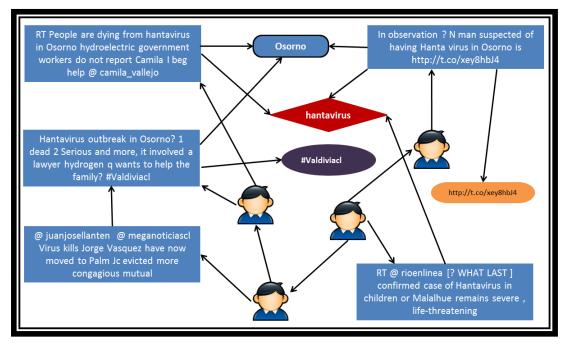


- Maximize a likelihood ratio statistic over all subsets of the "local neighborhoods" consisting of a center location s_i and its k-1 nearest neighbors, for a fixed neighborhood size k.
- Naïve search requires $O(N \cdot 2^k)$ time and is computationally infeasible for k > 25.
- For each center, we can search over all subsets of its local neighborhood in O(k) time using LTSS, thus requiring a total time complexity of O(Nk) + O(N log N) for sorting the locations.
- In Neill (2012), we show that this approach dramatically improves the timeliness and accuracy of outbreak detection for irregularly-shaped disease clusters.

Teaser #1: Detecting Rare Disease Outbreaks Using Twitter



Teaser #1: Detecting Rare Disease Outbreaks Using Twitter



Technical contributions:

- Modeling of Twitter data as a heterogeneous sensor network.
- Nonparametric subset scan to integrate data from multiple node types.
- Fast search algorithm scales to massive data.

<u>Evaluation</u>: 17 gold standard hantavirus outbreaks in Chile. Also applied to community health: predicting civil unrest and detecting emerging patterns of human rights violations.

Results: outperforms existing state-of-the-art methods with respect to timeliness of detection, detection power, and accuracy of outbreak characterization.

Detected Hantavirus outbreak, 10 Jan 2013

First news report: 11 Jan 2013





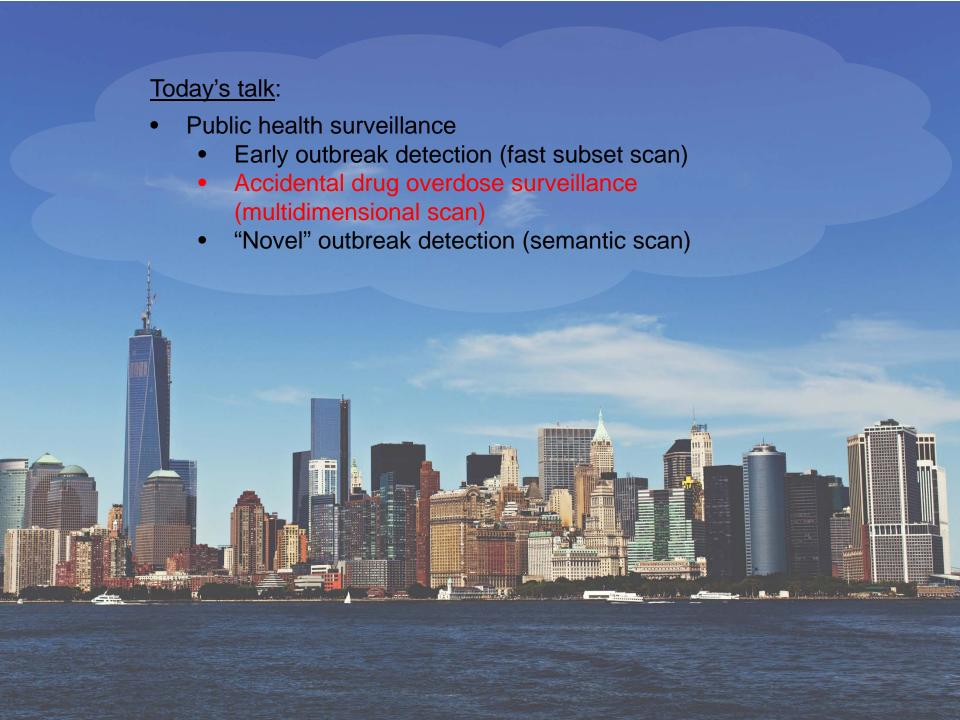
Uruguay

DO SUL

Locations
Users
Keywords
Hashtags
Links
Videos

Temuco and Villarrica, Chile

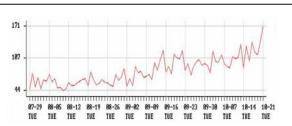
F. Chen and D.B. Neill. Non-parametric scan statistics for event detection and forecasting in heterogeneous social media graphs. Proc. 20th ACM SIGKDD Conf. on Knowledge Discovery and Data Mining, 1166-1175, 2014.



Multivariate event detection



Spatial time series data from spatial locations s_i (e.g. zip codes)



Time series of counts $c_{i,m}^{t}$ for each zip code s_{i} for each data stream d_{m} .

Outbreak detection

 d_1 = respiratory ED d_2 = constitutional ED d_3 = OTC cough/cold d_4 = OTC anti-fever (etc.)

Main goals:

Detect any emerging events.

Pinpoint the affected subset of locations and time duration.

Characterize the event, e.g., by identifying the affected streams.

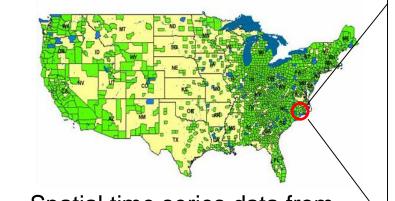
Compare hypotheses:

 $H_1(D, S, W)$

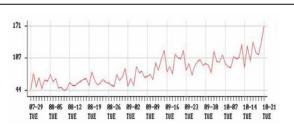
D = subset of streams
S = subset of locations
W = time duration

vs. H₀: no events occurring

Multidimensional event detection



Spatial time series data from spatial locations s_i (e.g. zip codes)



Time series of counts $c_{i,m}^{t}$ for each zip code s_{i} for each data stream d_{m} .

Outbreak detection

 d_1 = respiratory ED d_2 = constitutional ED d_3 = OTC cough/cold d_4 = OTC anti-fever (etc.)

Additional goal: identify any differentially affected **subpopulations** P of the monitored population.

Gender (male, female, both)

Age groups (children, adults, elderly)

Ethnic or socio-economic groups

Risk behaviors: e.g. intravenous drug

use, multiple sexual partners

More generally, assume that we have a set of additional discrete-valued attributes A₁..A_J observed for each individual case.

We identify not only the affected streams, locations, and time window, but also a **subset** of values for each attribute.

Multidimensional LTSS

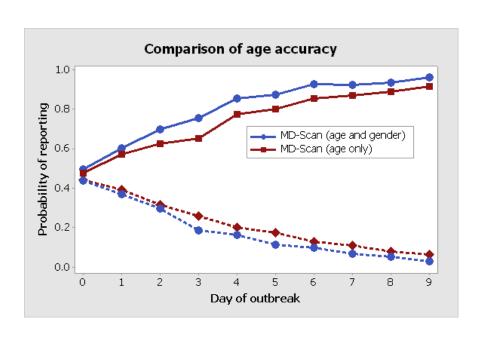
- Our MD-Scan approach (Neill and Kumar, 2013) extends LTSS to the multidimensional case:
 - For each time window and spatial neighborhood (center + k-nearest neighbors), we do the following:
 - 1. Start with randomly chosen subsets of **locations** S, **streams** D, and **values** V_j for each attribute A_j (j=1..J).
 - 2. Choose an attribute (randomly or sequentially) and use LTSS to find the highest scoring subset of values, locations, or streams, conditioned on all other attributes.
 - 3. Iterate step 2 until convergence to a local maximum of the score function F(D,S,W, {V_j}), and use multiple restarts to approach the global maximum.

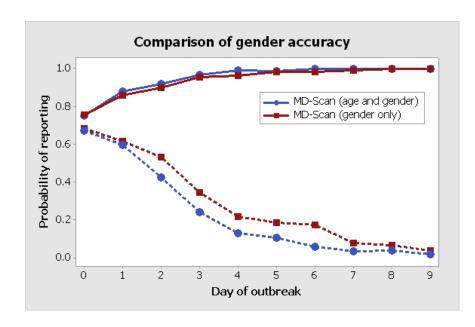
Empirical evaluation

- We first evaluated the detection performance of MD-Scan for detecting disease outbreaks injected into real-world Emergency Department data from Allegheny County, PA.
- We considered outbreaks with various types and amounts of age and gender bias.

1) Identifying affected subpopulations

By the midpoint of the outbreak, MD-Scan is able to correctly identify the affected gender and age deciles with high probability, without reporting unaffected subpopulations.





Proportions of correct and incorrect groups reported vs. time since start of outbreak.

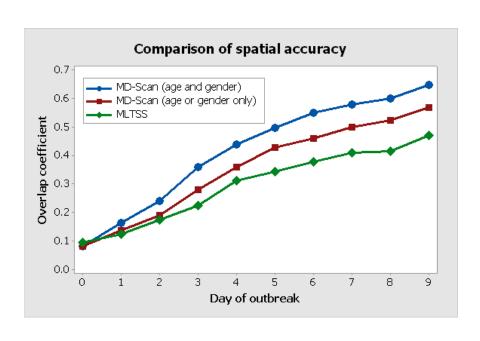
Solid lines: affected gender and/or age deciles. Dashed lines: unaffected.

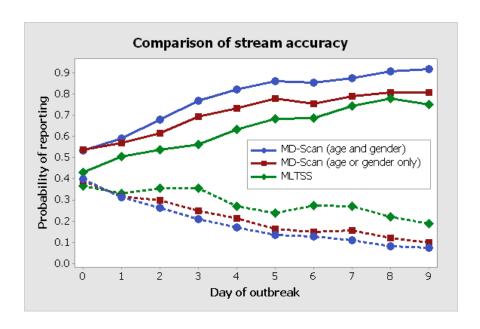
Blue lines: outbreaks with differential effects by both age and gender (easier).

Red lines: outbreaks with differential effects by age or gender only (harder).

2) Characterizing affected streams

As compared to the previous state of the art (multivariate linear-time subset scanning), MD-Scan is better able to characterize the affected spatial locations and subset of the monitored streams.





Left: overlap coefficient between true and detected subsets of spatial locations. Right: Proportions of correct and incorrect streams reported vs. day of outbreak.

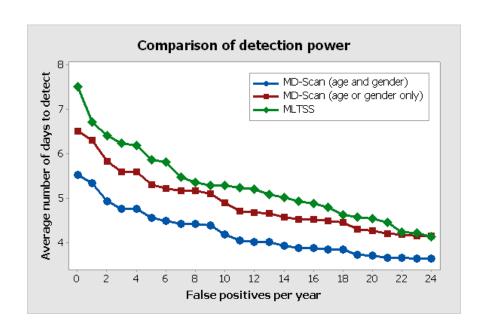
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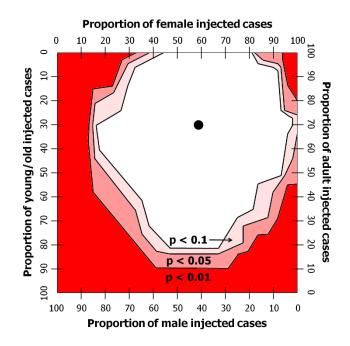
Red lines: outbreaks with differential effects by age or gender only (harder).

Green lines: MLTSS, ignoring age and gender information

3) Timeliness of outbreak detection

MD-Scan achieved significantly more timely detection for outbreaks that were sufficiently biased by age and/or gender.





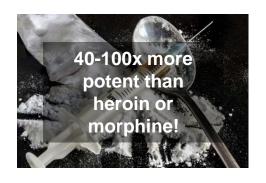
For outbreaks with strong age and gender biases, time to detection improved from 5.2 to 4.0 days at a fixed false positive rate of 1/month.

Smaller biases in age or gender were sufficient for significant improvements; even when no age/gender signal is present, MD-Scan performs comparably to MLTSS.

Allegheny County Overdose Data

- Collaboration with Allegheny County's Department of Human Services, including retrospective analysis (2008-2015) and plans to build a prospective surveillance tool.
- <u>~2000 cases</u>: for each overdose victim, we have date, zip code, age, gender, race, and which drugs present.
- We used an extension of MD-Scan, the multidimensional tensor scan (MDTS), to detect emerging geographic, demographic, and behavioral patterns, many of which DHS had not previously identified.
 - Earlier detection of emerging overdose clusters.
 - Better characterization of who and where is affected by identifying affected subset in each dimension.
 - Quantifying the effects of drug legislation and other policy changes.

MD-Scan Overdose Results (1)



Fentanyl is a dangerous drug which has been a huge problem in western PA.It is often mixed with white powder heroin, or sold disguised as heroin.

January 16-25, 2014: 14 deaths county-wide from fentanyl-laced heroin. March 27 to April 21, 2015: 26 deaths county-wide from fentanyl, heroin only present in 11.

January 10 to February 7, 2015:

Cluster of 11 fentanyl-related deaths, mainly black males over 58 years of age, centered in Pittsburgh's downtown Hill District.

Very unusual demographic: common dealer / shooting gallery?

Started in the SE suburbs of Pittsburgh, including a cluster of 5 cases around McKeesport between March 27 and April 8.

Cluster score became significant March 29th (4 nearby cases, white males ages 20-49) and continued to increase through April 20th.

Fentanyl, heroin, and combined deaths remained high through end of June (>100).

MD-Scan Overdose Results (2)

Another set of discovered overdose clusters each involved a combination of Methadone and Xanax.



Methadone: an opioid used for chronic pain relief and to treat heroin addiction, but also addictive and risk of OD.



Xanax (alprazolam): a benzodiazepine prescribed for panic and anxiety disorders. The combination produces a strong high but can be deadly (~30% of methadone fatal ODs).

From 2008-2012: multiple M&X OD clusters, 3-7 cases each, localized in space and time.

From 2013-2015: no M&X overdose clusters; 33% and 47% drops in yearly methadone and M&X deaths respectively.

Why did these deaths cluster, when methadone and methadone + other benzo deaths did not?

What factors could explain the dramatic reduction in M&X overdose clusters?



MD-Scan Overdose Results (2)

Another set of discovered overdose clusters each involved a combination of Methadone and Xanax.



Methadone: an opioid used for chronic pain relief and to treat heroin addiction, but also addictive and risk of OD.



Xanax (alprazolam): a benzodiazepine prescribed for panic and anxiety disorders. Increased state oversight of methadone clinics and prescribing physicians after passage of the Methadone Death and Incident Review Act (Oct 2012).

Approval of generic suboxone (buprenorphine + naloxone) in early 2013 lowered cost of suboxone treatment as an alternative to methadone clinics.

Why did these deaths cluster, when methadone and methadone + other benzo deaths did not?

What factors could explain the dramatic reduction in M&X overdose clusters?

Teaser #2: Discovering Anomalous Patterns of Care

Extensions of the multidimensional subset scan can be used to discover **heterogeneous treatment effects** in both experimental and observational data.

Using Highmark claims data from ~125K patients with diseases of the circulatory system, we discovered patterns including the following:

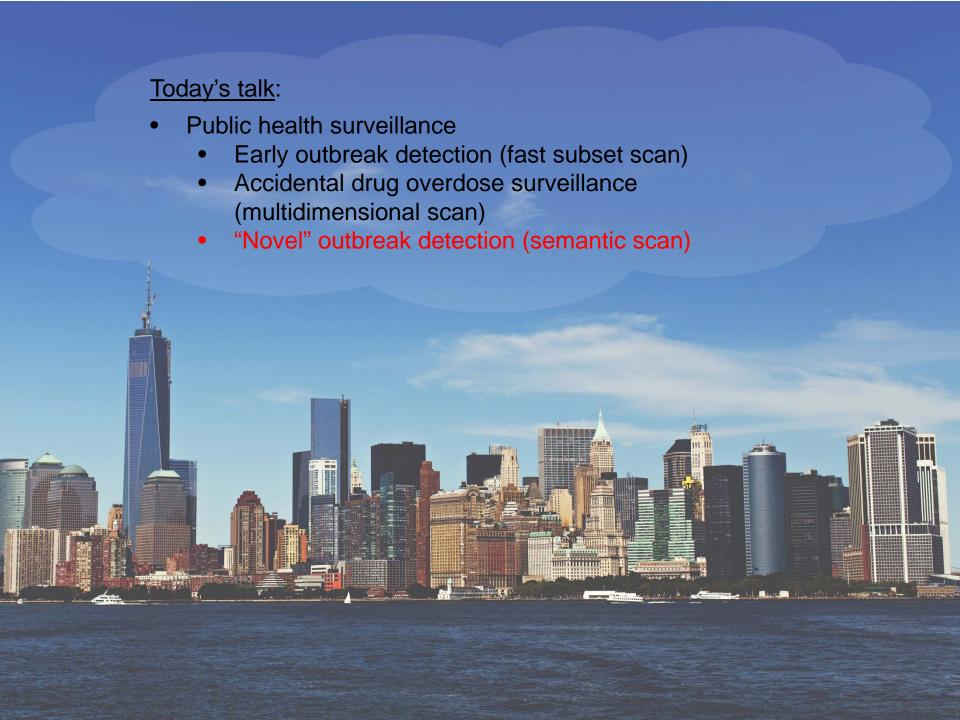
Glucocorticoids significantly increase mean number of hospitalizations following treatment in the subpopulation of hypertensive, overweight/obese males with endocrine disorders.

Regression on held-out data, controlling for observed covariates:

Glucocorticoids are associated with:

10.6% increase in hospitalizations across the entire population.

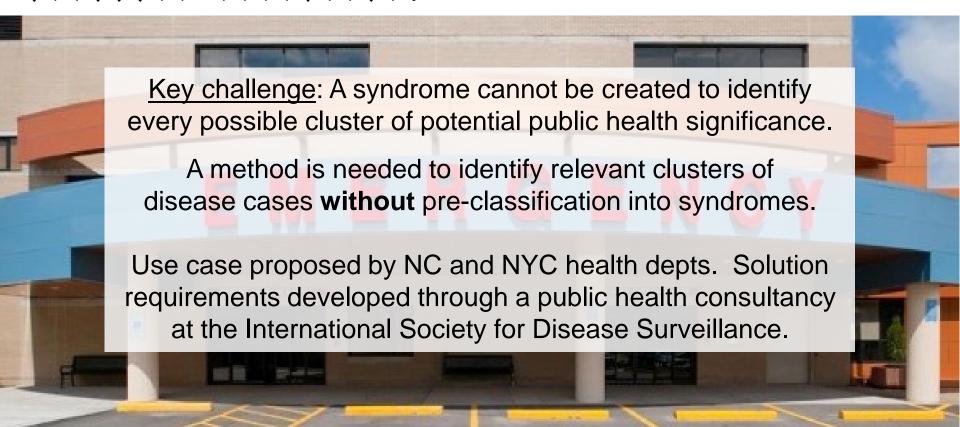
50.6% increase in hospitalizations for this subpopulation.



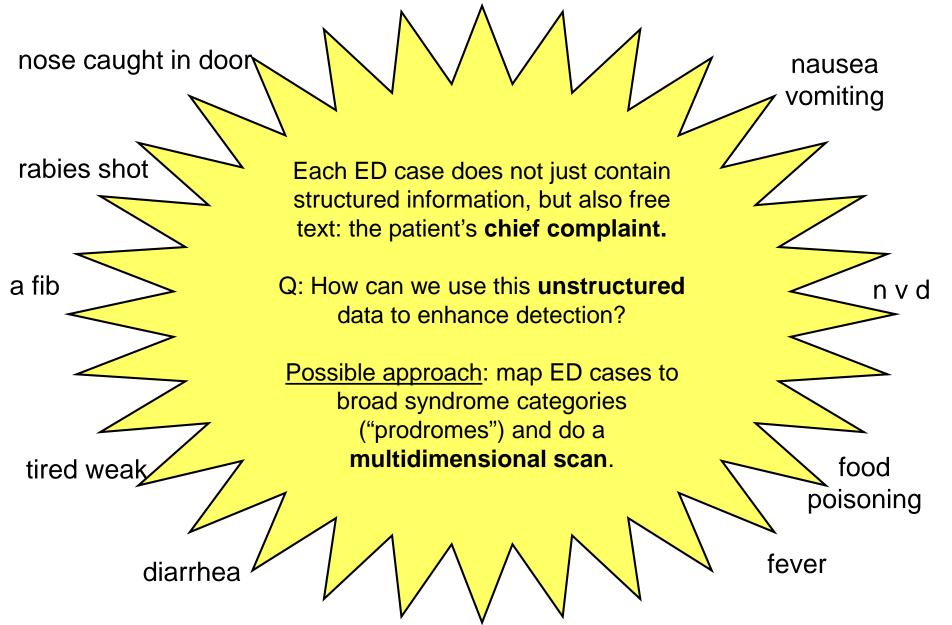
Asyndromic surveillance

Date	<u>/time</u>	Hosp.	Age	Complaint
Jan 1	08:00	Α	19-24	runny nose
Jan 1	08:15	В	10-14	fever, chills
Jan 1	08:16		0-1	broken arm
Jan 2	08:20	С	65+	vomited 3x
Jan 2	08:22	Α	45-64	high temp
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Free-text ED chief complaint data from hospitals in New York City, North Carolina, and Allegheny County, Pennsylvania.



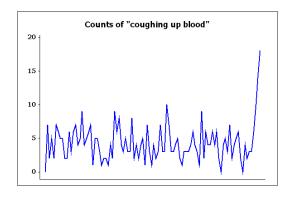
From structured to unstructured...



Where do existing methods fail?

The typical, prodrome-based scan statistic approach can effectively detect emerging outbreaks with commonly seen, general patterns of symptoms (e.g. ILI).

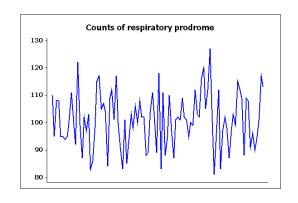
If we were monitoring these particular symptoms, it would only take a few such cases to realize that an outbreak is occurring!



What happens when something new and scary comes along?

- More specific symptoms ("coughing up blood")
- Previously unseensymptoms ("nose falls off")

Mapping specific chief complaints to a broader symptom category can dilute the outbreak signal, delaying or preventing detection.



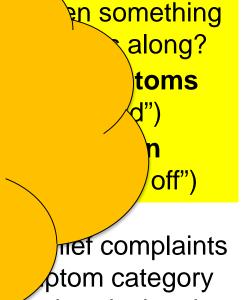
Where do existing methods fail?

The typical, production scan statistic effectively outbread seen sy

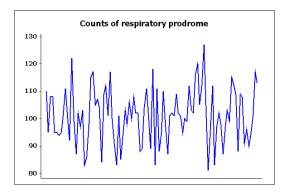
Our solution is to combine textbased (topic modeling) and event detection (multidimensional scan) approaches, to detect emerging patterns of keywords.

If we we particular sy take a few such that an outb

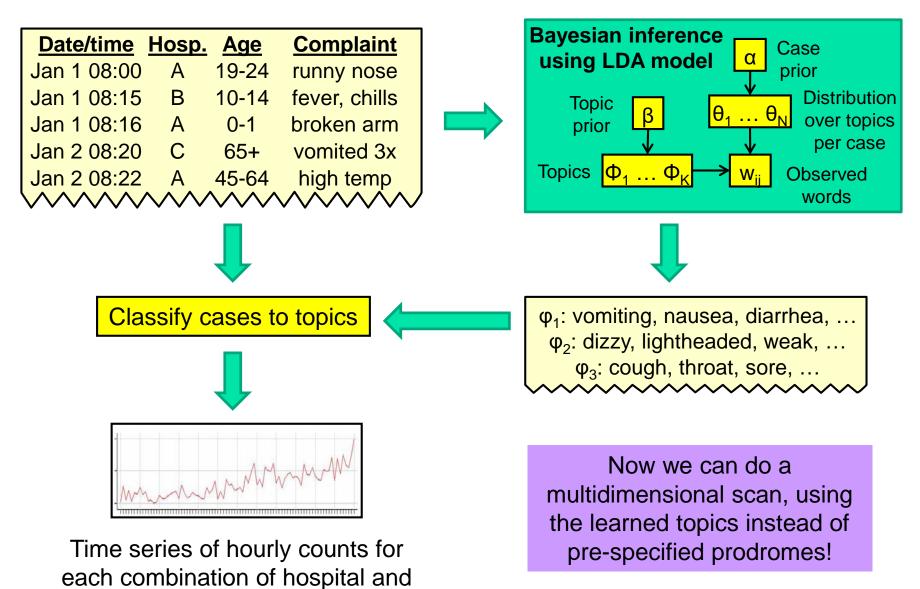
f "coughing up blood"



ying or preventing detection.



The semantic scan statistic



age group, for each topic ϕ_{i}

Multidimensional scanning

(for learned topics)

For each hour of data (~8K):

For each combination S of:

- Hospital
- Time duration (1-3 hours)
- Age range
- Topic

Count: C(S) = # of cases in that time interval matching on hospital, age range, topic.

Baseline: B(S) = expected count (28-day moving average).

Score: $F(S) = C \log (C/B) + B - C$, if C > B, and 0 otherwise (using the expectation-based Poisson likelihood ratio statistic)

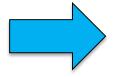
We return cases corresponding to each top-scoring subset S.

Semantic scan results (1)

(3 yrs. of data from 13 Allegheny County, PA hospitals)

Semantic scan detected simulated novel outbreaks more than twice as quickly as the standard prodrome-based method: 5.3 days vs. 10.9 days to detect at 1 false positive per month.





green
nose
possible
color
greenish
nasal
...

Simulated novel outbreak: "green nose"

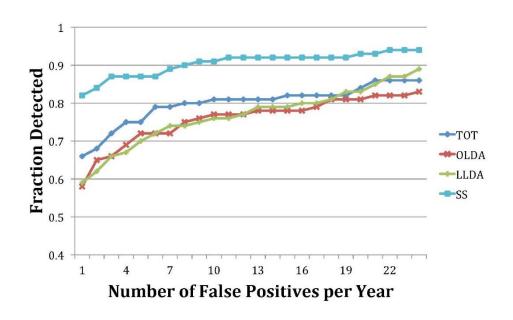
Top words from detected topic

Semantic scan results (2)

(3 yrs. of data from 13 Allegheny County, PA hospitals)

Using a "leave one out" approach in which we hold out one International Classification of Diseases (ICD) code and inject cases as if from a novel outbreak, we observe huge improvements in detection power and accuracy vs. competing methods (Online LDA, Topic Over Time, Labeled LDA).

These gains resulted from development of a new **contrastive topic modeling** approach with higher power to detect newly emerging topics.



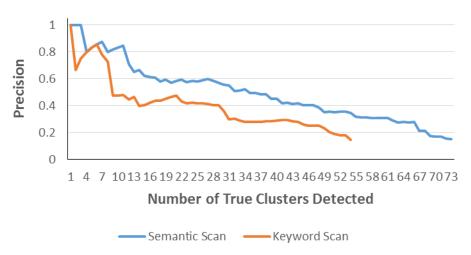
- 1) Learning a set of "background" topics from historical data.
- 2) Learning a set of "foreground" topics from recent data.
- Combined LDA inference, holding the background topics constant, leads to discovery of foreground topics that are maximally different.

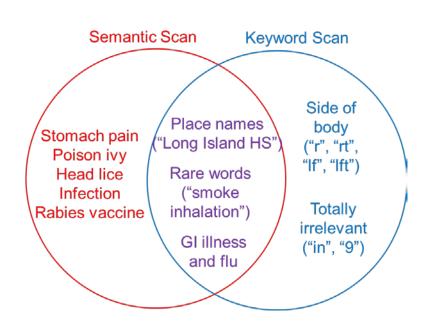
Semantic scan results (3)

(1 year of data from 3 hospitals in North Carolina)

We compared the top 500 clusters found by the semantic scan and a keyword-based scan in a blinded evaluation, with NC DOH public health officials labeling each cluster as "relevant" or "not relevant".

Comparison of Semantic Scan and Keyword Scan





Semantic scan: for 10 true clusters, had to report 12;

for 30 true clusters, had to report 54.

Keyword scan: for 10 true clusters, had to report 21;

for 30 true clusters, had to report 83.

Semantic scan results (4)

(5 yrs. of data from 10+ New York City hospitals)

Arrival Date	Arrival Time	Hospital ID	Chief Complaint	Patient Sex	Patient Age
			EVAUATION, DRANK COFFEE		
11/28/2014	7:52:00	HOSP5	WITH CRUS	M	45-49
11/28/2014	7:53:00	HOSP5	DRANK TAINTED COFFEE	M	65-69
11/28/2014	7:57:00	HOSP5	DRANK TAINTED COFFEE	F	20-24
11/28/2014	7:59:00	HOSP5	INGESTED TAINTED COFFEE	M	35-39
11/28/2014	8:01:00	HOSP5	DRANK TAINTED COFFEE	M	45-49
11/28/2014	8:03:00	HOSP5	DRANK TAINTED COFFEE	M	40-44
11/28/2014	8:04:00	HOSP5	DRANK TAINTED COFFEE	M	30-34
11/28/2014	8:06:00	HOSP5	DRANK TAINTED COFFEE	M	35-39
11/28/2014	8:09:00	HOSP5	INGESTED TAINTED COFFEE	M	25-29

This detected cluster (in data from NYC DOHMH) represents patients complaining of ingesting tainted coffee, and demonstrates Semantic Scan's ability to automatically detect rare and novel events.

To extend our approach to the NYC data, we had to deal with additional questions of scale (~20M records) and complexity; much noisier text data required additional pre-processing steps.

Other NYC events identified by Semantic Scan include:

Accidents

Motor vehicle
Ferry
School bus
Elevator

Contagious Diseases

Meningitis

Scabies

Ringworm

Other

Drug overdoses

Smoke inhalation

Carbon monoxide poisoning

Crime related, e.g., pepper spray attacks

The progression of detected clusters immediately following Hurricane Sandy highlights the variety of strains placed on hospital emergency departments following a natural disaster:

Acute cases: falls, SOB, leg Injuries



Mental health disturbances: depression, anxiety



Burden on medical infrastructure: methadone, dialysis

Conclusions

The continually increasing **size**, **variety**, and **complexity** of data available for population health and disease surveillance necessitate development of new detection methods to make use of these data.

Fast subset scanning (with constraints) can serve as a fundamental building block for efficient, scalable pattern detection in massive data.

Extensions to the **multivariate** and **multidimensional** settings, and incorporation of novel **topic modeling** approaches to handle free text data, enable us to address a variety of public health challenges.



Early outbreak detection



Drug overdose surveillance



Discovery of novel outbreaks

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Thanks for listening!

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