Hydro Nation International Centre

Utility of wastewater surveillance for detecting and monitoring emerging and re-emerging pathogens and endemic infections

Eulyn Pagaling[1], Urmi Ghosh[1], Clare Harkins[1], Claus-Dieter Mayer[2] and Lisa Avery[1]

[1]The James Hutton Institute, Craigiebuckler, Aberdeen AB15 8QH
[2]Biomathematics and Statistics Scotland, JCMB, The King's Buildings, Peter Guthrie Tait Road, Edinburgh, EH9 3FD

Research Purpose

Wastewater-based epidemiology (WBE) was successfully used to monitor infectious disease markers at population level, exemplified by SARS-CoV-2, obtaining near real-time population level data. To merit further investment, policy teams need assurance that improved surveillance benefits health protection in Scotland.

The main objective of Scotland's Wastewater Monitoring Programme Strategic Plan 2025-2028 is to deliver a quality-assured WBE program that fulfils the following needs:

- Delivers on the One Health agenda
- Is at the forefront of developments in WBE applied to public health practice
- Contributes to Scotland's future pandemic preparedness

Project Findings

The aim of this project was to review the utility of wastewater surveillance for detecting and monitoring emerging and re-emerging pathogens and endemic infections, including blood-borne viruses and enteric viruses. The findings under each of the four project objectives are detailed below.

Objective 1. The effectiveness of wastewater surveillance in detecting emerging and re-emerging pathogens and endemic infections compared to traditional surveillance methods, including:

a. Key factors influencing the detection sensitivity and specificity of wastewater surveillance for different/distinct pathogens, particularly in environments with multiple pathogens present.

A review of grey literature, including the UK Health Security Agency list of 24 priority pathogens, provided a list of over 60 emerging and re-emerging priority pathogens, including viral (e.g. *Coronaviridae*), bacterial (e.g. *Streptococcus pneumoniae*) and protozoal (e.g. *Entamoeba histolytica*) pathogens.

Pathogen detection methods were categorised as culture-based, culture-independent detection of whole organisms, PCR-based, isothermal amplification, sequencing, spectrometry, microfluidics, biosensors and emerging and integrated methods. There was inconsistent reporting on sensitivity and specificity of these methods (e.g. difference in units measured), making it difficult to compare. Culture-based methods cannot detect viable but non-culturable organisms (VBNC). Nucleic acid-based methods are affected by DNA extraction bias. PCR-based methods were affected by inhibition, competitive binding and primer bias. Spectrometry-based methods bypass issues with VBNC and inhibition but are affected by lack of reference standards. Both PCR-based and spectrometry-based approaches may be less effective in wastewater where multiple pathogens are present. The more established technologies have already been validated for use in wastewater, while some emerging technologies still require validation in wastewater.

Other factors should also be considered to assess the effectiveness of WBE, including spatio-temporal trends in pathogen load, potential degradation during sample transport and storage and methods for the primary concentration step. Nevertheless, correlations between WBE data and the population have been demonstrated for SARS-CoV-2, *Salmonella* spp., Influenza virus and MPOX.

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Objective 2. The cost-effectiveness of wastewater surveillance for monitoring emerging and re-emerging pathogens, compared to traditional surveillance methods (e.g., clinical testing, active case finding).

Costs for WBE need to account for personnel salaries (e.g. sampling team, laboratory technicians, bioinformaticians and specialists), sampling equipment, sample transport, and technology costs (e.g. laboratory equipment and laboratory consumables and reagents). International experience showed that WBE for SARS-CoV-2 was estimated to be $USD0.07 – $USD0.10/person in Malawi and $USD0.07 – $USD0.13/person in Nepal. Meanwhile, WBE for SARS-CoV-2 was estimated to be $USD0.10/person in rural areas and $USD0.005/person in urban areas of the USA. Costs for clinical testing or active case finding in the UK could not be found in the literature. Given international experience, it is anticipated that WBE would incur a lower cost per person, however other surveillance is unlikely to be applied at population level, therefore comparisons are difficult to evaluate. A direct comparison is difficult due to the different nature of clinical vs. WBE-type programmes.

Objective 3. Ethical/legal considerations associated with wastewater surveillance.

Ethical considerations concerning WBE include i) Privacy and the protection of personal data where results could potentially be traced back to an individual or groups of individuals, ii) Data analytics, big data and decision making where WBE data may make it possible for third parties to target specific groups of individuals, iii) Public health ethics where WBE may offer a more equitable solution to disease surveillance, iv) Research ethics where WBE results may lead to disproportionate measures on groups of individuals, and v) Environmental and water ethics where decisions over wastewater treatment may differ according to risks to human health versus risks to aquatic animals or ecological health. Legal issues arise when enforcement of measures (e.g. stay at home orders, sanitary cordons or quarantines) violate an individual's protections against searches, seizures and discrimination.

Objective 4. Gaps in the current body of research, recommendations including additional studies that are needed to improve global health monitoring.

To address research gaps, we recommend further research into specific technologies, for example, reference standards for advanced technologies, validation of emerging technologies on wastewater and validation of technologies for specific pathogens. We also recommend research into other factors affecting WBE efficacy such as spatio-temporal fluctuations in pathogen load (for example relative shedding of different pathogens by the human population), effects of sample transport and storage on pathogen degradation, efficacies of various primary concentration methods and best methods that link pathogen signals back to human numbers in a catchment. Finally, cost comparisons between WBE and traditional methods (e.g. clinical testing) will need to be conducted by relevant stakeholders to assess the cost-effectiveness of WBE.

Recommendations pertinent to Scotland include determining priority pathogens based on likelihood, prevalence and severity of health risk. Thereafter, specific recommendations for detection of those prioritised pathogens include identifying best available methodology, identifying technical capabilities, defining populations of interest, determining monitoring requirements and establishing External Quality Assessment Schemes to ensure comparability across testing laboratories. Finally, we recommend development of protocols to assess ethical aspects of inclusion/exclusion, anonymity and human genomic by-catch.

To improve pathogen reporting, we recommend regular re-assessment or 'horizon scanning' of emerging pathogens with pandemic potential, agreement on a standard detection method for WBE that could be implemented globally (especially in resource-limited areas), and standardised reporting of WBE results. Finally, implementation of WBE trials for monitoring of prioritised pathogens should be undertaken to provide evidence of utility, efficacy and integration with clinical testing and contact tracing.

Following generation of evidence of cost-effectiveness and to implement coordinated monitoring, we recommend investment in global infrastructure for sampling, transport and testing laboratories, development of a global open access database where WBE data and clinical data can be deposited for constant pathogen surveillance and vigilance, and development of a decision support tool to translate data into resource planning. We also recommend that formulation of pandemic action plans include the use of WBE to aid disease monitoring.