DroMedArio Project
Methodological Report

Drogen, **Med**ikamente, **A**lkohol- und Tabak**r**ückstände:
Abwasserbas**i**erte Epidemi**o**logie in der Schweiz
(Illicit drugs, pharmaceuticals, alcohol and tobacco residues:
wastewater-based epidemiology in Switzerland)

Client: FOPH
Project partners: Eawag and UNIL
Term of project: 2021-2024

Introduction/concept

In the DroMedArio project, substances of abuse and their metabolites are analyzed in wastewater to serve as independent indicators of community-wide consumption.

Up to now, the use of addictive substances has been investigated mainly by means of surveys to assess self-consumption (self-assessment), statistics from the police/health services and sales figures for pharmaceuticals. Analysing wastewater is a way of obtaining anonymous and timely information on consumption at the community level. It is important to note that wastewater data do not contain information about individuals. Wastewater analysis should not be seen as a substitute for traditional methods of estimating consumption, but as a complementary tool that allows regular estimates of consumption trends and comparison with other data sources.

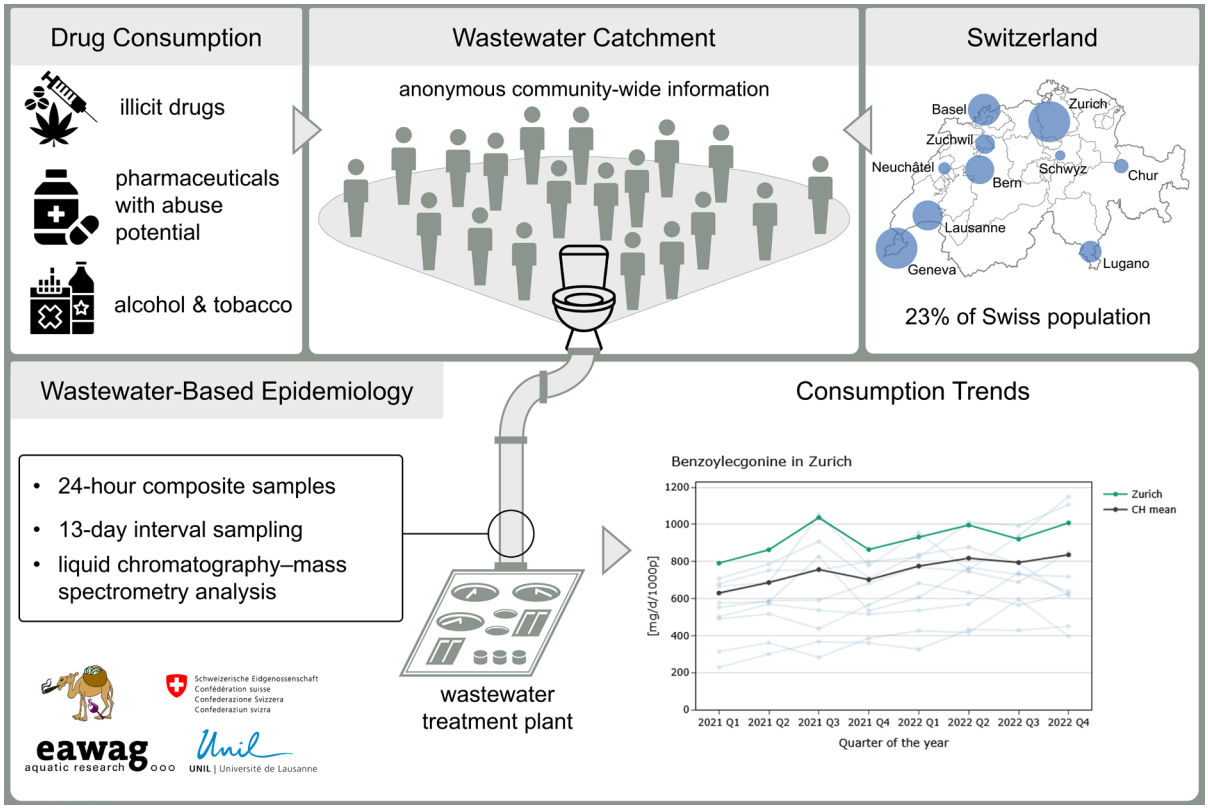

Figure 1: DroMedAri project overview

Wastewater-based epidemiology

Wastewater-based epidemiology is a scientific discipline based on the analysis of human excreta in municipal wastewater to study the temporal and spatial distribution of indicators of human population health. Typically, this involves analysing flow proportional 24-hour composite samples that are collected at the influent of wastewater treatment plants. These samples contain anonymous, community-wide information on the drug/pharmaceutical consumption, health conditions and exposure to foreign chemicals and pathogens of the population in the catchment area.

Substances

Chemicals that are ingested, unconsciously absorbed or produced in the human body and leave traces in excreta are potential subjects for wastewater-based epidemiology studies. Such traces may represent unchanged parent compounds or metabolic products.

The concept of wastewater-based epidemiology has been used to study community-wide consumption of illicit drugs, pharmaceuticals, diet and lifestyle products and the exposure to industrial chemicals, pesticides and pathogens.
The analysis of endogenous and exogenous substances in wastewater can also provide information on the health status of the population in the catchment area.
In recent times, wastewater-based epidemiology (WBE) has gained attention for its efficiency in monitoring pathogen exposure, as evidenced during the Covid-19 pandemic through the analysis of SARS-CoV-2 genetic material in wastewater.

Calculation

Wastewater-based epidemiology data are communicated in accordance with the international guidance in milligrams of substance per 1,000 inhabitants per day [mg/1000p/d]. This involves multiplication of the measured analyte concentration by the daily flow rate of the wastewater treatment plant and subsequent division by the population in the catchment area. The first step is to use the permanent resident population as the normalisation value. Normalised values make it possible to compare locations of different sizes as well as different sewer systems and weather conditions (all of which have an influence on wastewater flow). The exploratory research also involves estimating a day-specific number of people, including commuters and tourists, who contribute to wastewater.
For illicit drugs and pharmaceuticals, in certain cases correction factors for conversion in the consumer's body or purity (narcotics) are known, which allows an additional back-calculation to determine actual consumption.
However, especially in the case of illicit drugs, it is also important to know the degree of purity of the product on the market as well as the consumption method (e.g. smoking or snorting) and form (e.g. methamphetamine consumed in the form of either crystals or pills). These variables have an influence on the back-calculations and must be specifically taken into account.

Project structure

Sampling

The DroMedArio project involves collecting wastewater samples from **ten wastewater treatment plants** over a four-year period (Jan. 2021 - Dec. 2024) at 13-day intervals. This sampling strategy allows seasonal and weekly variations to be properly captured, with 28 samples per year. Evenly distributed over the year, seven samples are collected per quarter and each weekday is sampled four times per year. In total, the ten treatment plants treat the wastewater of almost two million people, which corresponds to about 23% of the Swiss population. The treatment plants of the five largest Swiss cities (Zurich, Geneva, Basel, Lausanne and Bern), but also treatment plants of smaller cities (Lugano, Chur, Neuchâtel) and those with a more rural catchment area (Schwyz, Zuchwil-Solothurn) take part in the project. This makes it possible to cover a large part of the Swiss population and different socioeconomic and geographic structures.

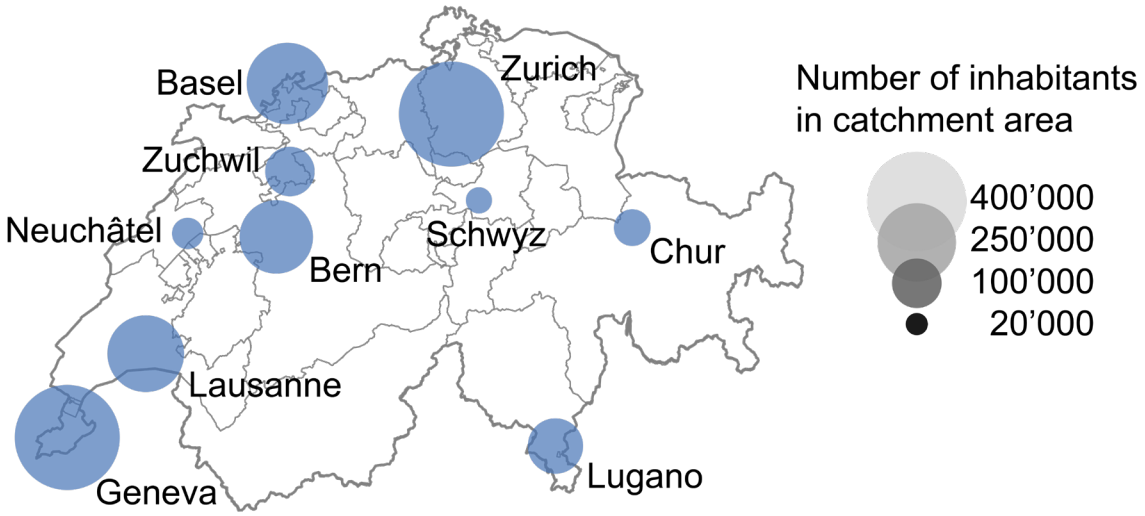

Figure 2: Wastewater treatment plants participating in the project

Since 2012 four wastewater treatment plants, in Basel, Bern, Geneva and Zurich, have been part of the SCORE European network for monitoring illicit drugs in wastewater.

Choice of substances

The project focuses on the long-term monitoring of illicit drugs and pharmaceuticals with abuse potential. This includes five illicit drugs, alcohol, as well as pharmaceuticals that are of interest from a public health perspective owing to the volumes sold and their psychoactive properties.

Table 1: Project wastewater markers

Basic part	Illicit drugs		• Amphetamine • Benzoylecgonine and cocaine • Cannabis (as THC-COOH) • MDMA • Methamphetamine
	Alcohol		• Ethanol (ethyl sulphate)
	Pharmaceuticals	Antidepressants	• Citalopram • Venlafaxine
		Opioids	• Codeine • Dextromethorphan (as dextrorphan) • Fentanyl • Methadone • Morphine • Oxycodone • Tramadol
		Sedatives	• Midazolam • Oxazepam
		Stimulants	• Methylphenidate (as ritalinic acid)
Exploratory part			• Tobacco (as nicotine metabolites) • NPSs • Endogenous metabolites

The project has an exploratory component that focuses on the development of analytical methods for the measurement of additional substances such as nicotine metabolites, novel psychoactive substances (NPSs) and endogenous metabolites.

Analytical measurement method

The main analytical challenges in wastewater analysis are the low analyte concentrations and the complex matrix composition.

Liquid chromatography coupled with tandem mass spectrometry has established itself as a sensitive and reliable analytical method for quantifying illicit drugs and pharmaceuticals in wastewater samples. In the DroMedArio project, the target substances in the wastewater samples are detected and quantified in this way directly or after pre-concentration with solid-phase extraction. Beyond routinely determining key metrics for internal quality assurance during measurements, such as analyte recovery in different wastewater matrices, external quality assurance is also implemented. This involves the participation of both the Eawag and UNIL laboratories in the annual SCORE interlaboratory exercise for selected illicit drugs. Detailed technical information about the analytical methods employed can be referenced in the literature.

Results and interpretation

The analyte concentrations measured in the 24-hour composite samples are communicated as amounts per day (mg/d), taking into account the day-specific wastewater volumes. For comparison between cities of different sizes, the number of inhabitants in the respective wastewater treatment plant catchment area can also be included. This results in population-normalised values, which are expressed as quantities per thousand inhabitants per day (mg/d/1000p).

Consumption patterns differ for the substances analysed and can lead to fluctuations in the daily amounts measured. This is particularly pronounced for some illicit drugs, where consumption at weekends can differ greatly from that on working days. For this reason, average analyte-specific quantities per year are also calculated, which allows a better comparison of consumption over the term of the project.

The results are made available to the public on the project website.

Further information

SCORE: pan-European wastewater-based epidemiology network

MonAM: Swiss Monitoring System of Addiction and Noncommunicable Diseases (FOPH)

EMCDDA: European Monitoring Centre for Drugs and Drug Addiction

Literature on the measurement methods used by UNIL and Eawag:

Benaglia, L., Udrisard, R., Bannwarth, A., Gibson, A., Béen, F., Lai, F. Y., Esseiva, P., Delémont, O. (2020). Testing wastewater from a music festival in Switzerland to assess illicit drug use. Forensic Science International, 309, 110148. doi: 10.1016/j.forsciint.2020.110148

Hollender, J., Schymanski, E., Singer, H., Ferguson, P. (2017). Nontarget Screening with High Resolution Mass Spectrometry in the Environment: Ready to Go? Environmental Science and Technology, 51:11505-12,doi: 10.1021/acs.est.7b02184

Anliker, S., Loos, M., Comte R., Ruff, M., Fenner, K., Singer H. (2020). Assessing Emissions from Pharmaceutical Manufacturing Based on Temporal High-Resolution Mass Spectrometry Data. Environmental Science & Technology, 54:4110-20. doi: 10.1021/acs.est.9b07085