

Monitoring sexually transmitted Infections Via wastewater analysis (MALDIVES)

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Context:

The research project is part of the Swealth [Surveillance of wastewater for public health] project¹, which is supported by the 4EU+ alliance to promote the development of wastewater-based epidemiology for a better understanding of population health.

As a receptacle for the molecules and infectious agents released in people's feces and biological fluids, wastewater is an ideal matrix for detecting and monitoring infectious diseases. Wastewater-based epidemiology (WBE) brings together all the approaches - mainly microbiological, chemical and mathematical/bioinformatical - used to assess the health status of a population by exploring the composition of wastewater². WBE strategies differ from "classic" epidemiology - which relies on individual data collection - in that they offer a macro-epidemiological approach, at lower cost, that can be applied to a region (wastewater treatment plant sampling), a city (main sewer), a neighborhood (sewer) or a building (school, hospital, nursing home, prison, etc.) and can be focus on a wide range of analyzed factors (bacteria, viruses, fungi, etc).

Chlamydia, gonorrhea, trichomoniasis, and syphilis are sexually transmitted infections (STI) whose infection rates remain very high throughout the world³. STIs are transmitted primarily through sexual contact, including vaginal, anal, or oral and according to the WHO reports, more than a million new cases of these STIs are recorded every day. STIs also include infections linked to oncogenic papillomaviruses, the main agents responsible for cervical cancer, against which there is, however, an extremely effective vaccine⁴, but whose use remains underdeveloped. Human papillomavirus (HPV) infection is associated with more than 311,000 deaths from cervical cancer each year⁵.

In the absence of a systematic individual screening policy, epidemiological data remains patchy, and the dynamics of these infections remain difficult to assess.

Most of these pathogens are detectable in urine⁶ and some, such as papillomaviruses, have already been detected in wastewater^{7,8}. Therefore, the main agents of STIs can in principle be detected, quantified, and genetically characterized in wastewater, which allows for a precise photograph and a dynamic vision of these infections in watersheds. Moreover, the presence of pathogens can also be monitored indirectly by monitoring their natural predators – bacteriophages⁹. Although there are no phage indicators developed for

¹ <https://4euplus.eu/4EU-12.html?newsID=19891>

² Maréchal V, Maday Y, Wallet C, Cluzel N, Borde C; SIG OBEPINE. Wastewater-based epidemiology: Retrospective, current status, and future prospects. *Anaesth Crit Care Pain Med*. 2023 Oct;42(5):101251. doi: 10.1016/j.accpm.2023.101251. Epub 2023 May 24. PMID: 37236316.

³ [https://www.who.int/news-room/fact-sheets/detail/sexually-transmitted-infections-\(stis\)](https://www.who.int/news-room/fact-sheets/detail/sexually-transmitted-infections-(stis))

⁴ Kluczynski MA, Rodriguez EM, McGillicuddy CS, Schlecht NF. Human Papillomavirus Vaccination in Pediatric, Adolescent, and Young Adult Cancer Survivors-Opportunity to Address Gaps in Cancer Prevention and Survivorship. *Vaccines (Basel)*. 2024 Jan 24;12(2):114. doi: 10.3390/vaccines12020114. PMID: 38400098; PMCID: PMC10892003.

⁵ Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2018 Nov;68(6):394-424. Epub 2018 Sep 12. Erratum in: *CA Cancer J Clin*. 2020 Jul;70(4):313.

⁶ Aaron KJ, Griner S, Footman A, Boutwell A, Van Der Pol B. Vaginal Swab vs Urine for Detection of Chlamydia trachomatis, Neisseria gonorrhoeae, and Trichomonas vaginalis: A Meta-Analysis. *Ann Fam Med*. 2023 Mar-Apr;21(2):172-179. doi: 10.1370/afm.2942. PMID: 36973065; PMCID: PMC10042575.

⁷ Di Bonito P, Iaconelli M, Gheit T, Tommasino M, Della Libera S, Bonadonna L, La Rosa G. Detection of oncogenic viruses in water environments by a Luminex-based multiplex platform for high throughput screening of infectious agents. *Water Res*. 2017 Oct 15;123:549-555. doi: 10.1016/j.watres.2017.06.088. Epub 2017 Jul 5. PMID: 28704770.

⁸ GIS Obepine, unpublished data.

⁹ Ballesté E, Blanch AR, Muniesa M, García-Aljaro C, Rodríguez-Rubio L, Martín-Díaz J, Pascual-Benito M, Jofre J. Bacteriophages in sewage: abundance, roles, and applications. *FEMS Microbes*. 2022 Mar 17;3:xtac009. doi: 10.1093/femsmc/xtac009. PMID: 37332509; PMCID: PMC10117732.

STIs detection, such an approach seems to be an interesting scientific challenge that may result in a new tool in STIs epidemiology.

The GIS Obépine (Epidemiological observatory in wastewater) is a research network supported by Sorbonne University that has acquired extensive experience in the field of wastewater epidemiology¹⁰. **The project aims, for the first time, to develop a WBE strategy specifically oriented toward pathogens associated with STIs by bringing together three countries, France, Poland and the Czech Republic. This pilot project could subsequently be extended to all members of the alliance and in particular involve teams specialized in human, microbial, and social sciences.**

Scientific objectives:

The thesis project, led in collaboration with Vincent Maréchal (Sorbonne Université), Piotr Golec (University of Warsaw), and Milena Busova (Charles University), will fulfill the following objectives:

- Develop **techniques for detection, quantification, and characterization** of the main agents responsible for STIs (chlamydia, gonorrhea, syphilis, and papillomaviruses) in wastewater. This work package will be developed in collaboration with the research teams of GIS Obépine, which has all the required molecular techniques (year 1)
- **Select wastewater treatment plants, in the three partner countries**, in which samples can be taken at regular intervals, over 2 years (year 1)
- **Collect regional epidemiological individual data on STIs** in the areas concerned (years 2 and 3)
- Search for and **quantify relevant pathogens in wastewater** (years 2 and 3)
- Develop **indirect techniques to detect STIs bacteria in wastewater**, based on the identification of bacteriophages (years 2 and 3)
- **Produce a dynamic model of STIs** from data from wastewater analysis (year 3). This component will be developed with Prof Yvon Maday (Mathematician, Sorbonne University).
- **Cross-analyze data from wastewater with individual data** collected from populations (year 3).

The project will be conducted in strong collaboration with a French research engineer in Paris.

Justification of the approach and suitability for the themes indicated in the call for projects:

This pilot project will be offered to a student with good training in microbiology and molecular biology, with a strong appetite for epidemiology. All labs involved commit to monthly meetings online and annual in-person meetings. The PhD student will have research stays in the other labs to facilitate the exchange of expertise.

It will make it possible, for the first time to our knowledge, to develop an integrated approach for monitoring sexually transmitted infections which today constitute a major public health concern. A pilot project par excellence, it fits perfectly into **global health issues** which constitutes a major area of research and training within member universities of the 4EU+ alliance. The thesis project pools various skills (knowledge of sanitation networks, epidemiology, infectious diseases). It could serve as a support to **extend this theme to all the partners of the alliance** by integrating questions relating to the **human and social sciences**: social and psychological determinants of the increase in STIs, particularly in the youngest populations, difficulty integrating population surveillance plans, determinants of the sexual health of young people and particularly student populations, resistance to vaccination, etc. This problem also extends to **economic issues** (benefit/cost ratio of indirect monitoring by wastewater), and **ethics** and aims to **provide decision-makers with new arguments to take specific awareness and prevention actions against STIs**, particularly concerning **the urban and most vulnerable populations**.

¹⁰ Wurtzer S, Marechal V, Mouchel JM, Maday Y, Teyssou R, Richard E, Almayrac JL, Moulin L. Evaluation of lockdown effect on SARS-CoV-2 dynamics through viral genome quantification in waste water, Greater Paris, France, 5 March to 23 April 2020. Euro Surveill. 2020 Dec;25(50):2000776. doi: 10.2807/1560-7917.ES.2020.25.50.2000776. PMID: 33334397; PMCID: PMC7812418.