

Review Article

Wastewater Surveillance System as a Complementary Approach for Rapid Identification of Infectious Diseases Outbreaks

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Abstract

The rapid identification of infectious disease outbreaks is critical, both for effective initiation of public health intervention measures and timely alerting of government agencies and the general public. Surveillance capacity for such detection can be costly, and many countries lack the public health infrastructure to identify outbreaks at their earliest stages. Wastewater surveillance is a promising complementary approach to clinical surveillance for monitoring community outbreaks. This approach can help detect the presence of pathogens across municipalities, and estimate disease incidence independent of individual testing. Wastewater surveillance may help overcome known limitations of clinical surveillance, such as low population coverage, high costs, testing and reporting delays, and the uncertain likelihood of an individual to seek health care. It is less resource intensive than large scale clinical testing, making it an optimal and cost-effective tool for long term monitoring as well as early identification of pathogens circulating in the population.

Keywords: Wastewater, surveillance, infectious diseases, outbreaks, monitoring, public health

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BACKGROUND

Infectious diseases are acknowledged as one of the most critical threats to global public health today. Climatic changes, unprecedented population growth with accelerated rates of antimicrobial resistance, have resulted in both the emergence of novel pathogenic organisms and the re-emergence of infections that were once controlled. The consequences have led to an increased vulnerability to infectious diseases globally. Even with the advancement of infectious disease surveillance over the last century, communicable diseases still pose significant risks to public health.^(1, 2)

Surveillance is a continuous systematic collection, analysis, and interpretation of health-related data in describing and monitoring a health event. In addition to providing information that is used for planning, implementing, and evaluating public health interventions and programs. Surveillance serves as an

early warning system for impending outbreaks that could become public health emergencies, enables monitoring and evaluation of the impact of an intervention, helps to track progress towards specific goals, monitors and clarifies the epidemiology of health problems, and guides priority setting and planning and evaluation public health policies and strategies.⁽³⁾

Infectious diseases surveillance types

A. Event-based infectious surveillance is most commonly conducted at the health center or the clinic,⁽⁴⁾ either through passive detailing or active case finding.^(3, 5) This event-based infectious disease surveillance monitors morbidity and mortality trends and alerts health systems when a statistically improbable uptick of events occurs. In this way, the number of cases, hospitalizations, and deaths from infectious

diseases can be monitored.⁽⁶⁻⁸⁾

- B. Environmental surveillance, on the other hand, is a broad category for systems that monitor the presence or absence of a pathogen in the environment, while still providing information regarding risks to human health. For example, environmental surveillance may routinely test known vectors for pathogens, alerting the public to the detection of, or an increase in, the pathogen in the vector population.⁽⁹⁾
- C. Wastewater surveillance is a type of environmental surveillance that has historically been utilized to track water-borne or fecal-orally transmitted pathogens.

The origin of wastewater surveillance hail back to the London cholera epidemic of the mid-1800's, John Snow, and the Broad Street Pump, when a cesspool near a house with multiple cholera deaths was excavated and found to be leaking into the pump's water supply. Scientists began hunting sewage not only for cholera but also for other pathogens including salmonella typhi bacteria, coxsackie viruses, and polioviruses.⁽¹⁰⁻¹²⁾ From the 1970s ahead, wastewater surveillance formed a basic component of worldwide activity to eradicate poliomyelitis,⁽¹³⁾ and perhaps poliomyelitis provides the best contrast between event-based and environmental surveillance systems. Whereas event-based polio surveillance relies on an unexpected increase in acute flaccid paralysis (AFP) which occurs in only 0.5% of polio cases,⁽¹⁴⁾ wastewater surveillance can detect poliovirus circulating in a community before any paralysis occurs.^(15, 16)

Efficient monitoring of infectious disease transmission is critical to prevent and manage infectious disease epidemics. The World Health Organization (WHO) stated top 10 threats to global health in 2019, four on the list directly refer to infectious diseases: Human immunodeficiency virus, pandemic influenza, dengue, and Ebola.⁽¹⁷⁾ Several major outbreaks of infectious diseases occurred during the past 20 years; including severe acute respiratory syndrome (SARS) (2002–2003),⁽¹⁸⁾ Ebola (2014–2016), H1N1flu (swine flu) (2009–2010),⁽¹⁹⁾ Zika virus (2015–2016) and COVID-19 (2019–up till now).⁽²⁰⁾

Wastewater-Based Epidemiology (WBE)

Rapid monitoring the spread of diseases is a key for their prevention and control; however, several limitations exist for current surveillance systems and the capacity to cope with the rapid population growth and environmental changes. WBE is a new epidemiology tool that has potential to act as a complementary approach for current infectious disease surveillance systems and an early warning system for disease outbreaks.⁽²⁾ WBE is an efficient approach with great potential for early warning of infectious disease transmission and outbreaks. By analyzing infectious disease biomarkers in water samples, the transmission of infectious disease in certain area can be monitored in near real time.⁽²¹⁾ These serious diseases caused by pathogens have made the effective monitoring of infectious diseases increasingly important. Integral components of public health are including; strengthening the supervision of infectious diseases, realizing early warning, and preventing infectious disease pandemics, especially emerging infectious diseases.⁽²⁾

There are many surveillance methods for infectious diseases, such as sentinel surveillance, routine reporting, clinical-based surveillance, surveys and special studies, and case and outbreak investigation, which hold great significance for infectious disease surveillance. However, most of these approaches depend on acquired data and information, such as incidence and mortality rates, prescription data, and hospitalization information, and herein, most of these systems are passive monitoring forms. Therefore, these techniques are subject to; bias, resource insensitivity, detection blindness, and high cost. Novel monitoring and management approaches are needed for the prevention and early warning of infectious diseases. These technologies should be flexible, cost-effective, and scalable and should provide comprehensive and objective data in real time. Meanwhile, they also need to monitor multiple diseases, even rare diseases.^(22, 23)

A systematic review revealed that the major pathogens monitored in wastewater are infections with the families Picornaviridae, Adenoviridae, Calciviridae, Hepeviridae, and Reoviridae, three of which are known to contribute to diarrheal infections, ⁽¹⁾ as shown in Figure 2.

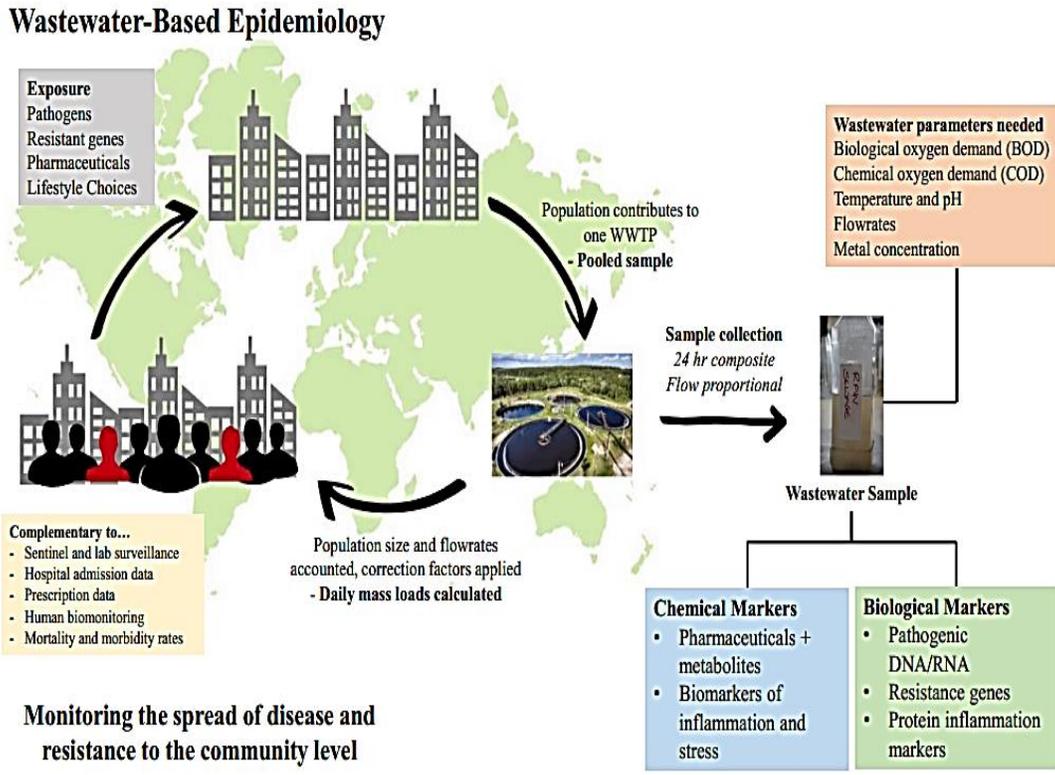


Figure 1: Wastewater-Based Epidemiology Concept

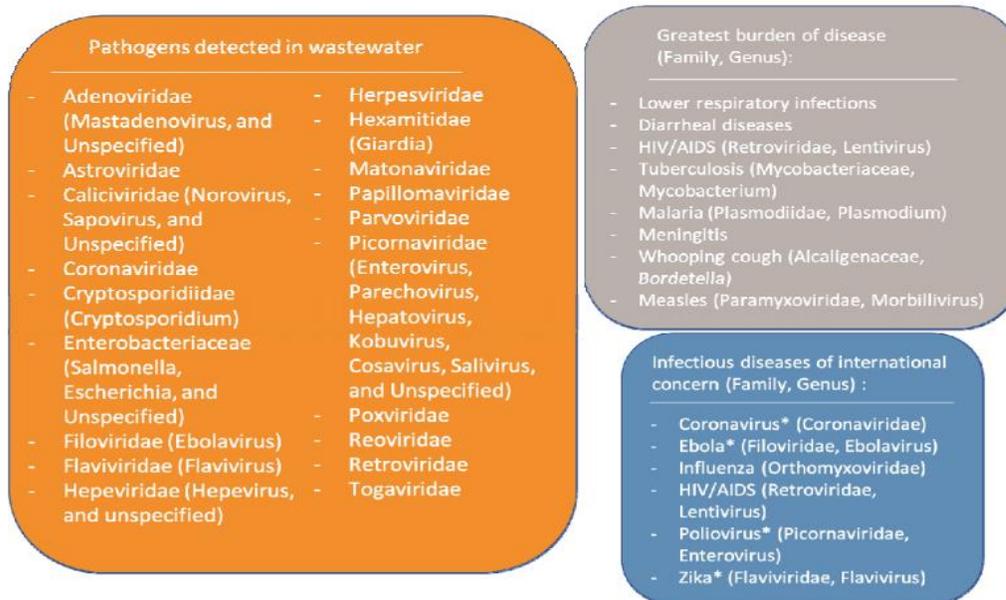


Figure 2: Pathogens surveilled in wastewater system⁽¹⁾

Human pathogens discharged in substantial liquids were monitored to decide the source of natural agents in the sewer and the length of agent discharge. Diverse sources of biological agents in sewers are feces, pee, skin from the shower and hand washing, and saliva from respiratory discharges.⁽²⁴⁾ Wastewater monitoring was commonly used to assess waterborne and fecal-oral pathogens that cause diarrhea. However, many other types of pathogens have been tracked using wastewater. Therefore, it should be considered as a potential tool for many infectious diseases. Observational studies of wastewater could be improved by consolidating other measures of infection transmission at the population level by counting infection frequency and hospital admissions.

Steps of wastewater surveillance:⁽²⁵⁻²⁷⁾

1. **Identify public health data needs.** The public health data needs depend on the status of the local epidemic and other available health indicators. Based on the current state of the science, wastewater surveillance can be used to support the following response objectives:
 - **Detect the presence of the pathogen of interest within a sewershed,** potentially earlier than with established case surveillance. The pathogen can be detected in wastewater several days prior to reported cases within the community. Knowing the pathogen is present in wastewater can be an important indicator when monitoring higher-risk communities with no known case patients.
 - **Monitor trends in pathogen spread within a sewershed,** including both reported cases and unreported infections. Analyzed wastewater data can provide trends in pathogen concentration over time. Using wastewater surveillance as a leading indicator of pathogen trends may be useful when trends in the number of new case patients are fluctuating or for assessing possible impacts of community mitigation efforts.
2. **Assess wastewater sampling and testing capacity.** When evaluating wastewater sampling and testing capacity, it is critical to include people with expertise in environmental microbiology and wastewater systems. Methods for accurately and precisely sampling and quantifying the pathogen RNA in wastewater that are representative of viral shedding within a community are available and continue to be improved. Effective use of limited wastewater testing capacity will require balancing population coverage and timely trend information that requires more frequent sampling.

3. **Develop a sampling plan.** The sampling plan should address the following questions: where to sample, how often to sample, what to sample, how to sample, and how to safely collect, store, and ship samples.

Criteria for selection of wastewater treatment plants for community wastewater monitoring:⁽²⁵⁻²⁷⁾

It is necessary to cover a certain percentage of the population, provide data on communities at higher risk for disease or at increased risk for severe illness from pathogen, and provide data on communities where timely disease clinical testing is underutilized or unavailable. Prior to selecting a wastewater treatment plant for community wastewater surveillance, it is critical to consult with wastewater engineers and utility managers to understand the geographic area and population served by the utility, relative contribution of the types of waste inputs (industrial, commercial, residential), operating factors that could influence the detection of pathogen e.g. pre-treatment of incoming wastewater, available sampling locations at the treatment plant, and utility capacity for sample collection, documentation, and shipping. Pathogen RNA concentrations are more variable upstream from the wastewater treatment plant than at the plant intake because upstream wastewater has had less time to mix and contains feces from fewer people. Access to sewer lines serving only the intended target population may require infrastructure alterations or may not be possible. Depending on the size of the target population, conducting effective targeted wastewater surveillance may be more costly and logistically challenging than case surveillance.

Frequency of sampling wastewater:⁽²⁵⁻²⁷⁾

Wastewater sampling frequency depends on how the data will be used for public health and the prevalence of disease in the community. Single samples or very infrequent (e.g., monthly) sampling will likely not be informative for establishing trends, but could be used for establishing presence of disease in a community. If the goal of wastewater surveillance is to screen for the presence of pathogen in wastewater, sampling once per week may be adequate, while if the goal is early indication of infection trends, at least three sampling points are needed within a trend period of interest for surveillance. National wastewater surveillance system analyses use a 15-day surveillance window for trend reporting. There are little data available describing how rapidly wastewater concentrations may change under various epidemic scenarios.

Type of waste water sample and method of selection:⁽²⁵⁻²⁷⁾

Sample type is an important consideration for collecting representative samples and will depend on

the sample collection location and factors specific to the wastewater treatment plant. Closely consult with treatment plant staff to determine appropriate sample types that will best represent the target population. Samples should be collected at locations that precede addition of chemicals or mixing of waste streams at the wastewater treatment plant.

1. Untreated wastewater:

Waste from household or building use (e.g., toilets, showers, sinks), which contains human fecal waste, as well as waste from non-household sources (e.g., rainwater, industrial use). Untreated wastewater may be sampled from wastewater treatment plant influent (prior to primary treatment) or upstream in the wastewater collection network. Changes in pathogen RNA concentrations in wastewater samples collected from wastewater treatment plant influent have been shown to correlate with trends in reported cases. In most cases, untreated wastewater will likely require concentration prior to RNA extraction. The number of infections needed to detect the virus in wastewater without concentration is difficult to determine because it depends on both the method detection limit and the amount of virus in feces, for which there are few data.

2. Primary sludge:

Primary sludge comprises suspended solids that settle out of wastewater during the first solids removal (“sedimentation”). Primary sludge is distinct from secondary sludge, which has undergone initial treatment that may remove pathogen RNA. Secondary sludge should not be used for wastewater surveillance. Changes in pathogen RNA concentrations in primary sludge samples have been shown to correlate with trends in reported cases. An advantage of primary sludge samples compared to untreated wastewater is that pathogen RNA concentrates in sludge may eliminate the need to concentrate the sample prior to quantification.

Untreated wastewater and primary sludge are both acceptable community wastewater surveillance sample types. For upstream targeted wastewater surveillance, only untreated wastewater samples are available. If laboratory methods are available, the Centers for Disease Control and Prevention (CDC) recommend sludge sampling to evaluate infection presence within a sewershed with few known case patients because the virus will be more concentrated in sludge, while the CDC recommend using untreated wastewater samples if wastewater treatment plants apply disinfectant before sludge can be sampled or sludge testing demonstrates high assay inhibition or poor virus recovery.

Wastewater surveillance system (WWSS) for COVID 19: A new frontier for public health ⁽²⁵⁻²⁷⁾

Wastewater surveillance for COVID-19 can be tested for RNA from SARS-CoV-2, the virus that causes COVID-19. While SARS-CoV-2 can be shed in the feces of individuals with COVID-19, there is no information to date that anyone has become sick with COVID-19 because of direct exposure to treated or untreated wastewater.⁽²⁸⁾ Sampling wastewater for SARS-CoV-2 as it enters a treatment plant (referred to as untreated influent) is used to evaluate trends in infection within the community contributing water to the sewer system. Select the number of treatment plants for community-level wastewater disease surveillance based on the public health data needs in the region and availability of resources. COVID-19 rates and trends in the community, distribution of the population, and characteristics of the sewer system may also influence the selection.

Wastewater sampling safety:

There is no evidence to date that anyone has become sick with COVID-19 because of direct exposure to wastewater. Standard practices associated with wastewater treatment plant operations should be sufficient to protect wastewater workers from SARS-CoV-2.

Wastewater sampling storage rules:

Samples should never be stored at temperatures higher than refrigeration (4°C), and samples should be refrigerated during the collection process, if possible, samples should be processed within 24 hours of collection. Effective actionable wastewater surveillance relies on rapid data collection. Remaining samples can be frozen at -70°C for archiving, avoid more than one freeze-thaw cycle. Data have shown potential loss of signal following freezing.

Shipping wastewater samples:

The CDC recommends that samples be packed in ice packs (4°C) and shipped the same or next day. Packaging and shipping of samples that are Class B infectious substances (UN 3373) according to United States Department of Transportation hazardous materials regulations.

Overview of wastewater sample processing and testing for SARS-CoV-2

After sample collection, the following steps should be followed: (Figure 3)

1. Sample preparation is the first step in SARS CoV-2 wastewater testing. A matrix recovery control should be spiked into the sample during this step.
2. Sample concentration is the second step.
3. RNA extraction from the concentrated wastewater sample is the third step.
4. RNA measurement is the final step. Along with measurement of SARS-CoV-2 RNA in this step, several laboratory controls should also be measured, including matrix recovery controls, human fecal normalization, quantitative measurement controls, and controls to assess molecular method inhibition.

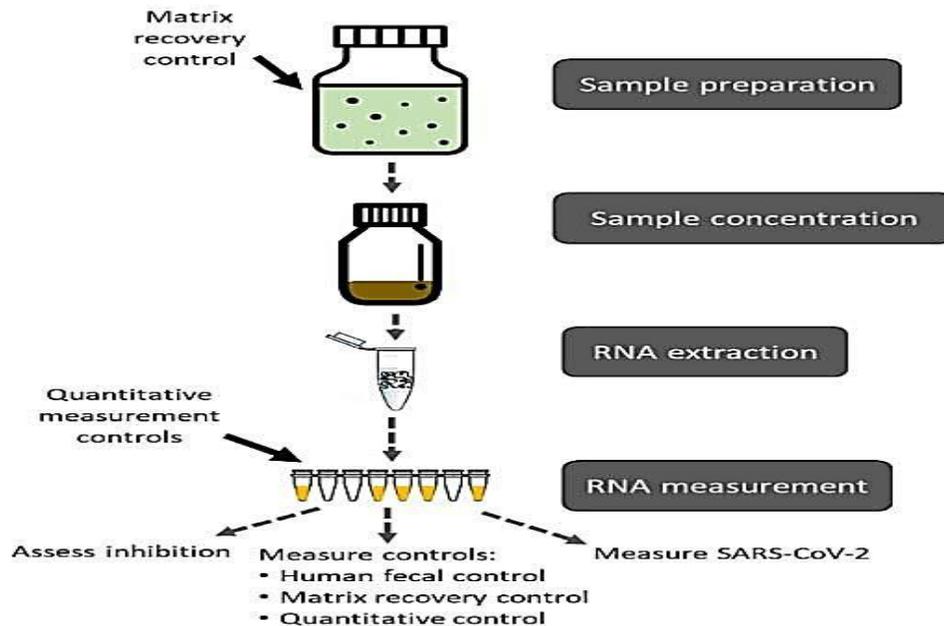


Figure 3: Wastewater surveillance testing method

Key public health advantages of wastewater surveillance⁽²⁹⁾

Wastewater analysis has been successfully used as an early detection strategy for other diseases such as poliomyelitis. SARS-CoV-2 can be shed in the feces of people with symptomatic or asymptomatic infections. Wastewater monitoring can therefore gather information on both types of pollution either symptomatic or asymptomatic infection. Depending on the reproducibility of testing, waste observations can be a key indicator of changes in community exposure to COVID-19. Detection of SARS-CoV-2 RNA in wastewater serves as a marker for his COVID-19 independent of health-conscious behavior and is included in clinical studies. Sewage monitoring can quickly determine the proximity of COVID-19 contamination to an entire city. This is one of the most cost-effective ways to get an overview of infectious agents in your community. It helps gather information from people and communities that need effective health care facilities. It provides real-time information on the spread of diseases, which helps to identify

future waves and even identify new evolutionary variants.

This method can be used to counter different viruses, like those that cause dengue, Zika, or TB in addition to antimicrobial resistance genes. It is important to monitor the infection, spread, and changing trends of COVID-19 at a population-wide scale and the waste-water based surveillance method is said to be a key tool in monitoring COVID-19 outbreaks and also minimizing such domino effects. Ability to identify changes in SARS-CoV-2 transmission trends. Changes on average 4-6 days before clinical cases show the same trend of changes.

Challenges and limitations of wastewater surveillance include:^(28, 29)

Potential exclusion of communities which do not have a drainage system and depend on septic tanks or facilities provided by such a decentralized sewer system, such as some prisons, universities, or hospitals that treat their own wastewater. Accurate and reliable prediction of the number of infected people in a

community based on sewer testing is unthinkable. More information on viral concentrations in the feces of infected individuals is needed to determine the relationship between concentrations of SARS-CoV-2 RNA in wastewater and infected populations in wastewater systems. Not all wastewater treatment plants may be suitable for target visits due to their operational coordination (for example, if the wastewater has recently been pretreated, it will reach wastewater treatment plant).

Situation in Egypt regarding wastewater surveillance system (WWSS):^(3, 28)

On 11 February 2013, in Egypt, wild poliovirus type 1 (WPV1) was isolated from sewage samples collected on 2 and 6 December 2012 in two areas of greater Cairo. Virus has been detected in sewage only; no case of paralytic polio has been reported. Genetic sequencing shows that the virus strains are closely related to virus from northern Sindh, Pakistan. Pakistan is one of three countries worldwide affected by ongoing indigenous transmission of WPV (together with Nigeria and Afghanistan). The isolates were detected through routine environmental surveillance in Egypt that involves regular testing of sewage water from multiple sites.

Polio surveillance in Egypt

Egypt has a vast and well-functioning polio surveillance system, consisting of surveillance for AFP by health workers across the country, and environmental surveillance of sewage runoff. Egypt consistently meets both of the international standards of polio surveillance, even during outbreak: the non-polio AFP rate is typically around three (the international standard is two or more) and the stool adequacy rate is usually in the high eighties (the international standard is 80%). Environmental surveillance has been in place in Egypt since 2000 and workers are given regular training and refresher sessions.

Forty-six collection sites operate across the country's 27 provinces, with at least one in each province. Wastewater testing provides a more complete snapshot of community spread than clinical testing and can serve as an early warning system for emerging outbreaks. The novel coronavirus has already been detected in wastewater which was demonstrated by the detection of SARS-CoV-2 RNA in primary sewage sludge during the early weeks of the outbreak.

Supporting COVID-19 prevention, early diagnosis and case management^(30, 31)

The United States Agency for International Development (USAID) supports the Egyptian government to curb the spread of COVID-19 by strengthening the health system in prevention, detection, and response. Starting in the 1990s, the USAID established Egypt's hospital-based national electronic disease surveillance system and reinforced the Central Public Health Laboratory structures, which is now diagnosing and analyzing COVID-19 cases in Egypt. The USAID programs are implemented in both the Ministry of Health and Population and university hospitals.

In 2020, the USAID donated 250 U.S.-made ventilators to Egypt to enhance the care of patients suffering from the most severe symptoms of COVID-19, as well as other diseases, for years to come. The USAID is supporting the Government of Egypt to detect SARS-CoV-2, the virus that causes COVID-19, in sewer systems to better understand outbreaks and reduce the time and cost of contact tracing. This early warning system supports public health measures to contain and control new COVID-19 outbreaks. This program provides technical support to improve the Government of Egypt's ability to plan for, sample, test, and disseminate information related to an early warning system for SARS-CoV-2 outbreaks.

CONCLUSION

Wastewater surveillance should be considered a general tool for public health going forward. Wastewater surveillance for infectious diseases at the level of sewerage and treatment plant should be a top priority of public health at the local, national and international level with the aim of acquiring actionable community-level information needed to navigate pandemics like COVID-19. It is widely acknowledged that effective surveillance system is a key for the rapid intervention and control of infectious disease outbreaks. The viral load of SARS-CoV-2 in wastewater represents the sum of both asymptomatic and symptomatic shedding, and thus indicating viral circulation in a community at any level. Wastewater surveillance is an economical and scalable companion to essential individual testing. The success of surveillance requires public legitimacy and trust of such measures.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest to declare.

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