Estimating opioid use through wastewater epidemiology

Opioid use in a population can be estimated by analyzing the concentration of opioid metabolites in wastewater. This is possible because individuals that use drugs or pharmaceutical products excrete modified versions of the drugs (metabolites) in urine or stool, and those metabolites get naturally aggregated in the wastewater infrastructure. The field of wastewater epidemiology started more than a decade ago with scientific work carried out by European researchers (Castiglioni *et al*., 2006).

Normalization and estimation of use

Biobot applies a published method to convert concentrations of opioid metabolites into estimates of average opioid use (Zuccato *et al*., 2008). It is important to notice that each step in the calculation requires additional assumptions and data, therefore *Biobot* reports all metrics.

1. Calculate **average opioid excretion rate** (mg / day / 1000 people):

Equation 1:

$$Average\ excretion\ rate\ of\ drug\ X\ [mg/day/1000\ people] = \frac{Concentration\ metabolite\ Y\ x\ Daily\ flow\ rate}{Population\ size}$$

Concentration metabolite Y [mg/L]: Concentration of opioid metabolite Y in wastewater composite sample collected over 24 hours as measured by liquid chromatography mass spectrometry.

Daily flow rate [L/day]: Average daily volumetric flow rate at the manhole where wastewater is sampled.

Population size [1000 people]: Population size in catchment as estimated from census data.

The largest source of uncertainty for Eq.1 is the catchment population size. Census data could over- or under-estimate the amount of people represented in the wastewater sample. Biobot is developing proprietary analytics to estimate population size from the wastewater sample itself to replace census estimates.

2. Calculate **average opioid use rate** (mg / day / 1000 people) by applying correction factors to average opioid excretion rate:

Equation 2:

$$Average\ consumption\ rate\ of\ drug\ X\ [mg/day/1000\ people] = \frac{Average\ excretion\ rate}{Fraction\ in\ urine} x \frac{Mol.weight\ parent\ drug\ X}{Mol.weight\ metabolite\ Y}$$

Average excretion rate [mg/day/1000 people]: see Equation 1.

Fraction in urine: Fraction of parent drug X that is excreted as metabolite Y in urine.

Mol. weight parent drug X: Molecular weight of opioid parent drug X.

Mol. weight metabolite Y: Molecular weight of opioid metabolite Y.

The largest source of uncertainty for Eq. 2 is the fraction of parent drug X that is excreted as metabolite Y in urine. Excretion ratios may vary across users and method of use, and may not be known at all for new drugs on the street.

3. Calculate **number of average use units** (# of doses / day / 1000 people):

Equation 3:

$$Average\ consumption\ units\ of\ drug\ X\ [\#\ of\ doses/day/1000\ people] = \frac{Average\ consumption\ rate}{Pure\ active\ drug\ X\ in\ average\ dose}$$

Average use rate [mg/day/1000 people]: see Equation 2.

Pure active drug X in average dose [mg/dose]: The amount of pure active drug X in average dose.

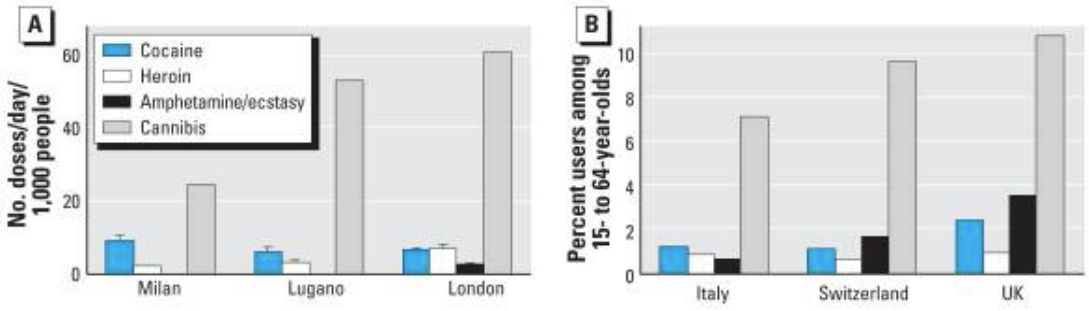
The largest source of uncertainty for Eq. 3 is the average dose of drug X, as this may vary considerably across users and method of use. The amount of pure active drug in a dose may not be known for street drugs.

Validation

Despite its limitations, drug consumption estimates from wastewater have been shown to be in agreement with other sources of data:

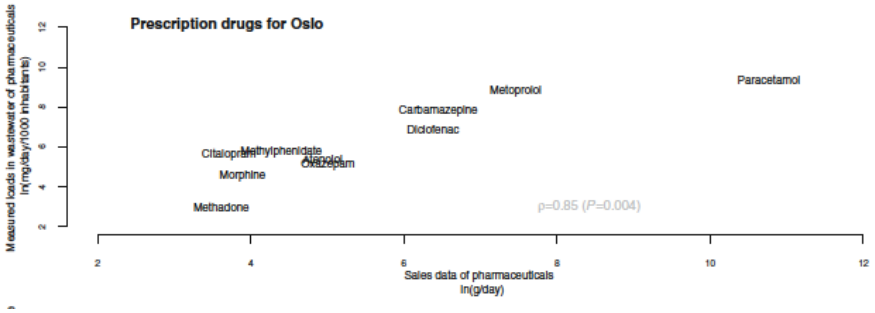
a) Validation of illicit drug use with drug surveys

Zuccato et al. (2008) compared local profiles of illicit drug use measured in wastewater (# of doses/day/1000 people) and national profiles of drug use (% users among persons 15-64 years old). Estimates of cocaine, heroin and cannabis consumption were in agreement. Consumption of amphetamine-type drugs was harder to estimate because metabolites in wastewater were less abundant.



b) Validation of prescription drug use with prescription data

Baz-Lomba et al. (2016) showed a high correlation between pharmaceuticals measured in wastewater and pharmaceuticals sales data in Oslo, confirming that wastewater data could be used with certainty to estimate drug use.



Data interpretation

Estimates of opioid use are useful for:

- Analyzing trends over time and geography, that is, to look at relative changes from a reference point.

These estimates are NOT useful for:

- Case finding, that is, to try to find heavy users in a population. If the method reports 10 doses / day / 1000 people in a community, it is NOT possible to know if this represents one person taking 10 doses or 10 people taking one dose.

Appendix. List of opioid drugs in *Biobot's* panel

Parent drug	Category
Heroin	Illicit
Fentanyl	Illicit
Codeine	Prescription
Oxycodone	Prescription
Tramadol	Prescription
Methadone	Substitution therapy
Buprenorphine	Substitution therapy
Naloxone	Substitution therapy and overdose reversal

Additionally, Biobot measures the concentrations of metabolites of morphine, oxymorphone, hydromorphone, hydrocodone and dihidrocodeine to make a bulk estimate of any opioid use.

References

Baz-Lomba, J.A. (2016) Comparison of pharmaceutical, illicit drug, alcohol, nicotine and caffeine levels in wastewater with sale, seizure and consumption data for 8 European cities. *BMC Public Health*

Castiglioni, S. *et al*. (2006) Identification and Measurement of Illicit Drugs and Their Metabolites in Urban Wastewater by Liquid Chromatography-Tandem Mass Spectrometry. *Analytical Chemistry*

Jacox, A. *et al*. (2017) Quantitative Analysis of Opioids and Cannabinoids in Wastewater Samples. *Forensic Sciences Research*

Zuccato E. et al. (2008) Estimating Community Drug Abuse by Wastewater Analysis. *Environmental Health Perspectives*