New Methodological Approaches for Opioid and Overdose Surveillance

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Drug overdoses

- Drug overdoses are an increasingly serious problem in the United States and worldwide.
  - In 2017, more than 72,000 drug overdose deaths occurred in the U.S., more than any year in recorded history.
  - Approximately 68% of these overdose deaths involved opioids.
  - Economic costs of the crisis are estimated at $78.5 billion annually.
- These statistics motivate public health to identify and predict emerging trends in overdoses, including geographic, demographic, and behavioral patterns, to better target interventions.
  - **Prevention** of high-risk prescribing and opioid use behaviors
  - **Treatment** of opioid addiction, e.g., medication-assisted therapy
  - **Rescue**, e.g., access to life-saving naloxone
  - **Recovery**, e.g., peer recovery coaches
Drug overdoses

- Machine learning has potential to **save lives** by:
  - **Integrating** multiple data sources
  - **Detecting** subtle, emerging patterns of overdoses in early stages
  - **Predicting** future overdose trends
  - **Targeting** an effective public health response
  - **Informing** prevention by quantifying effects of policy changes

- Here we present new machine learning methods for early detection, accurate characterization, and prediction of future overdose trends.

- Choice of methodology depends on goals and on desired spatial and temporal scales.
  - Early detection vs. near-term prediction vs. long-term forecasting
  - **Targeting of interventions**: geographic (city, neighborhood) vs. subpopulation (demographics, SES, risk behaviors) vs. individual.
Geographic surveillance

- Answers the question, **where** should I intervene?
- **Main goals**: estimate predicted overdose trends in space and time; identify anomalous spikes in overdose deaths.

**Useful predictors** include neighborhood characteristics and recent spatio-temporal trends in overdoses and leading indicator variables (e.g., behavioral risk factors).

**Gaussian processes** are a useful approach for modeling correlated spatio-temporal data. Our recent work* enables them to scale to real-world data, achieving state-of-the-art accuracy for long-term, small-area forecasting.

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We analyzed aggregate monthly counts of fatal opioid overdoses for six New York counties from 1999-2015.

We developed a new approach* which combines Gaussian processes (to model correlations) and subset scan (to identify the most anomalous space-time regions).

We compared our new method to typical anomaly detection approaches on real and synthetic datasets.

- GPSS > GP alone: nearby points matter for subtle anomalies
- GPSS > SS alone: covariance structure matters for correlated data

Case study: Geographic surveillance

Two statistically significant spikes in overdose cases:

- Brooklyn: End of 2015. Recent surge due to fentanyl.
Case study: Geographic surveillance

Simpler anomaly detection methods fail to capture the relevant trends.
Subpopulation-level monitoring

• Answers the question, for whom should I intervene?
• **Main goal**: provide early warning for newly emerging subpopulation-level spikes/clusters of overdose deaths.
• We developed a novel detection method, **multi-dimensional tensor scan**, to detect emerging geographic, demographic, and behavioral patterns.
  • **Earlier detection** of emerging overdose clusters through daily surveillance runs.
  • Better characterization of where and who is affected.

![Image of a map with markers indicating areas of concern.]

**X** white males aged 20-49

**X**
Multidimensional Tensor Scan

• In a nutshell: we identify subspaces of the attribute space (a subset of values for each attribute) with higher than expected numbers of recent case counts.
  • Spatial area (subset of locations) and time window
  • Affected genders, races, age ranges, and which drugs involved.

• We use a novel tensor decomposition approach to estimate how many counts we expect for each combination of attributes, while maintaining computational efficiency.

• Iterative conditional optimization: optimize over all subsets of values for each attribute conditional on the current subsets of values for all other attributes.

• Each conditional optimization step can be performed very efficiently, without exhaustive searching over subsets, by fast subset scanning (Neill, J. Royal Stat. Soc. B, 2012).
Overdoses in Allegheny County, PA

• We analyzed* county medical examiner data for fatal accidental drug overdoses, 2008-2015.
• ~2000 cases: for each overdose victim, we have date, location (zip), age, gender, race, and the set of drugs present in their system.
• Reduced to 30 dimensions (age decile, gender, race, presence/absence of 27 common drugs) plus space and time.
• Clusters discovered by MD-Scan were shared with Allegheny County Dept. of Human Services.

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.


March 27 to April 21, 2015: 26 deaths county-wide from fentanyl, heroin only present in 11.

Started in the southeast suburbs of Pittsburgh and spread across the city.

Our method could have detected this pattern on **March 29**, identifying a cluster of four overdose deaths with strong geographic and demographic similarities.

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?
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?
Individual-level opioid use monitoring

- Seven years of de-identified data from over 1M individuals provided by Kansas prescription drug monitoring program (PDMP), with unique patient, prescriber, and dispensary identifiers.
- Duration and quantity of prescribed opioids are used to create timelines of morphine milligram equivalents (MME) for individual patients.
- Can we identify **early indicators** in patient MME timelines which are predictive of later opioid misuse or unsafe prescribing?
Individual-level opioid use monitoring

- Patients are clustered using the $k$-shape algorithm (Paparrizos & Gravano, 2015) to group patients with similar patterns in MME timelines.

- Are some patient clusters associated with higher risk of red flags indicating misuse or unsafe practices?

- For a new patient, can we confidently assess risk of future red flags given a partial MME timeline?
Red Flag Analysis by Cluster:
# of Unique Opioid Types

Average # of Opioid Types

Cluster ID

1 2 3 4 5 6 7 8 9 10
Red Flag Analysis by Cluster:
# of Unique Prescriber Zip Codes

Average Unique ZIPs

Cluster ID

1 2 3 4 5 6 7 8 9 10
Early individual-level risk assessment by classifying partial trajectories
Early individual-level risk assessment by classifying partial trajectories

Partial trajectory assigned **low risk** based on MME and cluster shape.
Early individual-level risk assessment by classifying partial trajectories

Partial trajectory assigned to high risk cluster #5, and higher MME → high risk
Conclusions

Here we described several new methods that can be used for **early warning** and **advance forecasting** of overdoses at the geographic, subpopulation, and individual levels.

Our retrospective analyses of overdose and opioid use data from Pennsylvania, New York, and Kansas suggest high potential utility for **prospective** drug overdose surveillance systems, to facilitate targeted and effective interventions.

We are currently collaborating with an interdisciplinary team of investigators and public health practitioners, with the goals of deploying targeted interventions to prevent overdoses and evaluating their effectiveness through randomized trials.
Thanks for listening!

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