Facilitator guide for WES case study

Background

Wastewater and environmental surveillance (WES) have recently become an increasingly important tool for early warning detection of known and unknown pathogens. It is a modality that has been primarily for polio surveillance, as a tool to assess polio circulation and vaccine effectiveness[1].

Efforts during the COVID-19 pandemic have shown the value of WES, complementing clinical surveillance to monitor and manage the pandemic[2]. From that, WES has grown in interest and importance globally, with advancements in techniques and innovations to expand its scope beyond polio and SARS-CoV-2[3]. WES can potentially become a cost-effective, objective and real-time tool for public health infectious disease surveillance.

WES enables serial monitoring of populations with minimal interruption to daily life but generates real-time, objective and comprehensive data on the prevalence and distribution of pathogens in the community. However, to fully utilize the data, optimization of workflows for extraction, concentration, identification and quantification in the wastewater sample is needed, together with the understanding of the pathogen dynamics; and how and when the pathogen enters the sewage system[4]. Correlating the WES data with the burden of clinical disease is crucial for actionable public health intervention[3]. While data generated from WES has the potential for great public health benefits, issues on data ownership, privacy and governance also needs to be considered[5].

Considerations for WES system

Figure 1 illustrates the considerations for designing a WES system. The are several public health uses of a WES system such as new pathogen detection, tracking of variants and monitoring intervention efforts. This can inform public health actions such as guiding antimicrobial stewardship, development of vaccines for vaccine-preventable diseases and vector control for vector-borne diseases. Closed sewage infrastructure is a tributary network, with smaller collection points flowing into larger pipes and eventually to a treatment plant. Understanding the changes in the wastewater chemistry through the sewage infrastructure due to factors such as contamination and degradation will determine the sampling location and workflow optimization. For settings with a mix of open and closed sewage infrastructure, further considerations are needed to determine the optimum location of sampling.

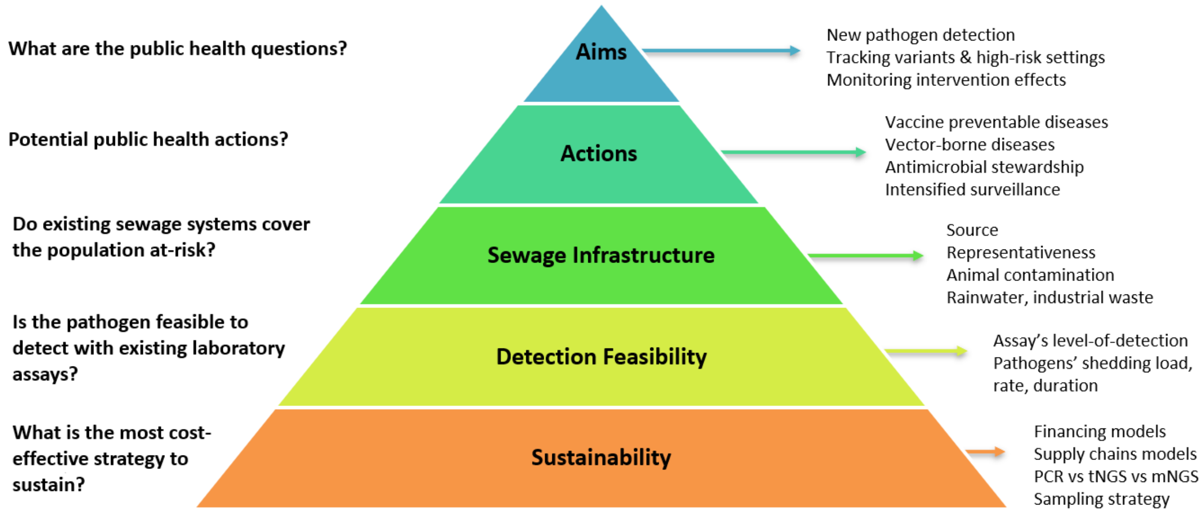

Figure 1. WES strategy framework.

Pathogen dynamics plays an important part in wastewater surveillance. For a pathogen to be detected and tracked in wastewater, its nucleic acid must be present in the wastewater. Further characteristics of the pathogens such as their hydrophobicity and the pathogen shedding load also influence its distribution in the wastewater. A list of pathogens that can potentially be detected in wastewater is shown in **Figure 2**.

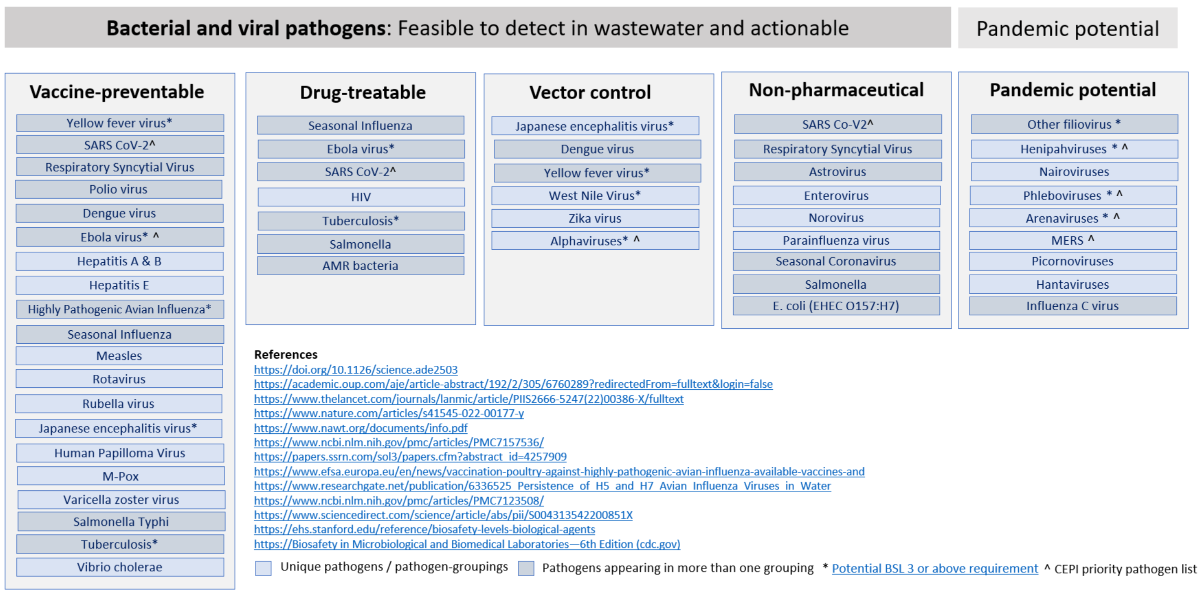

Figure 2. List of potential pathogens detected in wastewater.

An understanding of how each pathogen enters the sewage system, whether through secretions such as stool and urine or through activities from hand washing, teeth brushing or bathing will play a part in identifying the pathogens.

Designing a WES system requires a sustainability plan, especially in resource-limited settings. Efficient sampling strategies and complementary molecular techniques are required for a cost-effective system. An integrated financing model within national budgets will be helpful for sustainability.

Case study guide

Learning objectives for this case study:

1. Participants to understand the system requirements of WES for infectious diseases
2. Participants to understand the genomic utility of using WES for infectious diseases

This first part of the case study is developed to guide participants in understanding what are the components and system consideration of a WES including sewage infrastructure, the pathogen characteristics for detection in wastewater and sampling strategies suitable for WES. The second part investigates the genomic utility of example pathogens for public health interventions using 3 example pathogens/pathogen groups: rotavirus, Salmonella typhi and pathogens of pandemic potential.

Part 1: Country context and wastewater surveillance planning

Background
Country A is an LMIC in Asia with a population of 70 million people with centralized healthcare system and an established communicable disease surveillance system. It has a national reference lab with a network of satellite labs with a moderate capacity for genomic sequencing. Most cities in the country have a closed sewage system with a treatment plant. There are rural areas that use open sewage systems. Country A wants to use WES to assess other pathogens beyond SARS-CoV-2.
Question
Q1. Discuss the advantages and limitations of having a WES system. What are the capacities needed to establish a WES system.
Facilitator prompt
Facilitator should guide the discussion around the advantages of having a WES as a complementary system to clinical surveillance, level of monitoring (individual vs population), ability to monitor multi-pathogens in single sample. Discuss disadvantages such as accuracy or availability of protocols, ethical issues on data privacy and governance, technical challenges in processing wastewater samples and cost of setting up WES system. *Capacity wise, highlight the laboratory & bioinformatics capacity, infrastructure, expertise and governance issues needed to establish a WES.*
Facilitator notes

Pathogen characteristics and sampling strategies

Background
Question
Q2. Discuss the sampling strategies for WES in relation to the operational consideration below. ● Priority pathogens ● High risk populations ● Sampling frequency and location
Facilitator prompt
Facilitator should guide the discussion on what are the considerations for priority pathogens in a WES system, e.g. what is detectable, what is actionable. Discuss sampling strategy at population level, e.g. population where clinical burden is higher, high risk populations like elderly, etc. Discuss the sampling methods (manual vs automated samplers), frequency (time of day, number of times per day, etc) and location (sewage treatment plant vs manholes or location around high risk population – e.g. nursing home, POEs).
Facilitator notes

Part 2: Genomic utility

Background
Country A introduced the 3-dose rotavirus vaccine into its pediatric immunization schedule. Two years later, it reported an increase in rotavirus infections.
Question
Q3. Discuss the genomic utility in this scenario.
Facilitator prompt
Facilitator should guide the discussion around using genomic sequencing for genotype shift in the context of ongoing vaccination programme. What are the implications when cases still increase despite vaccination and what value can genomic sequencing add (vaccine mismatch/evasion)?
Facilitator notes

Background

Following the introduction of a typhoid vaccination program targeting Salmonella typhi in high-risk urban areas, WES analysis reveals decrease in overall prevalence. However, NGS analysis of S.typhi from wastewater demonstrates an increase in proportion of genes associated with resistance to ciprofloxacin and ampicillin.

Question

Q4. How does it guide antimicrobial stewardship in clinical settings, intervention effectiveness and overall public health surveillance?

Facilitator prompt

Facilitator should guide discussion around practical steps to communicate the data on AMR to guide antimicrobial stewardship – what communication needed to clinical management, how to promote better use of antimicrobials, how to track effectiveness.

Facilitator notes

Background

Country A subsequently adapted WES for the detection of pathogens for pandemic potential. In routine WES surveillance and analysis, Nipah virus was detected in the wastewater.

Question

Q5. What changes would you implement to the WES system in this event?

Q6. What implications in terms of One Health does a WES have on other sectors apart from human health?

Facilitator prompt

Facilitator should guide the discussion around the public health response of a potential Nipah outbreak. And subsequently in the outbreak or post outbreak, any changes can be made to improve the WES system – change in capacity, change in sampling strategy,

Discuss the One Health approach in using WES for pathogens of pandemic potential – who are the other stakeholders involved, what other surveillance systems needed, what are the challenges in the One Health perspective
Facilitator notes

References

1. Polo, D., *et al.* Making waves: Wastewater-based epidemiology for COVID-19 - approaches and challenges for surveillance and prediction. *Water Res* **186**, 116404 (2020).
2. Diamond, M.B., *et al.* Wastewater surveillance of pathogens can inform public health responses. *Nat Med* **28**, 1992-1995 (2022).
3. Parkins, M.D., *et al.* Wastewater-based surveillance as a tool for public health action: SARS-CoV-2 and beyond. *Clin Microbiol Rev* **37**, e0010322 (2024).
4. Cohen, A., *et al.* Making waves: The benefits and challenges of responsibly implementing wastewater-based surveillance for rural communities. *Water Res* **250**, 121095 (2024).
5. Gable, L., Ram, N. & Ram, J.L. Legal and ethical implications of wastewater monitoring of SARS-CoV-2 for COVID-19 surveillance. *J Law Biosci* **7**, lsaa039 (2020).