Drug epidemiology based upon municipal wastewater testing

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Presentation Outline

• Overview of Current Drug Abuse Indicators & Measurement limitations
• Wastewater Treatment Plant (WWTP) drug testing- rationale and methods
• WWTP testing for addictive drugs findings
• Questions to consider when deciding upon whether and how to use WWTP testing
Overview of Current Drug Abuse Indicator Data & Measurement Issues
Drug Abuse Surveillance - Importance

- Detect new and changing drug trends
- Document persistent drug trends
- Used to allocate resources for prevention, treatment and intervention
Drug Abuse Surveillance – Current Limitations

• Lack of **geographic** resolution - current surveys provide national-level drug use/abuse data – little at region/state or sub-state level
• Lack of **temporal** resolution (annual data) and timely availability (e.g. DAWN ED report 1-3 years after data collection)
• **Population coverage** - Large portion of drug-using community currently excluded
• Small # of “events” in many jurisdictions
Measurement Bias Examples

• Mortality data: only true population-level data
  – ‘Tip of the iceberg’ since mortality is biased toward more lethal drugs and generally lags behind entrance of drugs into ‘market’

• Current surveys usually:
  – Rely on self-reporting
    • Social desirability bias
    • Don’t know actual composition of drugs used
  – Exclude populations such as prisoners, unhoused

• ER and overdose data only for large cities

• Poison control center calls may decline as physicians recognize drug-related health problems and develop experience in treatment
Example - Annual trend data

Drug caused deaths, King County WA

- Small numbers, lots of noise (region with 2.2 million people)
- Fairly common drugs may have low lethality or vice versa
- Rapid changes over a few years mean data being compared must be from same time frame e.g. fentanyl
- Very reductionistic, most people use multiple drugs
Example- Trends by time and place

Police evidence testing

Fentanyl cases more than doubling in Q2 2020 versus average quarter in prior 3 years

- Analytic chemistry
- Small numbers
- Impacted by changes in police focus, priorities, procedures
- May not be comparable across time and place
Wastewater Treatment Plant (WWTP) drug testing - Rationale and methods
**Raw Wastewater Influent**

- Conveniently ‘focused’ and sampled at a central location
- Least amount of degradation compared to effluent
- Preserves privacy of individuals
- Samples collected daily
- Known flows for calculation of loads
WWTP derived data attributes

• Cover much of the population
  – Though areas with septic not covered
• Known catchment/geographic areas
• Generally follow political boundaries
  – Aids comparisons with other data types
  – Increases utility for local planners
• GIS/Mapping data often available from local municipalities
WWTP derived data attributes

- Drug specific
- Timely- available with short lag
- Time scale-able (within day, day, month, year)
- Geographically scale-able (could aggregate municipalities or go “up-stream”)
Population covered by WWTP

WWTPs provide coverage to 85% of the population of King County, WA based upon place of residence: 1,482,427 of 1,737,034 residents
Wastewater Catchment Areas for King County Area

- Multiple places
- Moderate size
- Alignment with cities varies
EMCDDA
INSIGHTS
Assessing illicit drugs in wastewater
Potential and limitations of a new monitoring approach

Table of contents
• Introduction to sewage epidemiology
• Estimating community drug use
• Drug metabolism
• On the occurrence and fate of illicit substances in sewer systems
• Georeferenced wastewater sampling and applied spatial statistics
• Integrating wastewater analysis with conventional approaches to measuring drug use
• Overall conclusions
Sample Collection and Preparation

- 24 hr, flow-normalized composites of raw WWTP influent
- 125 mL HPDE bottles, frozen
- Centrifuge 2350 rpm for 14 min
- 6 mL in autosampler vial, spike with internal standards + 20 µL 0.1% acetic acid
  - LOQ = low ng/L
  - Precision = < 10%
  - Matrix effects addressed by internal standards
Chemical analysis-

**LC-MS/MS Analysis and SPE**

- Illicit drugs are most frequently analyzed by liquid chromatography-tandem mass spectrometry (LC-MS/MS). These compounds are small molecules, often polar, and generally nonvolatile, characteristics suited to LC-MS/MS which provides unambiguous determination of the analyte (compound being analyzed) because of the technique’s selectivity. The chromatography separates analytes based on their physical and chemical properties causing different retention times through the stationary phase of the analytical column.

- Due to the low concentrations of drugs and their metabolites in wastewater, analysis is typically first performed with a concentration step to magnify the concentration of the analytes. Typically this extraction and concentration step is done with solid phase extraction (SPE).

Courtesy of Daniel Burgard University of Puget Sound
Sample analytical output

A) + MRM (300.2 -> 199.0) M-DRUG-20190815_MP2.d
   Counts
   Hydrocodone
   Acquisition Time (min)
   5.128 min.

B) + MRM (337.2 -> 188.1) M-DRUG-20190815_MP2.d
   Counts
   Fentanyl
   Acquisition Time (min)
   6.984 min.

C) + MRM (304.3 -> 182.3) M-DRUG-20190815_MP1.d
   Counts
   Cocaine
   Acquisition Time (min)
   6.790 min.

+ MRM (286.1 -> 199.2) M-DRUG-20190815_MP2.d
   Counts
   Nor-hydrocodone
   Acquisition Time (min)
   5.182 min.

+ MRM (233.2 -> 84.1) M-DRUG-20190815_MP2.d
   Counts
   Nor-fentanyl
   Acquisition Time (min)
   6.596 min.

+ MRM (290.3 -> 168.3) M-DRUG-20190815_MP1.d
   Counts
   Benzoylcegonine
   Acquisition Time (min)
   6.692 min.

Courtesy of Daniel Burgard University of Puget Sound
Human Urinary Biomarkers

- Calculated loads cannot account for changes in population (e.g., commuters, students, etc).
- Population served on any given sampling day may vary significantly from the ‘stated’ populations.
- **Human urinary biomarkers** can be used to normalize wastewater data (e.g., ratio drugs to biomarkers).

Nicotine/Cotinine
- Metabolite of nicotine
- Sales of nicotine
- Available by zip code

Caffeine
- Wide consumption

Creatinine
- Drug test standard
Dealing with <LOD and <LOQ

• Approaches sometimes used
  – treat results <LOD (and <LOQ) as 0
  – replace values between LOD & LOQ with a constant such as a mid-point

• However, these approaches have been shown to lead to biased results (Helsel, 2009).

• Appropriate statistical approaches exist to dealing with data that are “censored”.
Point Estimate + Error

- Incorporating error components
  - Analytic - provide by lab
  - Flow - literature
  - Sampling - estimated via modeling* (Ort)
  - Population - use city’s commute data (e.g. 31%/2)

\[
\sqrt{(\text{Analytical error})^2 + (\text{Flow error})^2 + (\text{Sampling error})^2 + (\text{population estimate error})^2} \\
5\% \quad 20\% \quad 20\% \quad 15.5\%
\]

0.034 +/- \sqrt{(0.0017)^2 + (0.0068)^2 + (0.0068)^2 + (0.0053)^2}

0.034 mg/p/d +/- 0.011 ; 0.023 - 0.045 mg/p/d ; 0.034 mg/p/d +/- 33%
Sample data presentation

Methamphetamine (top panel) and MDMA (bottom) index load distribution (mg/person/day).

Using wastewater-based epidemiology to estimate drug consumption—Statistical analyses and data presentation

Data trade offs

• With survey data you may end up with narrow confidence bounds around an estimated value that is likely wrong/biased
• With WWTP data you may end up with a large confidence bound around an estimate that is accurate
Essential data comparison problem

WW is Total Population

Everything else is not

- Missing highest frequency users
- Only high frequency users
- Populations being compared don’t align well
Questions to ask yourself

Questions to start with:
• What are the target analytes?
• What do they represent?
  – At the total population level
• Degradation, metabolismization
• What loads are likely present?
• Chemical structure impact analysis?
• Do I want to know
  – The exact level
  – The trend
  – Whether a drug is present or not
Interdisciplinary

• Expertise needed: chemistry, toxicology, engineering, medical and public health practice, pharmacology, epidemiology...