New Methodological Approaches for Opioid and Overdose Surveillance

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This talk is based on joint work with **William Herlands** & **Dylan Fitzpatrick** (EPD Lab, Carnegie Mellon), **Fan Xiong** (Washington State DOH), and **Reyne Kenton** (Kansas State Board of Pharmacy). Thanks to **Eric Hulsey** (Allegheny County DHS) and **NCSU Laboratory for Analytical Sciences**.

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
  - <u>Targeting of interventions</u>: geographic (city, neighborhood) vs. subpopulation (demographics, SES, risk behaviors) vs. individual.

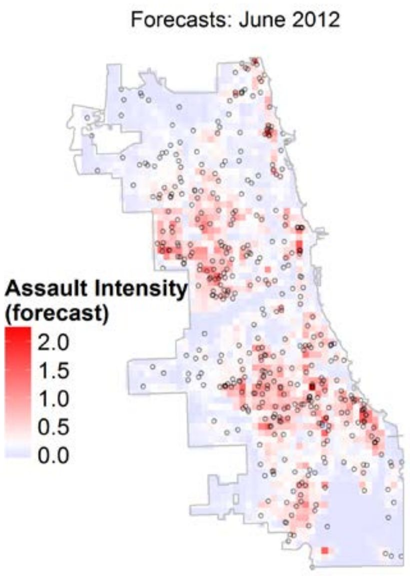
Geographic surveillance

- 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.



*SR Flaxman, AG Wilson, DB Neill, H Nickisch, AJ Smola. Fast Kronecker inference in Gaussian processes with non-Gaussian likelihoods. Proc. 32nd Intl. Conf. on Machine Learning, *PMLR* 37: 607-616, 2015.

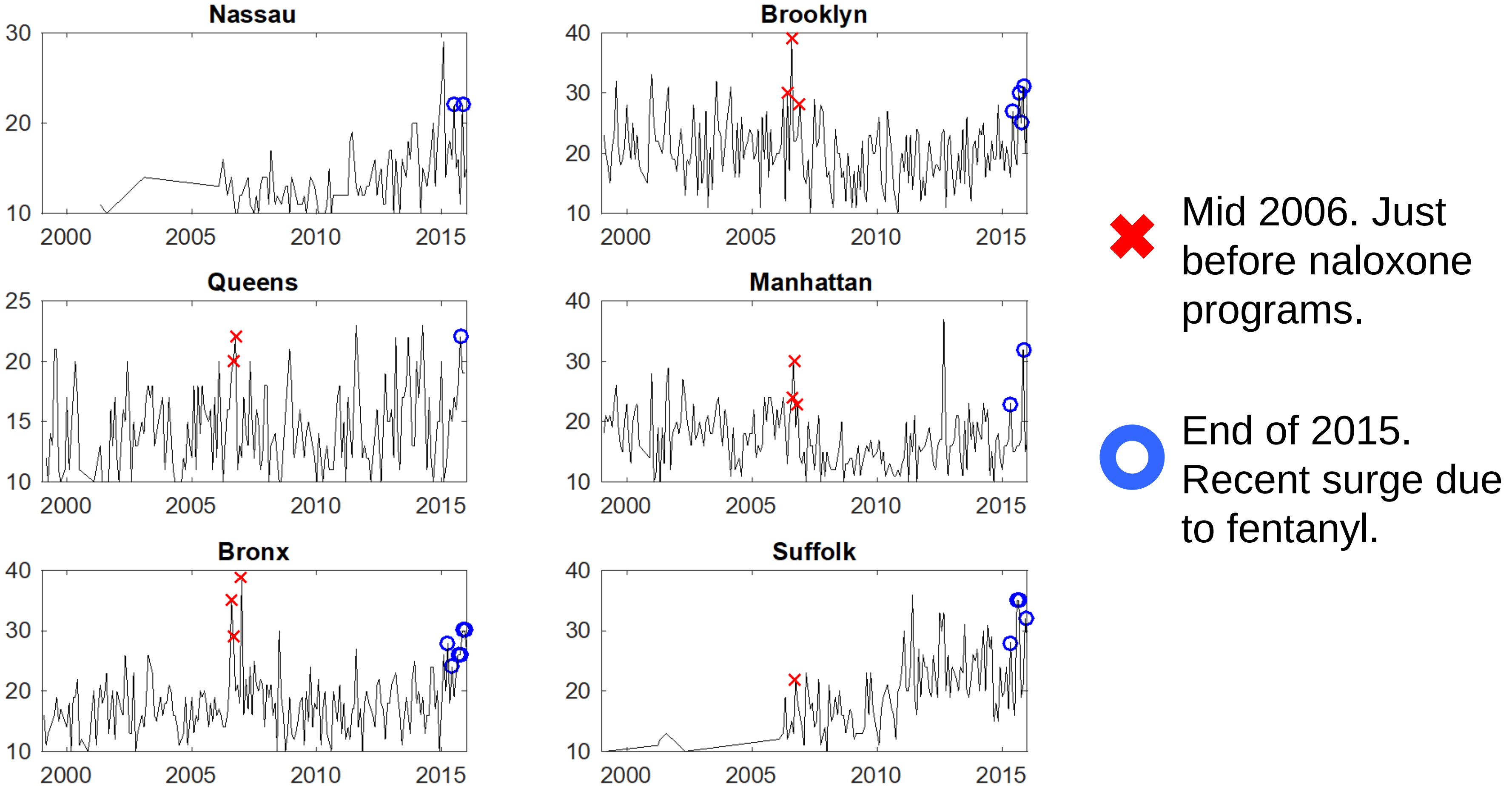
Case study: Geographic surveillance

- 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

*W Herlands, E McFowland III, AG Wilson, DB Neill. Gaussian process subset scanning for anomalous pattern detection in non-iid data. *Proc. 21st Intl. Conf. on Artificial Intelligence and Statistics, PMLR 84*: 425-434, 2018.

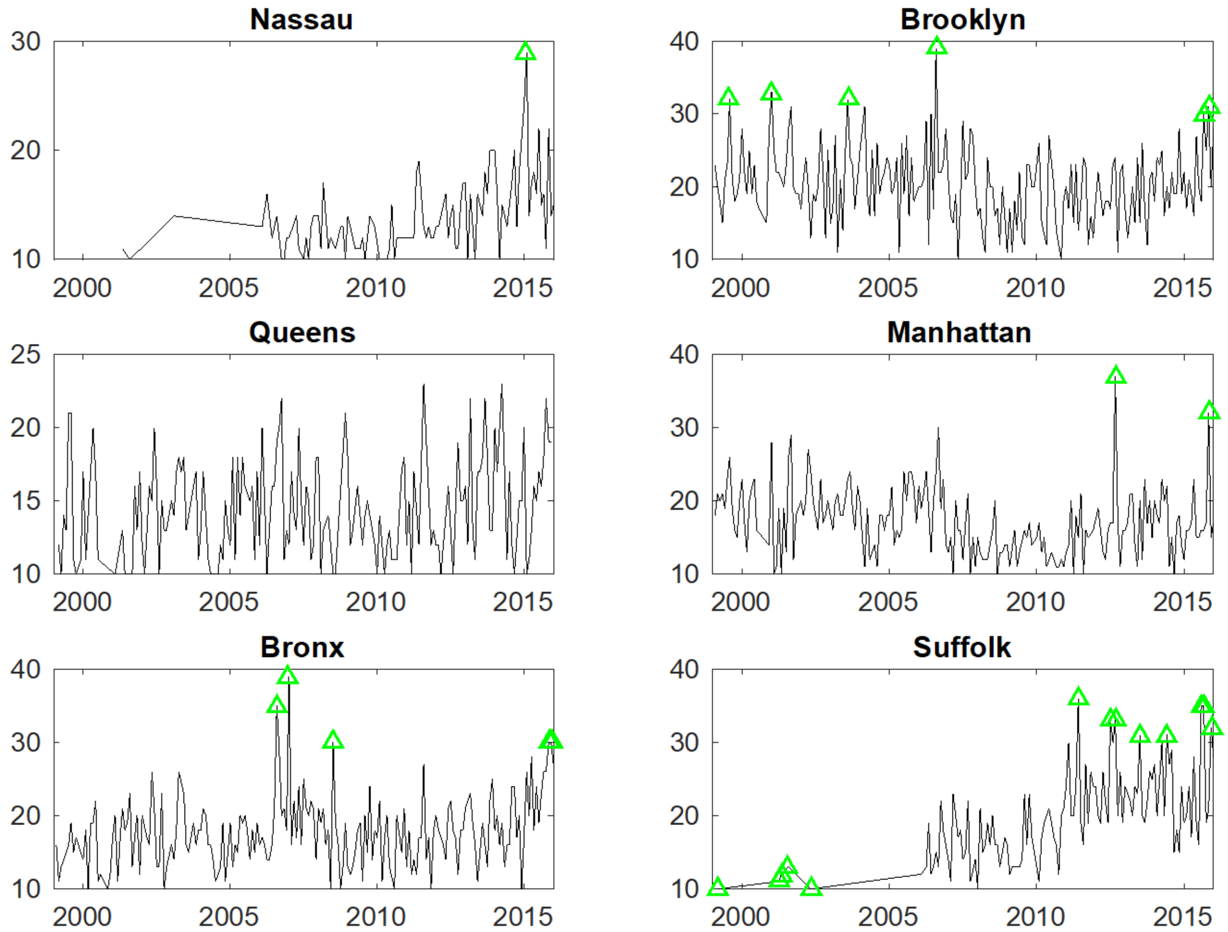
Case study: Geographic surveillance

Two statistically significant spikes in overdose cases:



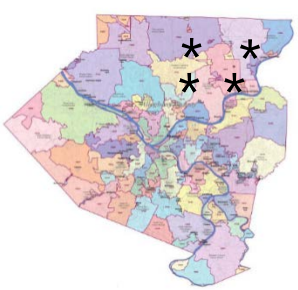
Case study: Geographic surveillance

Simpler anomaly detection methods fail to capture the relevant trends.



Subpopulation-level monitoring

- Answers the question, **for whom** should I intervene?
- <u>Main goal</u>: 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.



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.

*DB Neill, W Herlands. Machine learning for drug overdose surveillance. *J. Technology in Human Services* 36(1): 8-14, 2018.

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.

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?

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?

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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.

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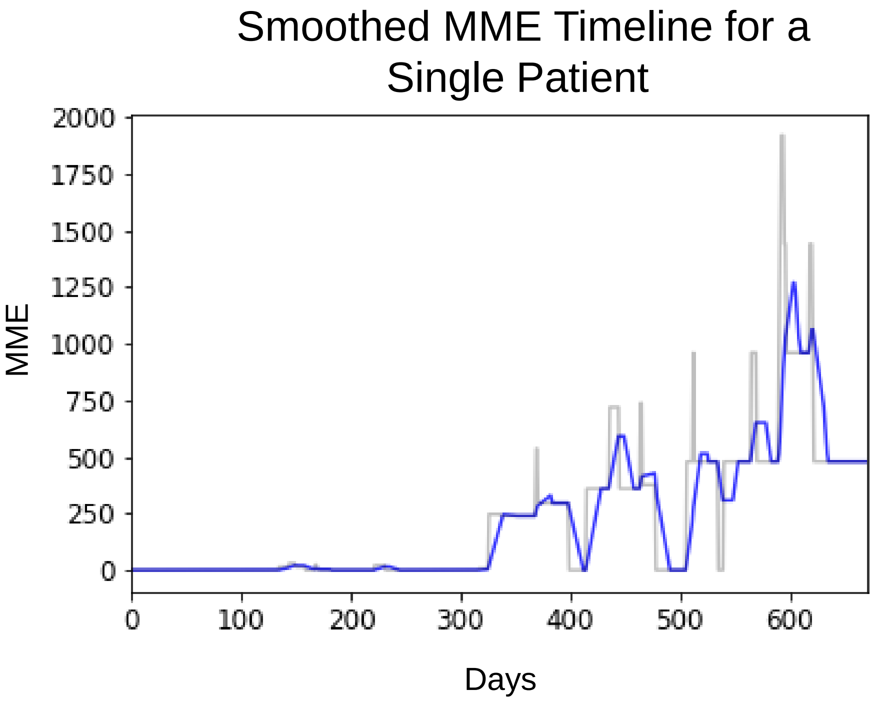
What factors could explain the dramatic reduction in M&X overdose clusters?

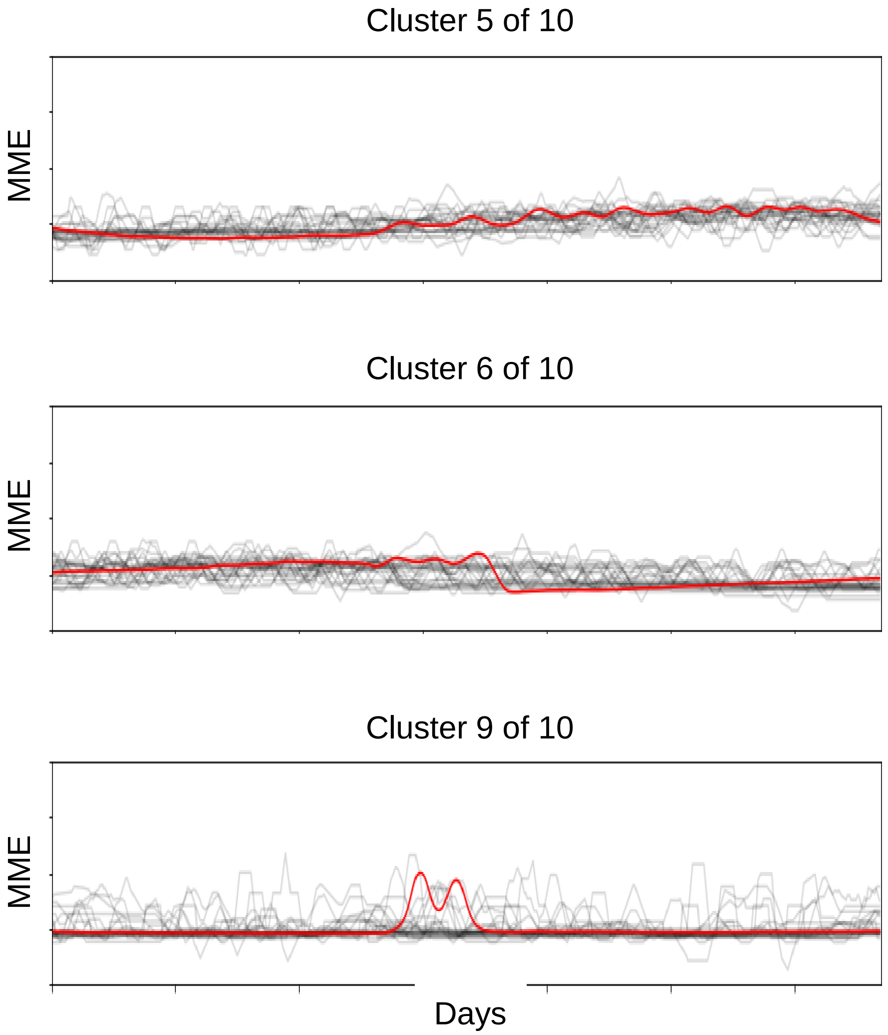
Individual-level opioid use monitoring

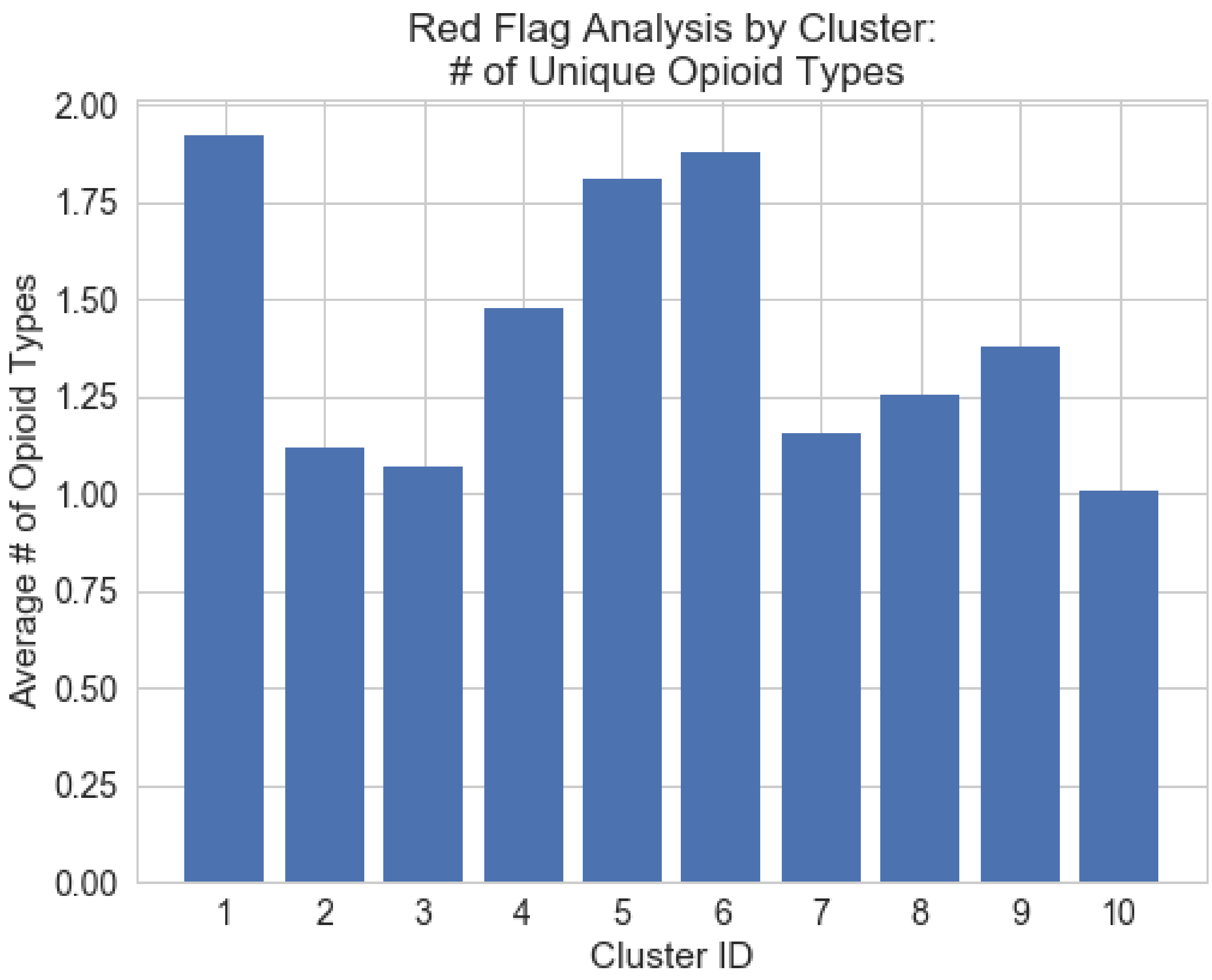
- Seven years of de-identified data from over 1M individuals provided by Kansas prescription drug monitoring program (PDMP), with unique patient, prescriber, and dispensary identifiers.
- Duration and quantity of prescribed opioids are used to create timelines of morphine milligram equivalents (MME)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

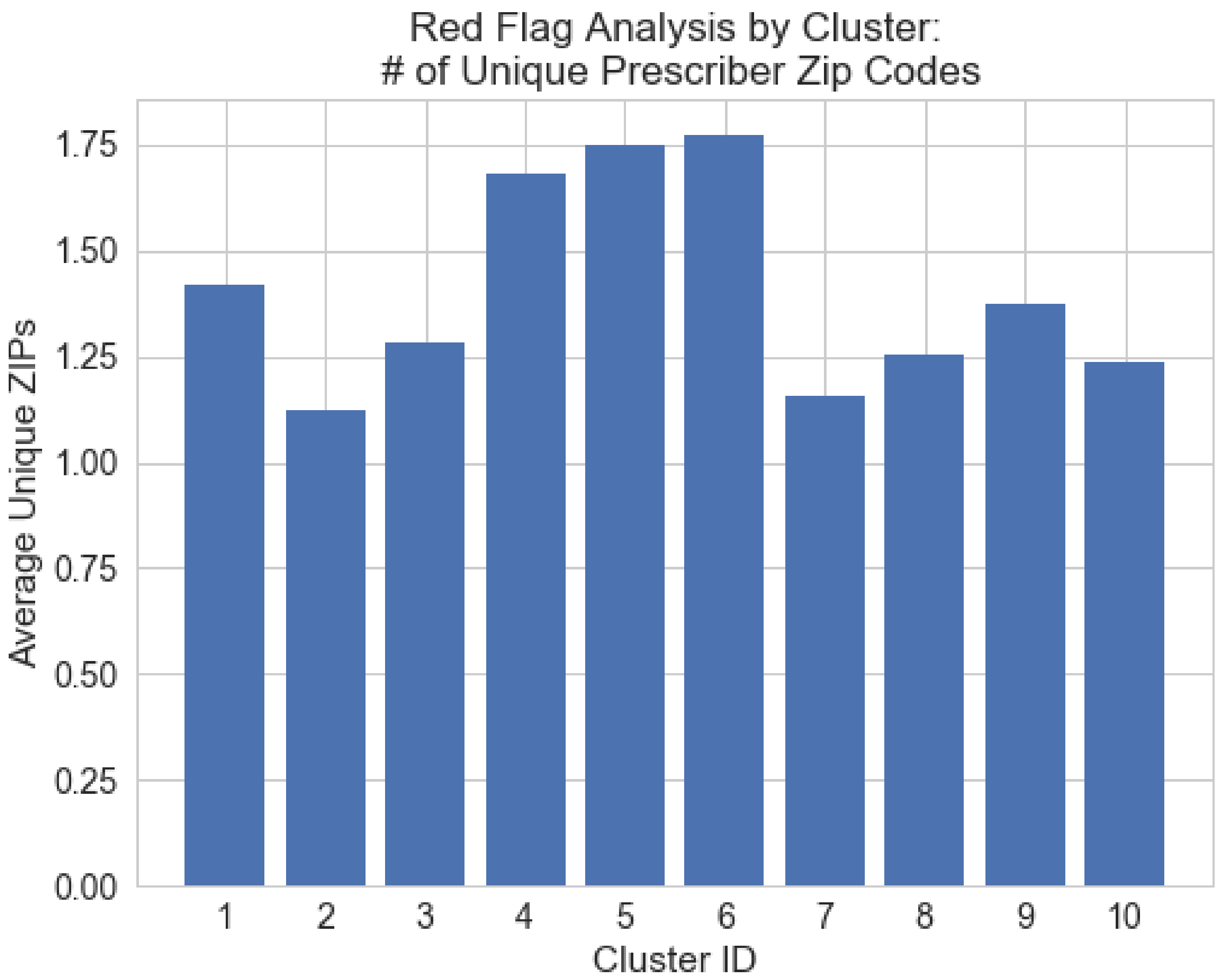


Individual-level opioid use monitoring

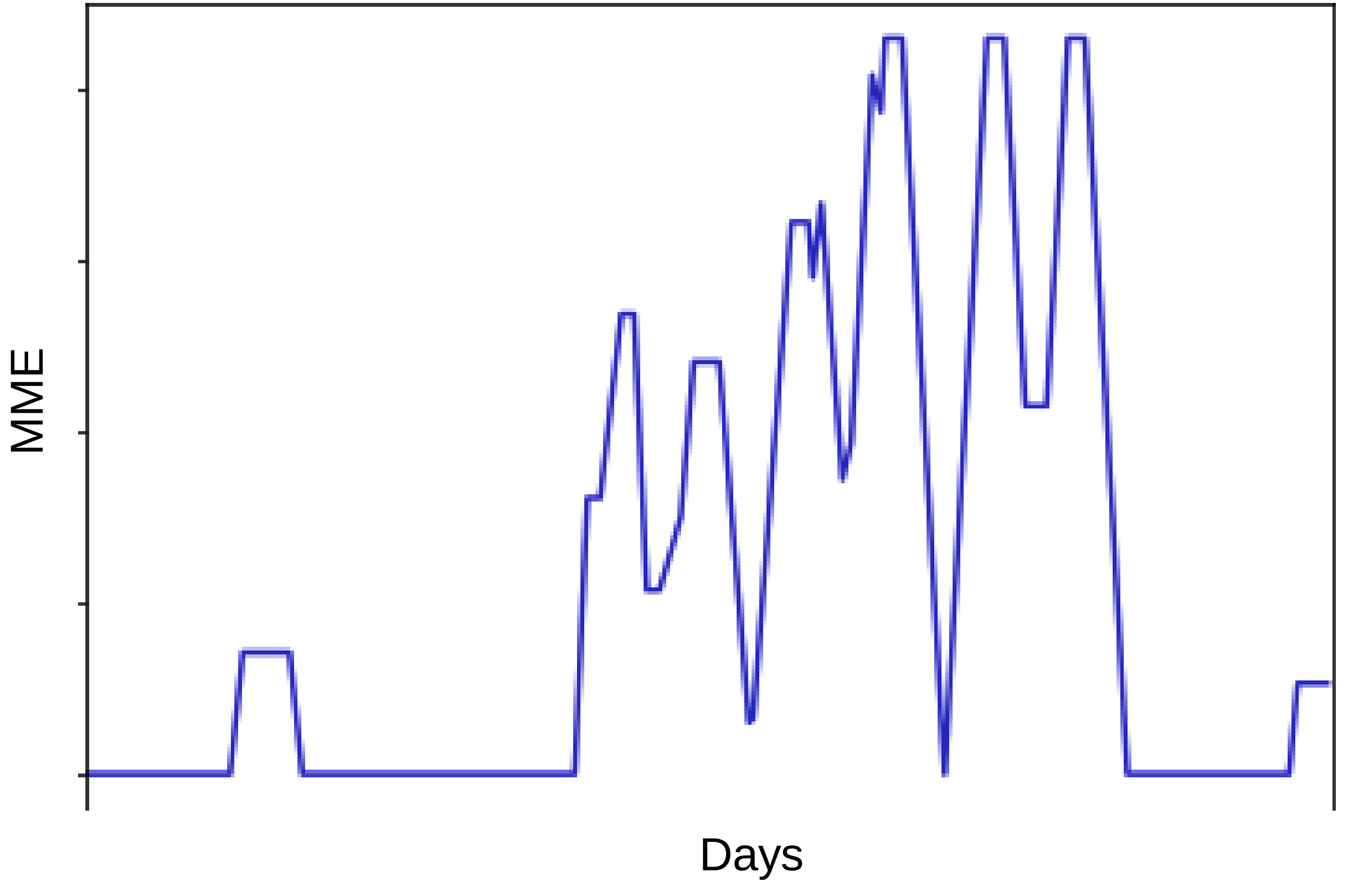
- Patients are clustered using the *k*-shape algorithm (Paparrizos & Gravano, 2015) to group patients with similar patterns in MME timelines.
- Are some patient clusters associated with higher risk of red flags indicating misuse or unsafe practices?
- For a new patient, can we confidently assess risk of future red flags given a partial MME timeline?



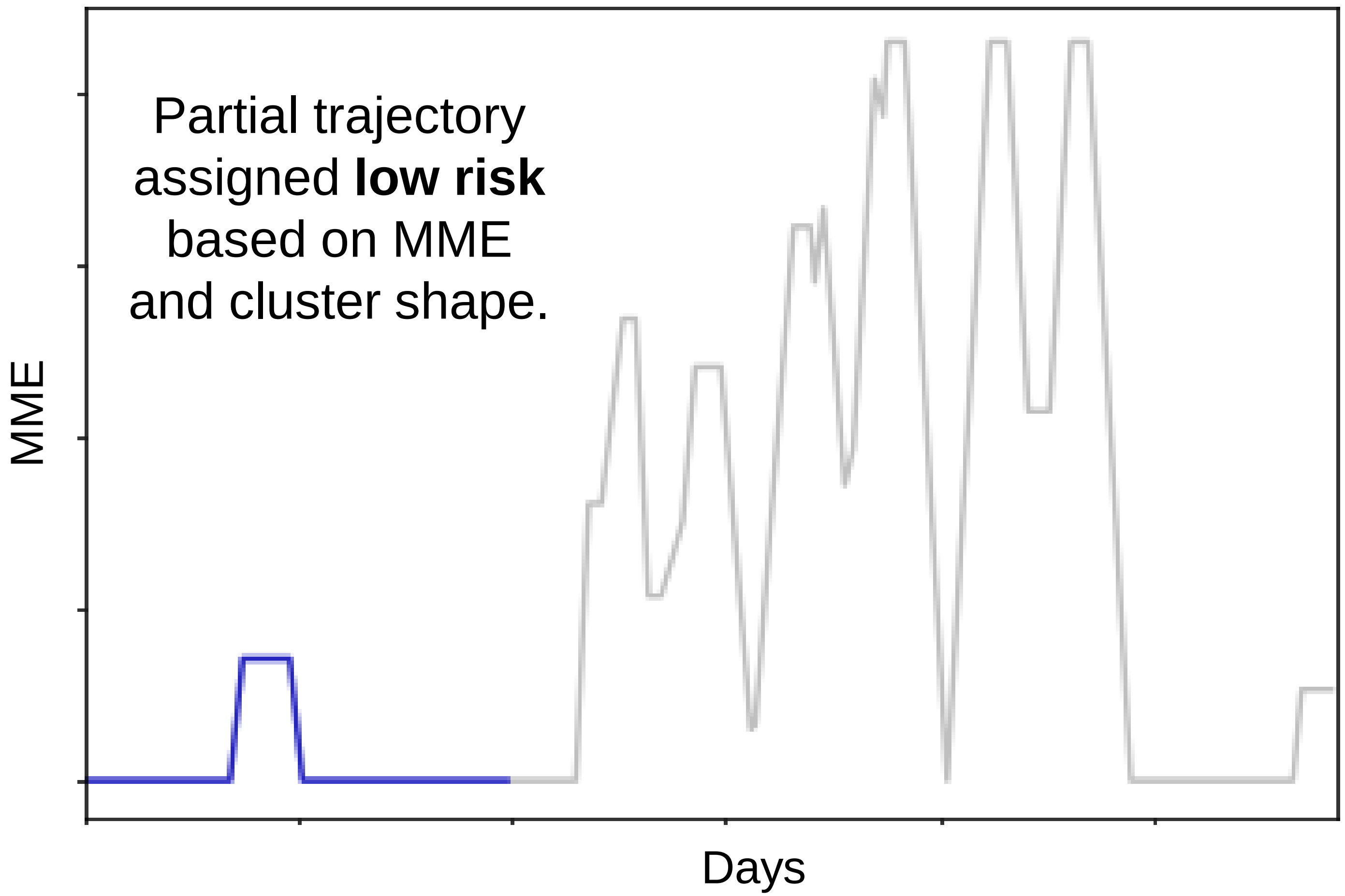

Red Flag Analysis by Cluster:
# of Unique Opioid Types
Average # of Opioid Types
0.00
0.25
0.50
0.75
1.00
1.25
1.50
1.75
2.00
1
2
3
4
5
6
7
8
9
10
Cluster ID


Red Flag Analysis by Cluster:
# of Unique Prescriber Zip Codes
Average Unique ZIPs
1.75
1.50
1.25
1.00
0.75
0.50
0.25
0.00
1
2
3
4
5
6
7
8
9
10
Cluster ID

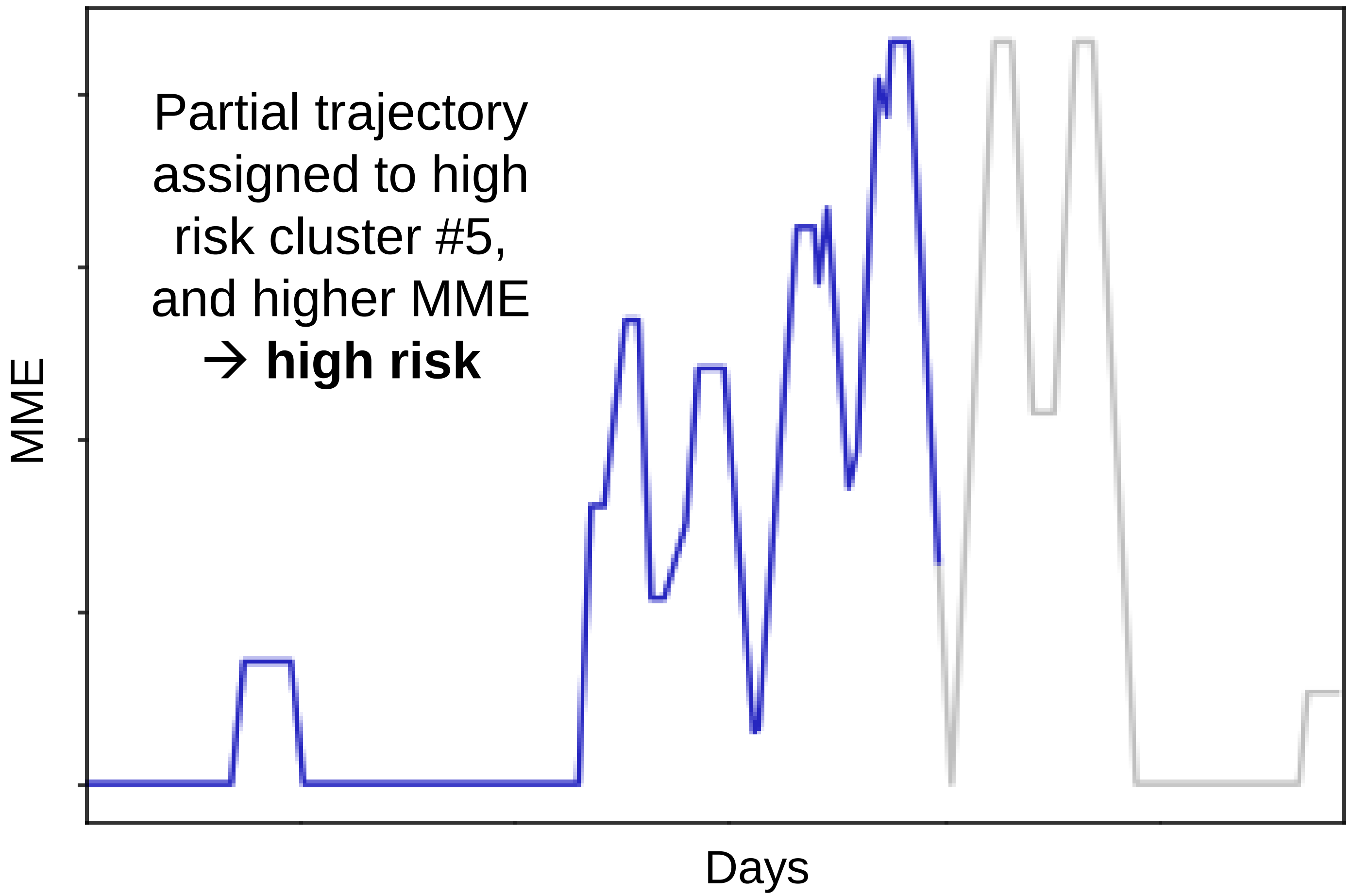
Early individual-level risk assessment by classifying partial trajectories



Early individual-level risk assessment by classifying partial trajectories



Early individual-level risk assessment by classifying partial trajectories



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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