**ACRONYM:** **DARWIN**

**Title:** **Dynamics of Antimicrobial Resistance in the Urban Water Cycle in Europe**

**Keywords:** **Environmental AMR reservoir, sewer catchment, pathogen ecology, horizontal gene transfer, omics, mathematical modelling**

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## Abstract:

While therapeutic antibiotic use directly impacts the evolution of AntiMicrobial Resistance (AMR), it has become increasingly clear that the environmental dimension of AMR is also of great importance. We postulate that urban water systems (UWS), which are our receptacle for excreted antimicrobials, AMR organisms and AMR genes, are central conduits of AMR to and from pathogens and environmental strains. This is because of high microbial densities and the co-mingling of different wastes, which promotes accelerated AMR gene transfer (HGT) and multi-resistance due to the co-occurrence of antibiotics, biocides, metals and microbes.

In DARWIN, we will undertake a never-previously-performed pan-European examination of the fate of key AMR organisms and genetic determinants in UWSs resulting from discharged hospital and community wastes, including transmission mechanisms in different stages of sewer catchments and receiving waters. We focus on the spread of AMR genes encoding clinically relevant extended spectrum β-lactam (ESBL) and carbapenem resistance in three countries with differing AMR profiles and sewage management practices.

We postulate that AMR genes readily transmit in UWSs from pathogens and commensal hosts in human wastes (after antibiotic use) to environmental strains better adapted to migrate through the sewer environment, which is driven by local ecologies, conjugal plasmid transfer and phage-mediated transduction.

Hence, we will, for the first time, determine specific bacterial hosts that carry AMR genes across UWSs, and identify where key HGT events occur with the ultimate goal of assessing the relative risk of AMR genes returning back to humans due to environmental exposure. To guide risk assessments, a predictive dynamic mathematical model for UWSs will bedeveloped to assist in health and sewage management decisions.