Pharmaceutical Contamination in Groundwater and Drinking Water

A Review and Non-Targeted Approach

ATV Jord og Grundvand
27. November 2025

Annaliese Nan Vernon
Environmental Forensics and Metabolomics Lab, Technical University of Denmark, Building 115, 2800 Kongens Lyngby, Denmark

Why?

- Relevance
- Sources
- Current Research

How?

- Methodology for Literature Search
- Methodology for Database Search
- Methodology for Margin of Exposure
- Role of Non-target Analysis

What?

- Key Pharmaceuticals
- Concentrations
- Findings from Database Search
- Safety Assessment with Margin of Exposure

Background on Pharmaceutical Pollution

Pharmaceuticals are Contaminants of Emerging Concern (CECs)

- Trace levels
- Risk is not well-characterized
- Not included in current regulations for environmental monitoring

Significant chemical footprint

- 600 different pharmaceuticals have been detected in aquatic environments globally[1]

Potential for toxicological impacts on humans and ecosystems

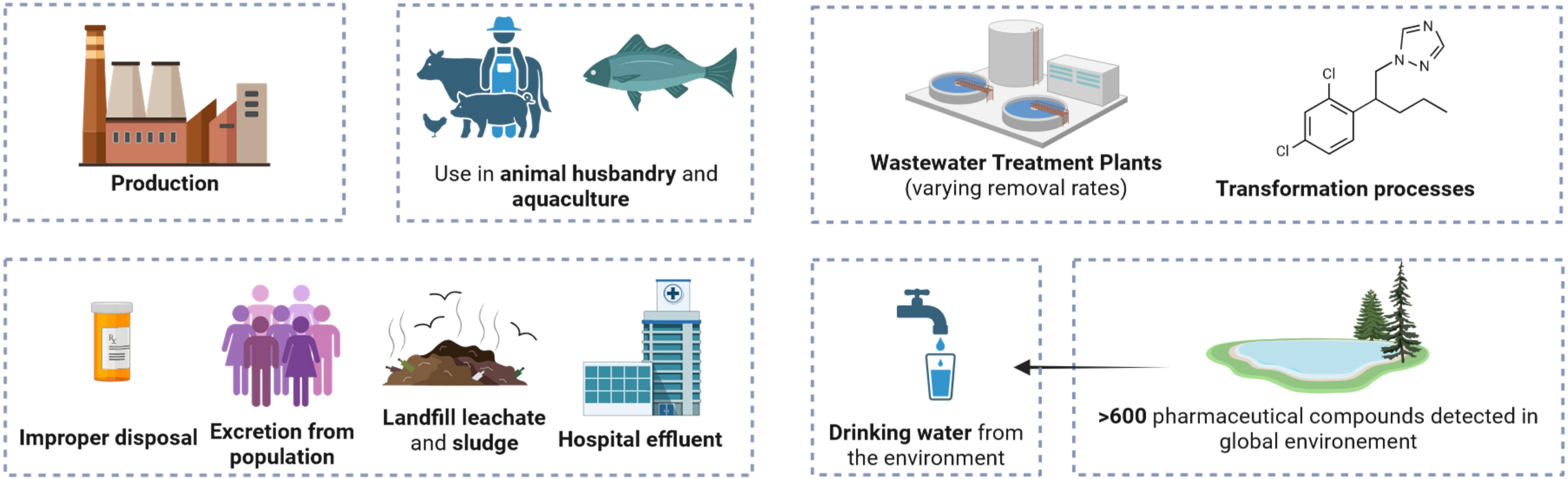
- Designed to be bio-active
- Endocrine disrupting compounds can have non-monotonic dose response effects
- Only 10% of currently prescribed pharmaceuticals have ecotoxicology data[2]

Tramadol[3]
SSRIs[2]
Synthetic Estrogens[4]

Squalius cephalus

Background on Pharmaceutical Pollution

Relevant Pathways



Current State of Research

47%

40%

8%

Study Aim

- Identify the most detected pharmaceutical compounds in European groundwater and drinking water and find their concentrations

Review Methodology

Search Criteria

- Analytical methods: LC-MS and GC-MS
- Region: Europe
- Sample Type: Groundwater and Drinking Water
- Quality Control: Concentrations above Limit of Detection and Limit of Quantification
- Publication date: after 2000

Literature Review

Database

- Pharmaceuticals in the Environment database (PHARMS-UBA)
  - Margin of Exposure calculation

Umwelt Bundesamt

Database Search

Results of Literature Search

- 28 articles were found that met the search criteria
- 147 unique pharmaceutical substances or transformation products were detected
- 11 countries were represented with Spain (7), Germany (6) and France (4) being the most common countries in the studies
- LC-MS was a more common analytical technique, used by 24 studies while 8 studies used GC-MS
- 5 studies included a health perspective and none considered ecotoxicity

Most Frequently Detected Pharmaceuticals and Concentrations (ng/L)

Analgesics and Anti-Inflammatories

- Ketoprofen: 3-62.6
- Diclofenac: 2-590
- Ibuprofen: .4-400
- Naproxen: .2-27.2
- Salicylic acid: 2-102
- Paracetamol: 4-210
- Phenazone: 9.2-400
- Propyphenazone: 80-100

Antibiotics

- Sulfamethoxazole: 2-410
- Trimethoprim: 1.4-100
- Erythromycin: 1-112

Anticonvulsants

- Sotalol: .4-560

Blood-Lipid Modifying Agents

- Clofibrate Acid: 1.36-100
- Bezafibrate: 3.4-12.4
- Gemfibrozil: 2-91

Hormones

- Estrogens: 3-77

Psychoactive Compounds

- Fluoxetine: .3-5.3
- Caffeine: 13-115
- Oxazepam: 10-91
- Diazepam: 9-24

Carbamazepine

Widespread

- Carbamazepine was detected in concentrations ranging from 0.09 to 900 ng/L across 16 different studies
- One study found carbamazepine in 42% of 164 groundwater samples from 23 European countries[5]

Persistent

- Resistant to hydrolysis and biodegradation

Degradation product

- 10,11-Epoxycarbamazepine was detected in studies from France, Serbia, and Spain

Removal efficiency

- Flocculation, sand filtration and sedimentation achieve ~30% removal, while ozonation reaches 99%[6]
- 10,11-Epoxycarbamazepine is harder to remove with 63% removal by ozonation but up to 72% removal with Granular Activated Carbon (GAC) filtration[6]

Non-Steroidal Anti-Inflammatory Drugs

Widespread

- Ibuprofen was found in 12 studies from 0.6 to 400 ng/L but values were lower in drinking water, typically under 5 ng/l
- Diclofenac was found in 8 studies in the range of 2 to 590 ng/L

Regulation

- In 2022, the European Commission proposed adding ibuprofen and diclofenac to the list of priority substances with respective limit concentrations of 220 ng/L and 40 ng/L for surface water[7]

Ecotoxicity

- One study found that Diclofenac pollution has been linked with the decline of vulture populations[8]

Sulfonamides and other Antibiotics

Widespread

- Antibiotics make up 20% of the substances identified in this review
- Sulfamethoxazole was the most frequently identified antibiotic, found in 9 studies in concentrations between 2-410 ng/L

Persistence

- Varies based on conditions such as temperature, pH, and other conditions
- One study found that the removal efficiency for 22 different antibiotics ranged from -34 to 72%
- Sulfamethoxazole is estimated to last over a year in the environment[9]

Ecotoxicity

- Antibiotic pollution can contribute to the spread of antibiotic resistance

PHARMS-UBA Database Overview

Initial dataset

- **276,895 entries** of **992 pharmaceuticals** from **89 countries**

Credibility & Relevance Filters

- Removed questionable sources → **220,801 entries**
- Included Measured Environmental Concentration (MEC) > 0 → **93,337 entries**

Geographic Focus

- Limited to European countries → **52,354 entries**

Water Type

- Focused on drinking & groundwater → **2,119 entries**

Detection Quality Filters

LOD > 0 and only positive detections →

979 entries with **149 compounds** across **22 pharmaceutical groups**

Results of PHARMS-UBA Database Search

Insights by Water Type

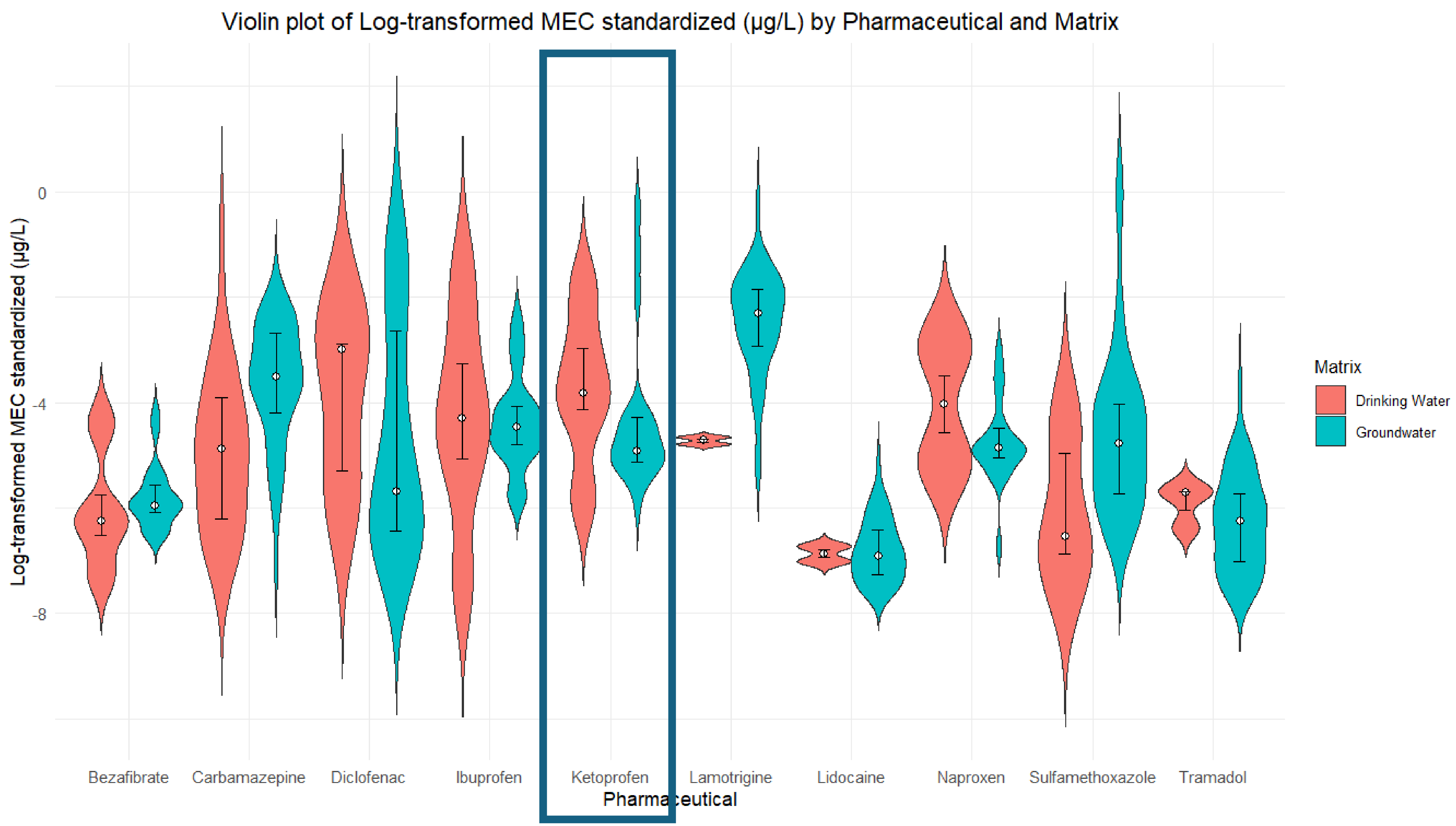
- 73% of pollutants identified were found in groundwater (n=717) with an average concentration of 98 ng/L
- 27% of pollutants identified were found in drinking water (n=262) with an average concentration of 35 ng/L

Insights by Pharmaceutical Type

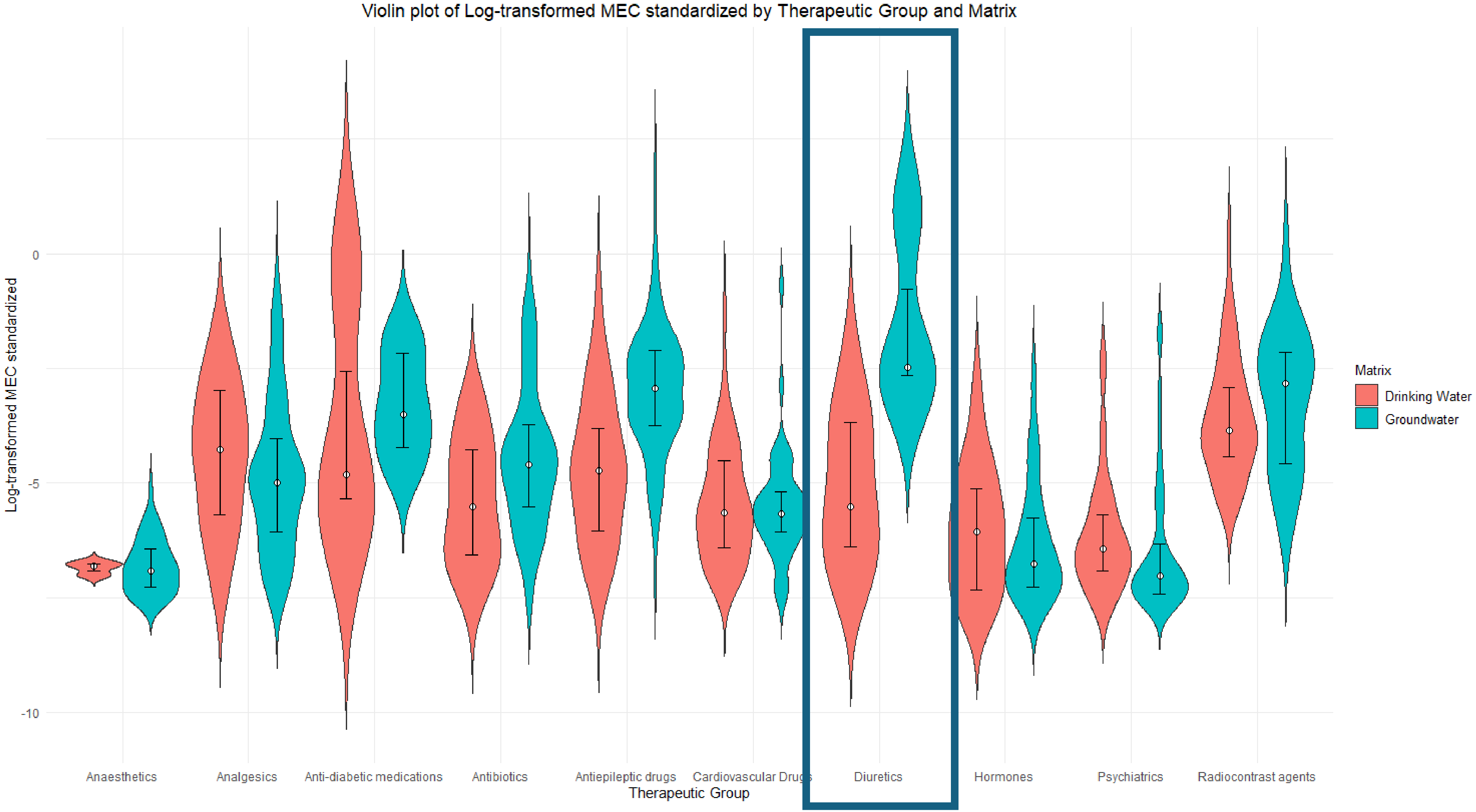
- The most frequently identified use-group is Analgesics
- The most frequently identified compound is Carbamazepine (n=129)

Insights by Geography

- 19 countries represented
- The most represented countries are Hungary (n=281), Germany (n=205), Spain (n=93) and Finland (n=890)
- These top 4 countries cover 68% of all data points



Violin plot of Log-transformed MEC standardized (µg/L) by Pharmaceutical and Matrix
Log-transformed MEC standardized (µg/L)
0
-4
-8
Bezafibrate
Carbamazepine
Diclofenac
Ibuprofen
Ketoprofen
Lamotrigine
Lidocaine
Naproxen
Sulfamethoxazole
Tramadol
Pharmaceutical
Matrix
Drinking Water
Groundwater



Violin plot of Log-transformed MEC standardized by Therapeutic Group and Matrix
Log-transformed MEC standardized
0
-5
-10
Anaesthetics
Analgesics
Anti-diabetic medications
Antibiotics
Antiepileptic drugs
Cardiovascular Drugs
Diuretics
Hormones
Psychiatrics
Radiocontrast agents
Therapeutic Group
Matrix
Drinking Water
Groundwater

Calculate Margin of Exposure for PHARMS-UBA Database

Data Availability

US EPA CompTox database had 21 of the 149 pharmaceuticals with Point of Departure (POD) values

Average Daily Dose (ADD) was calculated by

$$ADD=(C \times DWI \times FE \times ED)/(BW \times AT)$$

C = concentration in drinking water (mg/L)

DWI = daily water intake (L/day) (age specific)

BW = body weight (kg) (age specific)

FE = frequency of exposure (365 days/year)

ED = exposure duration (1 year)

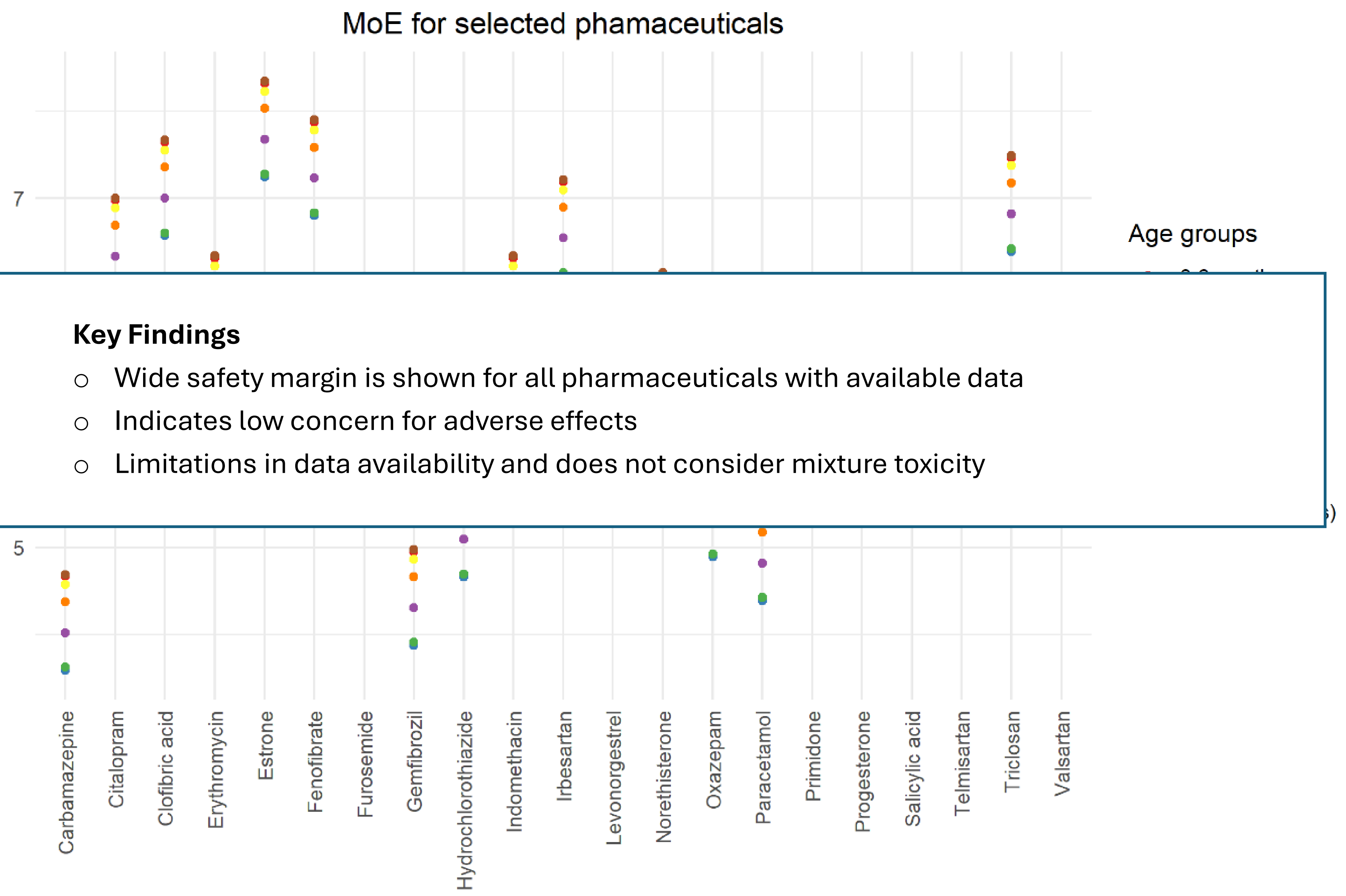
AT = average time (365 days)

Margin of Exposure was calculated by

$$MoE=0.2\ (POD/ADD)$$

Interpretation of MoE:

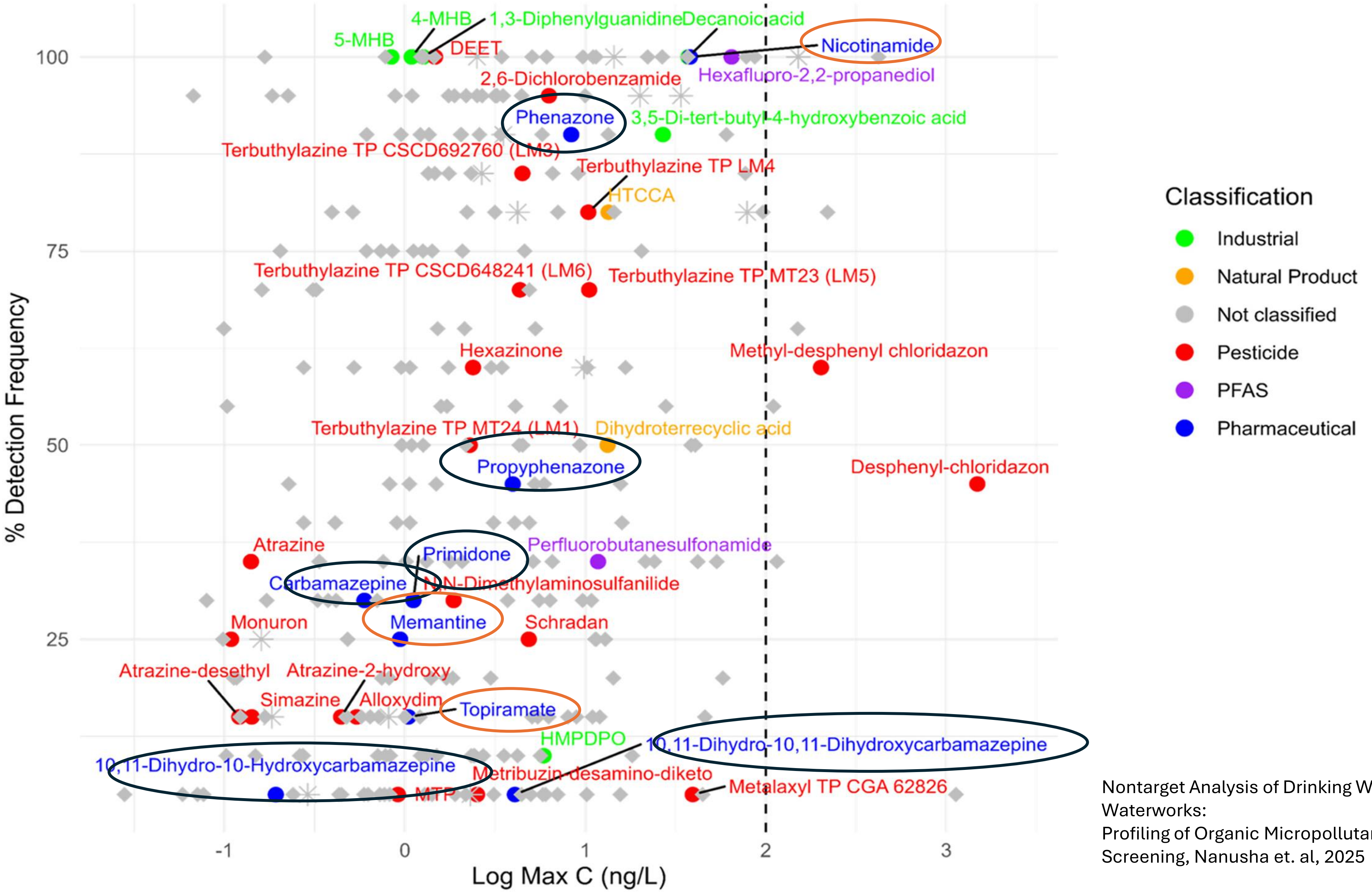
- **MoE < 100** → potential concern for sensitive groups
- **MoE < 1000** → potential concern for general population



Key Findings

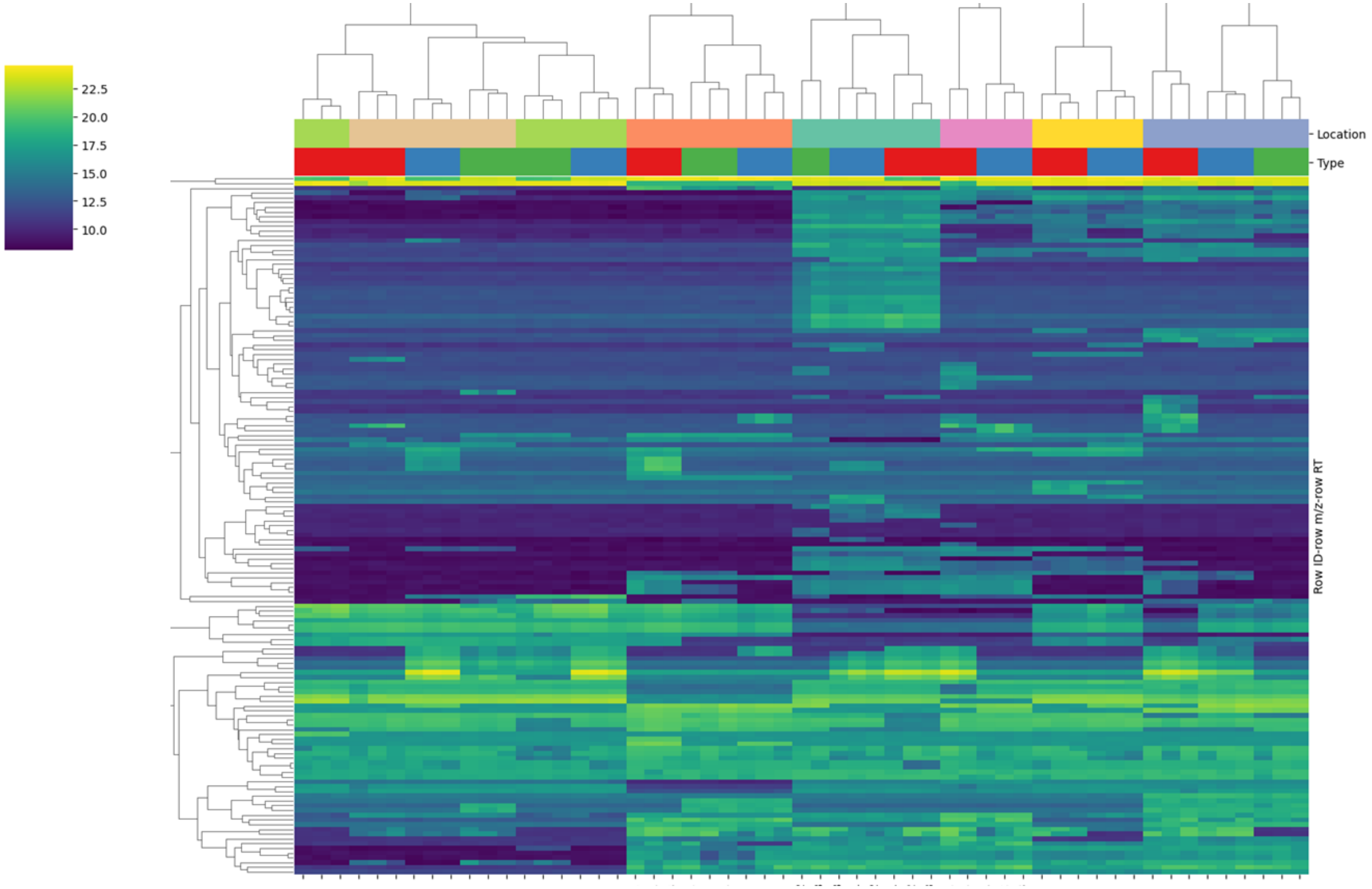
- Wide safety margin is shown for all pharmaceuticals with available data
- Indicates low concern for adverse effects
- Limitations in data availability and does not consider mixture toxicity

Organic Micropollutants in Danish Drinking Water



Nontarget Analysis of Drinking Water from Danish Waterworks:
Profiling of Organic Micropollutants and Health Risk Screening, Nanusha et. al, 2025

Non-Targeted Approach



Future Recommendations

Expand Analytical Coverage

- Opportunity in using Non-Target Analysis strategies to expand detected compounds
- Effect-directed analysis to prioritize pollutants

Further Investigate Human Toxicity

- Utilize strategies to incorporate real-life exposure scenarios such as low-level concentrations and a mixture of compounds

Further Investigate Removal Techniques

- Determine the efficacy of various treatments to remove these types of pollutants

Characterize Pollution Load in Denmark

- Conduct comprehensive monitoring of pharmaceutical pollution in Danish drinking water and groundwater
- Use findings to inform precautionary policy decisions and safeguard water quality

Thank you for listening! – **Questions?**

Sources

1. Aus Der Beek, T., Weber, F., Bergmann, A., Hickmann, S., Ebert, I., Hein, A., & Küster, A. (2016). Pharmaceuticals in the environment—Global occurrences and perspectives. *Environmental Toxicology and Chemistry*, *35*(4), Article 4. https://doi.org/10.1002/etc.3339
2. Whitacre, D. M. (Ed.). (2012). *Reviews of Environmental Contamination and Toxicology Volume 218* (Vol. 218). Springer US. https://doi.org/10.1007/978-1-4614-3137-4
3. Santos, M. E. S., Horký, P., Grabicová, K., Hubená, P., Slavík, O., Grabic, R., Douda, K., & Randák, T. (2021). Traces of tramadol in water impact behaviour in a native European fish. Ecotoxicology and Environmental Safety, 212, 111999. https://doi.org/10.1016/j.ecoenv.2021.111999
4. Gunnarsson, L., Snape, J. R., Verbruggen, B., Owen, S. F., Kristiansson, E., Margiotta-Casaluci, L., Österlund, T., Hutchinson, K., Leverett, D., Marks, B., & Tyler, C. R. (2019). Pharmacology beyond the patient – The environmental risks of human drugs. *Environment International*, *129*, 320–332. https://doi.org/10.1016/j.envint.2019.04.075
5. Molnarova, L., Halesova, T., Vaclavikova, M., & Bosakova, Z. (2023). Monitoring Pharmaceuticals and Personal Care Products in Drinking Water Samples by the LC-MS/MS Method to Estimate Their Potential Health Risk. *Molecules*, *28*(15), Article 15. https://doi.org/10.3390/molecules28155899
6. Huerta-Fontela, M., Galceran, M. T., & Ventura, F. (2011). Occurrence and removal of pharmaceuticals and hormones through drinking water treatment. *Water Research*, *45*(3), Article 3. https://doi.org/10.1016/j.watres.2010.10.036
7. Kulišťáková, A. (2023). Removal of pharmaceutical micropollutants from real wastewater matrices by means of photochemical advanced oxidation processes – A review. *Journal of Water Process Engineering*, *53*, 103727. https://doi.org/10.1016/j.jwpe.2023.103727
8. Oaks, J. L., Gilbert, M., Virani, M. Z., Watson, R. T., Meteyer, C. U., Rideout, B. A., Shivaprasad, H. L., Ahmed, S., Iqbal Chaudhry, M. J., Arshad, M., Mahmood, S., Ali, A., & Ahmed Khan, A. (2004). Diclofenac residues as the cause of vulture population decline in Pakistan. *Nature*, *427*(6975), 630–633. https://doi.org/10.1038/nature02317
9. Gao, L., Shi, Y., Li, W., Niu, H., Liu, J., & Cai, Y. (2012). Occurrence of antibiotics in eight sewage treatment plants in Beijing, China. *Chemosphere*, *86*(6), Article 6. https://doi.org/10.1016/j.chemosphere.2011.11.019
10. Houtman, C. J., Kroesbergen, J., Lekkerkerker-Teunissen, K., & Van Der Hoek, J. P. (2014). Human health risk assessment of the mixture of pharmaceuticals in Dutch drinking water and its sources based on frequent monitoring data. *Science of The Total Environment*, *496*, 54–62. https://doi.org/10.1016/j.scitotenv.2014.07.022
11. Vulliet, E., & Cren-Olivé, C. (2011). Screening of pharmaceuticals and hormones at the regional scale, in surface and groundwaters intended to human consumption. *Environmental Pollution*, *159*(10), Article 10. https://doi.org/10.1016/j.envpol.2011.04.033
12. Zühlke, S., Dünnbier, U., & Heberer, T. (2004). Detection and identification of phenazone-type drugs and their microbial metabolites in ground and drinking water applying solid-phase extraction and gas chromatography with mass spectrometric detection. *Journal of Chromatography A*, *1050*(2), Article 2. https://doi.org/10.1016/j.chroma.2004.08.051
13. Lopez, B., Ollivier, P., Togola, A., Baran, N., & Ghestem, J.-P. (2015). Screening of French groundwater for regulated and emerging contaminants. *Science of The Total Environment*, *518–519*, 562–573. https://doi.org/10.1016/j.scitotenv.2015.01.110

DTU