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Sewage-based Epidemiology Requires a Truly Transdisciplinary Approach

If asked whether you had consumed illicit drugs recently, would you admit it? If yes, could you precisely recall types of drug, times and amounts used? If you were the person commissioned with the task of quantifying drug use, what approach would you use given the social stigma attached with such behavior? We measure drug residues in sewage, which represents urine of entire populations, to provide an objective estimate of total drug use in a region. In transdisciplinary projects, sewage-based results provide valuable information at unrivaled spatiotemporal resolution complementing traditional data.

Christoph Ort, Caleb J. Banta-Green, Lubertus Bijlsma, Sara Castiglioni, Erik Emke, Coral Gartner, Barbara Kasprzyk-Hordern, Malcolm J. Reid, Jörg Rieckermann, Alexander L. N. van Nuijs

Sewage-based Epidemiology Requires a Truly Transdisciplinary Approach | *GAIA* 23/3 (2014): 266–268
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Context and Transdisciplinarity

Directly and indirectly, illicit drug use causes substantial global health problems and social harms (e.g., overdose, blood borne viruses, violence) (Degenhardt and Hall 2012). Accurate and reliable data on illicit drug consumption is needed to plan and assess the impact of interventions aimed at reducing drug use. Traditional monitoring methods that rely on self-report (e.g., population surveys) may underestimate drug use because it is an illegal, stigmatized activity. Additionally, these methods are expensive, time-consuming and incomplete (Banta-Green and Field 2011). Therefore, scientists have developed an innovative, complementary method of estimating community drug use by quantifying drug residues in sewage, which contains urine from the entire population: they 1. collect a sewage sample, 2. measure concentrations of drug residues in the samples, 3. calculate sewage drug loads (concentrations multiplied by sewage volume), 4. correct for human metabolism (excretion rate), and 5. normalize total loads with population size.

To ensure reliable results, sewage-based epidemiology (SBE) requires significant expertise from numerous disciplines: environmental engineers design sample collection to guarantee that sewage samples are representative of the community's excreted urine; analytical chemists develop methods to accurately quantify drug residues; environmental chemists investigate transformation in sewers; pharmacologists define the identity and amounts of excreted drug residues to estimate total consumption; epidemiologists identify how this information can complement traditional methods to estimate prevalence of substance use; and social scientists assess ethical aspects of sewage analysis.

This paper does not describe the outcomes of a specific project, but emphasizes the beneficial collaboration of individuals with a mutual interest, at various levels – without the involvement of specific funding and virtually no extra administration.

Sewage Systems, Sampling and Chemical Analysis

Flushed via toilets, excreted drug residues in sewers can be subject to high short-term dynamics and diurnal variations. Both need to be considered to obtain a representative sample (Ort et al. 2010). A thorough experimental design assesses the definition of catchment area, hydraulic properties and the sampling setup, which are elicited from utilities with specifically tailored questionnaires (Castiglioni et al. 2013). Typically, a sample of 500 milliliters of raw sewage, filtered and stabilized until analysis, is sufficient. Analyte concentrations are at the low nanogram per liter level which necessitates sample clean-up, pre-concentration and subsequent chemical analysis via highly specific and sensitive techniques, normally based on liquid chromatography coupled to tandem mass spectrometry (Van Nuijs et al. 2011).

Contact: *Dr. Christoph Ort* | Swiss Federal Institute of Aquatic Science and Technology (Eawag) | Urban Water Management | Ueberlandstr. 133 | 8600 Dübendorf | Switzerland | Tel.: +41 58 7655277 | E-Mail: christoph.ort@eawag.ch

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Back-calculation and Uncertainty

The analyte of choice in SBE is generally the primary urinary metabolite of the drug of interest. To differentiate between actual consumption and direct disposal of unused drugs, enantiomeric profiling can be applied with the usage of chiral chromatography coupled to mass spectrometry (Kasprzyk-Hordern and Baker 2012). To facilitate comparison among cities and to estimate consumption, sewage drug loads are normalized by the number of people and corrected for excretion rates of the metabolite and drug purity. Excretion rates are available from clinical studies, and drug purity is determined through analysis of drugs from local seizures or test purchases. Interestingly, a reliable estimate of the population contributing to the sewage is difficult: census may be outdated or not coincide with the geographical boundary of a sewer catchment, and accounting for commuters and tourists is challenging. One solution is to measure simultaneously specific compounds in the sewage samples to estimate population size. Ideally, a ubiquitous biomarker could be found that has no other source than human excretion and is stable during transport in sewers (Chen et al. 2014). So far, pharmaceutical residues have been successfully combined with Bayesian inference (O'Brien et al. 2014). Although transformation of certain drugs during transport in sewers may affect SBE, this is just starting to be investigated (Thai et al. 2014).

In most cases, sewage-based estimates of substance use – as pure substance per 1,000 people per day – have an uncertainty of about 40 percent. While this uncertainty may seem large, it is considered acceptable by epidemiologists as there is lower risk of the estimates being biased. By contrast, other monitoring methods (e.g., surveys) may have narrow variability components, but higher risk of bias. Currently, the estimation of the number of doses or even of individual users based on sewage samples requires a series of assumptions and remains speculative. Nevertheless, some studies have shown good qualitative agreement between sewage-based estimates and other data (Reid et al. 2012).

Applications, Ethical Considerations and Outlook

Most studies aimed at regional or national estimates of drug use, but international comparisons exist now (see figure). Sewage analysis can be carried out at high temporal frequency and spatial resolution. Daily variations can be identified (e.g., a weekend-effect for cocaine and ecstasy), and intra-day variability might discriminate between commuters and permanent residents (Brewer et al. 2012). The approach also allows investigating holiday periods, special events in sports or music with permission from the organizers (Lai et al. 2013). Given the negligible risk of (in)direct harm >

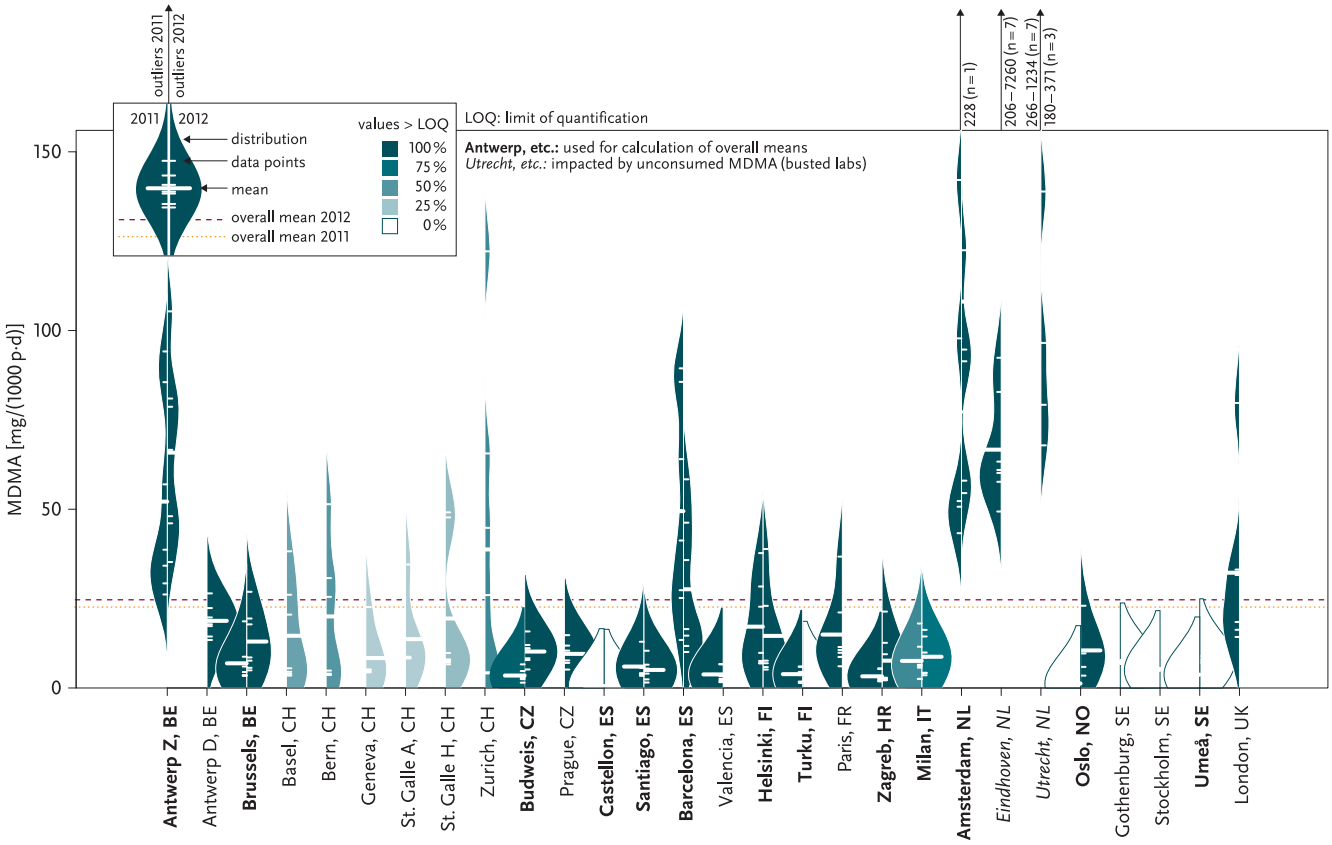

FIGURE: Population-normalized ecstasy (MDMA) sewer loads during two one-week periods (seven daily samples each) in 28 sewage treatment plant catchments (adapted from Ort et al. 2014).

to residents, minimal ethical issues are expected for SBE in large, general populations (≥ 10,000 people) if findings do not relate to specific groups (e. g., a disadvantaged suburb) (Hall et al. 2012).

SBE is not limited to illicit drugs. Examples encompass antihistamine use in the general population (Reid et al. 2011) or Attention Deficit Hyperactivity Disorder medications used by students during semester and examination periods (Burgard et al. 2013). Identifying doping used by athletes was suggested but may prove difficult due to sampling issues and other practical aspects (Harman et al. 2011). It is expected that SBE can expand to further public health aspects (e. g., lifestyle and diet) (Thomas and Reid 2011), and may serve as an early warning system in case of pandemics.

Collaboration with various stakeholders from, for example, public health and drug prevention institutes, forensics and law enforcement is now envisaged to apply SBE meaningfully in a local, relevant context. The innovative co-production of knowledge requires diverse perspectives from an early project stage onwards to reach the desired societal impact.

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CONTRIBUTING AUTHORS

Dr. Christoph Ort
Dr. Jörg Rieckermann
both: Swiss Federal Institute of Aquatic Science and Technology (Eawag), Dübendorf, Switzerland

Dr. Caleb J. Banta-Green
University of Washington, Alcohol and Drug Abuse Institute, Seattle, WA, United States

Lubertus Bijlsma, MSc
University Jaume I, Research Institute for Pesticides and Water, Castellón de la Plana, Spain

Dr. Sara Castiglioni
IRCCS – Istituto di Ricerche Farmacologiche Mario Negri, Department of Environmental Health Sciences, Milan, Italy

Erik Emke, BSc
KWR Watercycle Research Institute, Nieuwegein, The Netherlands

Dr. Coral Gartner
The University of Queensland, UQ Centre for Clinical Research, Royal Brisbane and Women's Hospital, Herston, QLD, Australia

Dr. Barbara Kasprzyk-Hordern
University of Bath, Department of Chemistry, Bath, United Kingdom

Malcolm J. Reid, BSc (Hons)
Norwegian Institute for Water Research (NIVA), Oslo, Norway

Dr. Alexander L. N. van Nuijs
University of Antwerp, Toxicological Center, Antwerp, Belgium

Christoph Ort

Born 1974 in Zurich, Switzerland. 2006 PhD in environmental engineering (ETH Zurich). 2008 to 2010 postdoc at the Advanced Water Management Centre (University of Queensland, Australia). Since 2011 group leader in the Urban Water Management Department (Eawag), Dübendorf, Switzerland. Research interests: water-related urban pollutant fluxes, modeling, sewer processes, sampling and monitoring design, source typing and tracking.