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Editorial: Wastewater-based epidemiology at the frontier of global public health

The COVID-19 pandemic demonstrated the necessity for highly interdisciplinary, multi-stakeholder collaboration to enable effective public health practice and response. The application of wastewater monitoring to support the pandemic response was demonstrated quickly, leveraging existing scientific and engineering capability to rapidly develop methods that enabled scaling of monitoring programmes across the globe (Naughton *et al.* 2021; The Economist 2022). The science and practice of wastewater monitoring, or wastewater-based epidemiology (WBE) as it is often termed in the context of surveillance, for public health threats is well-documented. As a highly socialised tool, national, regional, and international communities of interest have joined efforts to provide evidence of the value of the data derived and its application in practice. While the use of wastewater monitoring to detect and characterise targets of public health concern is not new, COVID-19 and the (re)emergence of rare, novel, or unexpected pathogens (e.g., Poliovirus (Klapsa *et al.* 2022; Ryerson *et al.* 2022; Zuckerman *et al.* 2022), Mpox (de Jonge *et al.* 2022), Enteric viruses (Reyne *et al.* 2023), Respiratory illnesses (Wolfe *et al.* 2022)) stresses the importance of continued research and development into the utility of wastewater monitoring and utility of the data it generates. As wastewater monitoring continues to move from the research community into applied public health agencies, there is a need to develop standard methods and data analytics for specific applications. Establishing wastewater-based epidemiology at the frontier of global public requires a clearer understanding and acknowledgment of its value by public health policy makers, regulators, and government.

This Special Issue presents a broad view of WBE thinking and practice, delineating the current understanding and future potential of the field. The topics covered range from geographically distinct reports on the use of WBE to inform on pathogen circulation in a population, through technical developments and data utility, to commentaries on future challenges and opportunities including for WBE 'beyond the Pandemic'.

As a pandemic, COVID-19 has seen a global public health response, with regional, national, and sub-national variation in surveillance and intervention. Although wastewater monitoring of the virus has not been adopted universally, a significant number of countries have or continue to provide complementary data on SARS-CoV-2 load or concentration in sewage (Naughton *et al.* 2021), the majority of which are large, well-resourced countries. However, the democratisation of WBE, to a large extent, has enabled less populated, geographically small, or lower resourced nations, to pursue monitoring campaigns. Markt *et al.* (2022) report on the results of a six month monitoring programme in the Principality of Liechtenstein, highlighting the potential of WBE as an 'early-warning' indicator ahead of clinical results in response to lower testing rates. This, and their observation that changes in phenotypic expression across variants may affect the interpretation of wastewater measurements, is not unique and demonstrates some inherent determinism in the use of WBE. Similarly, Fang *et al.* (2022), report on the wastewater monitoring programme in Scotland, and address the issue of variability in both structural and analytical terms, describing approaches to manage inherent and sporadic variation in the data.

Normalisation of wastewater measurements is discussed by Fang *et al.* (2022) as approach to account for systematic variation in the data (e.g., through extraneous, non-human flow contributions). Sakarovitch *et al.* (2022) focus explicitly on the use of normalisation to avoid misinterpretation of the data. Here, they recommend that multicomponent, or composite, normalisation can account for multiple sources of variability and evidence its improvement over single factor normalisation (e.g., using flow rate).

The management, analysis, and use of WBE data is a broad but important topic and assuring the methods employed for WBE is needed to provide reliable and comparable numeric estimates and predictions of community disease burden. Anneser *et al.* (2022) present an example of its use for modelling the relationship between viral concentrations (wastewater and settled solids) measured across three regions in New England, USA and corresponding individual case rates in those geographies. Several statistical models were employed, with promising results suggesting some high level of correspondence between the datasets.

While studies that employ models to ascribe a relationship between wastewater measurements and other measures of disease burden, may find a relationship, the fact that no metric provides complete confidence in the true state and all suffer from inherent biases and uncertainties, urges caution when interpreting modelled relationships. This is discussed by Faraway *et al.* (2022), who provide a summary of some of the data and methodological issues that complicate development of effective predictive models for disease case rates including temporal and spatial heterogeneity, and the effects of different levels of data aggregation.

While most WBE research and practice in recent years has focused on SARS-CoV-2, a groundswell of diverse applications for wastewater monitoring have arisen in the wake of the pandemic, based often on extant knowledge, and integrating recent advances in methods and data science. In the wake of easing COVID-19 restrictions and interventions, much speculation on the effect of these, and increased public health awareness, on other circulating diseases. Here, Abd-Elshafy *et al.* (2022), discuss the impact of increased hygiene practices on common enteric virus infections at a location in Egypt. By monitoring wastewater during a period of high COVID-19 prevalence and comparing enteric virus data to a similar period prior to the pandemic, the authors suggest that the public health impact of this behaviour amongst the population indirectly lessens the incidence of enteric diseases.

The global public health threat of antimicrobial resistance (AMR) has meant there is an increased requirement for effective monitoring. This has elevated debate on the value of wastewater monitoring in response. Understanding the relationship between the temporal variation in Antimicrobial Resistance Gene (ARG) levels and the presence of resistance markers in wastewater is a key challenge within this value proposition. Steenbeek *et al.* (2022) report a significant positive correlation between several antibiotics and ARGs, and integrons (i.e., the measure of microbial adaptation and evolution), as measured in wastewater. However, the authors also highlight the need to design appropriate sampling schemes to reduce the risk of mischaracterising the burden of antibiotic resistance.

WBE has the potential to provide an increasing level of resolution on community or aggregated population health, as the quality, quantity, and diversity of data extracted from wastewater is realised. Soller *et al.* (2022) demonstrate the utility of wastewater-based mechanistic models for normalisation of wastewater data to ensure that the collated information is consistent under variable conditions. Hence, the integration of assured WBE programmes, including best practice approaches, within public health systems will enable authorities and decision-makers to respond with the appropriate level of knowledge and confidence. During the COVID-19 pandemic, small-scale, community-organised wastewater-based monitoring initiatives emerged in parallel with larger, well-funded government programmes. One such study (Brooks *et al.* 2023), conducted in Yarmouth, ME, USA (pop. 8,900) was established to assist with the public health response to disease outbreaks, providing end-to-end surveillance, data analyses and dissemination at community level and affect a rapid response at local scale.

Although, during the pandemic, WBE has been integrated into some public health surveillance programmes, several important research gaps need to be resolved to expand the utility and reliability of WBE in the future both for SARS-CoV-2 and other public health applications. Robins *et al.* (2022) review these gaps in the context of WBE for pathogenic viruses, antimicrobial resistance, and chemicals. Additional research is needed in the areas of markers in stool and urine, environmental factors, and methodologies for sample collection and quantification (Robins *et al.* 2022).

Compounding the wider need for both empirical research, standardisation of methods and protocols, and greater, open communication between disciplines and sectors, Hyllestad (Hyllestad *et al.* 2022) conducted a systematic review of the value proposition for environmental surveillance as an early-warning of public health threats. Although focused on the large and expanding data and information evidence generated within the COVID-19 pandemic, this review and the aforementioned research gaps analysis (Robins *et al.* 2022) suggest that WBE sits firmly at the frontier of global public health – one that requires appropriate resourcing, evidence development, and stronger alignment with the plethora of public health functions that underpin societal health resilience into the future.

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