Wastewater-Based Epidemiology: Global Collaborative to Maximize Contribution in the Fight Against COVID-19

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Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a novel member of the *Coronaviridae* family, has been identified as the etiologic agent of an ongoing pandemic of severe pneumonia known as COVID-19[1]. To date there have been millions of cases of COVID-19 diagnosed in 184 countries with case fatality rates ranging from 1.8% in Germany to 12.5% in Italy[2]. Limited diagnostic testing capacity and asymptomatic and oligosymptomatic infections result in significant uncertainty in the estimated extent of SARS-CoV-2 infection[3]. Recent reports have documented that infection with SARS-CoV-2 is accompanied by persistent shedding of virus RNA in stool in 27%[4] to 89% of patients at densities from 0.8 to 7.5 log10 gene copies per gram[5]. The presence of SARS-CoV-2 RNA in stool raises the potential to survey sewage for virus RNA to inform epidemiological monitoring of COVID-19, which we refer to as wastewater-based epidemiology (WBE)[6], but is also known as environmental surveillance[7].

Several studies have reported the detection of SARS-CoV-2 RNA in wastewater in the early stages of local outbreaks, further supporting the technical viability of WBE[8–10]. WBE could be especially informative given that oligosymptomatic infections are likely not captured in clinical surveillance. In such instances, WBE can be used to determine the burden of undiagnosed infections at the population level, which is critical to refining estimates of case-fatality rates. Additionally, wastewater offers an aggregate sample from an entire community that is more easily accessible than pooled clinical samples[11]. Along with clinical data and other technological approaches such as contact tracing, WBE could provide critical monitoring of COVID-19 transmission within a community including the beginning,tapering, or re-emergence of an epidemic (Figure 1). This approach mirrors previous efforts in environmental monitoring, for example poliovirus RNA, to inform mechanistic models of pathogen transmission dynamics[12].

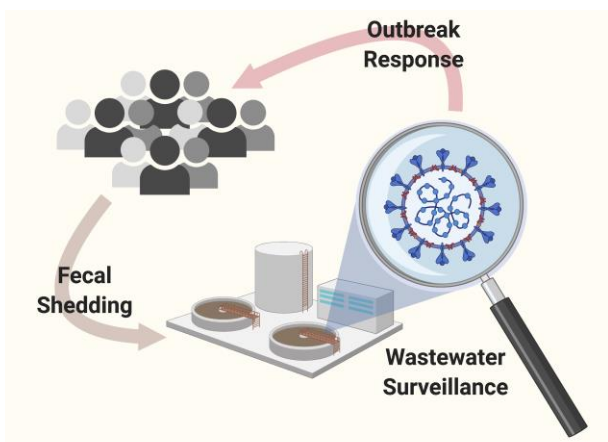

FIGURE 1 | In wastewater-based epidemiology (WBE), the prevalence of SARS-CoV-2 infections in a community could be estimated by enumerating the virus RNA in that community's sewage and performing mass balances on virus shedding using population and sewage flow rate data. Such information can then inform public health responses to the outbreak.

The ongoing pandemic provides a meaningful opportunity to field-test the hypothesis that WBE can be used to detect and manage infectious disease transmission in communities. Many research groups across the globe are mobilizing to monitor wastewater for SARS-CoV-2 RNA for this purpose. However, the quantitative relationship between RNA densities in sewage and human infection prevalence is dependent on many spatial and temporal variables. Importantly, these relationships must be examined in both urban settings with centralized wastewater facilities and rural and low-income settings with decentralized wastewater infrastructure. Assessing variation and uncertainty across such diverse settings requires the systematic harmonization and validation of methodologies across research groups. Therefore, to maximize the potential of the diverse WBE efforts underway, we propose a global effort to coordinate methodologies and data-sharing to maximize the yields of WBE for the current and future outbreaks of disease. The community will also benefit from including appropriate fully quantitative controls and standards as described previously by Bustin et al. 2009[13] to ensure cross laboratory comparability and data defensibility. Efficient harmonization of sampling, quality control, and analysis methods in the near term and, in the future, widespread dissemination of the resulting datasets and publications will help to ensure a high-quality evaluation of WBE.

In partnership with the Sewage Analysis CORe group Europe (SCORE) network and the Global Water Pathogen Project, we have launched the COVID-19 WBE Collaborative (https://www.covid19wbec.org/) as a hub to coordinate and promote the efforts of research groups undertaking WBE for COVID-19. The website will include content such as press releases, commentaries, and media content for public outreach and will be used to solicit participation in the collaborative and advertise events relevant to WBE. In the future, the site could also be used to host datasets and promulgate publications and presentations that result from the COVID-19 WBE Collaborative. We are pleased to invite our colleagues to join this effort at a level commensurate with their discretion.

The website also links to two important platforms for ongoing collaboration. The first is a protocols.io working group for methodological coordination. Research groups currently undertaking wastewater surveillance for SARS-CoV-2 are invited to share their protocols to help produce comparable results across geographies and time scales. Important details include, but are not limited to, the timing, frequency, location, and volume of sampling, relevant metadata, sample storage, means of concentration, extraction, and quantification of nucleic acids and observed processing recoveries. As previously mentioned, harmonization in the execution, or at minimum the reporting of relevant details, will greatly enhance the robustness of resulting datasets for analyzing transmission dynamics at various spatial and temporal levels. The second platform linked through the website is a Slack workspace for informal communication regarding COVID-19 WBE. The ongoing COVID-19 pandemic continues to evolve rapidly; therefore, any collaborative effort must include a platform for rapid communication.

As we work to sample sewage in the midst of this pandemic, biosafety remains paramount. Beyond protocols for sample analysis, we encourage all interested parties to work together to ensure appropriate biosafety measures while conducting this important work. Additionally, we ask funding agencies and the wastewater industry to consider funding for collaborative research related to COVID-19 WBE. The ongoing COVID-19 pandemic affords the occasion for engineers and scientists to collaborate with population-based scientists, such as epidemiologists, mathematical modelers and public health agencies to make high impact and timely contributions to society at large. The magnitude of such an opportunity calls for interdisciplinary coordination on a global scale to multiply the impacts of individual efforts. To that end, we have established the COVID-19 WBE Collaborative to facilitate such collaboration and we encourage all interested parties to join us.

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