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Centralized and decentralized wastewater-based epidemiology to infer COVID-19 transmission – A brief review

José Gonçalves [a,b,*], Andrés Torres-Franco [a,b], Elisa Rodriguéz [a,b], Israel Diaz [a,b], Tom Koritnik [c], Priscilla Gomes da Silva [d,e,f], João R. Mesquita [d], Marija Trkov [c], Metka Paragi [c], Raúl Muñoz [a,b], Pedro A. García-Encina [a,b]

[a] *Institute of Sustainable Processes, Valladolid University, Dr. Mergelina s/n, Valladolid 47011, Spain*
[b] *Department of Chemical Engineering and Environmental Technology, University of Valladolid, Dr. Mergelina s/n, Valladolid 47011, Spain*
[c] *Department for Public Health Microbiology, National Laboratory of Health, Environment and Food, Ljubljana, Slovenia*
[d] *ICBAS – School of Medicine and Biomedical Sciences, Porto University, Porto, Portugal*
[e] *Epidemiology Research Unit (EPIUnit), Instituto de Saúde Pública da Universidade do Porto, Porto, Portugal*
[f] *Laboratório para a Investigação Integrativa e Translacional em Saúde Populacional (ITR), Porto, Portugal*

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ABSTRACT

Wastewater-based epidemiology has shown to be a promising and innovative approach to measure a wide variety of illicit drugs that are consumed in the communities. In the same way as for illicit drugs, wastewater-based epidemiology is a promising approach to understand the prevalence of viruses in a community-level.

The ongoing coronavirus disease 2019 (COVID-19) pandemic created an unprecedented burden on public health and diagnostic laboratories all over the world because of the need for massive laboratory testing. Many studies have shown the applicability of a centralized wastewater-based epidemiology (WBE) approach, where samples are collected at WWTPs. A more recent concept is a decentralized approach for WBE where samples are collected at different points of the sewer system and at polluted water bodies. The second being particularly important in countries where there are insufficient connections from houses to municipal sewage pipelines and thus untreated wastewater is discharged directly in environmental waters.

A decentralized approach can be used to focus the value of diagnostic tests in what we call targeted-WBE, by monitoring wastewater in parts of the population where an outbreak is likely to happen, such as student dorms, retirement homes and hospitals. A combination of centralized and decentralized WBE should be considered for an affordable, sustainable, and successful WBE implementation in high-, middle- and low-income countries.

1. Introduction

The continuous changes in the emerging dynamics of viruses have led to their discovery and diagnosis playing an increasingly important role in clinical diagnostics and public health. The globalization of travel and trade in pets and animal products, trade-in bushmeat, political instability and bioterrorism, as well as climate change and its impact on vector distribution, have all contributed to the emergence and re-emergence of zoonoses [1]. Viruses that were previously confined to one host species or geographic region may now appear in unexpected places, confusing clinicians who are not prepared to recognize new syndromes or detect new pathogens with their existing diagnostic tests [2].

Individual sampling and testing of individuals is the most accurate measure of active transmission and disease prevalence [3]. Nevertheless, the temporal and spatial extent of individual testing that is needed to accomplish sufficient penetrance to obtain information is unreasonable and economically prohibitive in many countries. Moreover, surveillance systems based on clinical diagnosis depend heavily on the reporting and the severity of clinical symptoms and how these symptoms correspond to existing diseases in the population [4–8]. This can lead to significant underestimation, which is exacerbated by asymptomatic infections [5,9].

Due to these challenges, wastewater-based epidemiology (WBE) was proposed. WBE was first described in 2001 [10], and was initially used to trace cocaine and other illegal drugs [11]. This approach is based on

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* Corresponding author at: Institute of Sustainable Processes, Valladolid University, Dr. Mergelina s/n, Valladolid 47011, Spain.
E-mail address: zemcg5@gmail.com (J. Gonçalves).

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the assumption that any substance that is stable in wastewater and that is excreted by humans can be used to calculate the initial concentration [6,10,12–14].

A recent review concluded that WBE can rapidly detect trends in the consumption of illicit drugs and it is a very useful tool to generate data on illicit drug usage [14].

Just as with illicit drugs, WBE can also be used for infectious diseases. Since viruses are unable to grow outside of host cells, their concentrations in wastewater might represent the concentrations that are excreted by the corresponding population [15,16]. Thus, WBE is a promising approach to understand the prevalence of viruses at the community-level [17].

The use of WBE based on samples from raw sewage treatment plants is widespread and is referred to as centralized WBE. On the other hand, studies have also been conducted using samples from sewer networks, rivers, and sewage collectors instead of samples from WWTPs (decentralized WBE). In this review, we discuss the applications of wastewater-based epidemiology with special attention to the ongoing COVID -19 pandemic and discuss the idea of a decentralized approach to WBE.

2. Challenges in the implementation of WBE surveillance systems

A WBE approach for virus surveillance typically consists of three steps: 1) sampling; 2) virus recovery and concentration; and 3) virus detection and/or quantification. Each of these steps has its own challenges that limit the implementation of WBE [6,18] (Fig. 1).

The temporal and spatial challenges associated with sampling for WBE may affect the generated data representing the studied population. Sampling time needs to be based on the expected critical pathways [19]. The size of the catchment area and its vulnerability to daily changes in water flow and detection rates of viruses needs to be considered [20]. Autosamplers are often used to collect composite samples over a period of time with cooling units that help prevent virus degradation. Viral degradation and fate is affected by temperature [21,22] and may differ for systems with enclosed underground sewers and storm tanks and for systems using septic tanks, catchment basins and the open environment. Urban wastewater systems differ from rural wastewater systems as in rural areas there may be no wastewater collection systems and no proximity to testing facilities, whereas in urban wastewater systems the wastewater of the entire population is ultimately collected via catchment basins that can be used to subdivide the population. Despite the dilution of viral particles by industrial wastewater and others, urban wastewater systems are able to provide a more representative sample compared to rural systems [19]. Weather factors, such as dilution by rain are also important to access the viral load in wastewater, as well as for the disease transmission in the community [23,24].

The quantification of viruses is one of the most important steps in WBE, as a rise in the concentration of viruses in wastewater can indicate the possible outbreak of future diseases and/or increasing trends in infections and the number of hospitalisations [6]. Wastewaters often contain qPCR inhibitors such as urea, bile salts, ethanol, phenol, polysaccharides, sodium dodecyl sulphate, tannic acid, humic acids and melanin. Various proteins such as collagen, myoglobin, haemoglobin, lactoferrin, immunoglobin G (IgG) and proteinases are also abundant and known to have qPCR inhibitory effects [25]. In addition, environmental samples often contain small amounts of viral particles and thus high sensitivity methods are required. Before molecular detection of viral RNA or DNA, a concentration step is usually used as a preparatory step prior to molecular detection. Adsorption-elution based methods to concentrate enteric viruses are widely used. These primary concentration methods use either electropositive or electronegative filters, sedimentation by flocculation, size exclusion by ultracentrifugation and ultrafiltration [26,27]. After concentration, the gold standard for detection and quantification of RNA viruses is classical reverse transcription PCR (RT-PCR) and reverse transcription real-time PCR (RT-qPCR). These methods are used to obtain both qualitative and quantitative data [18].

Different calculations are required to associate viral RNA concentrations to epidemiological data. Depending on local sewer infrastructure, viral decay and flow rate in wastewater systems could be necessary to accurately relate the concentration of viruses in a sample to the viral

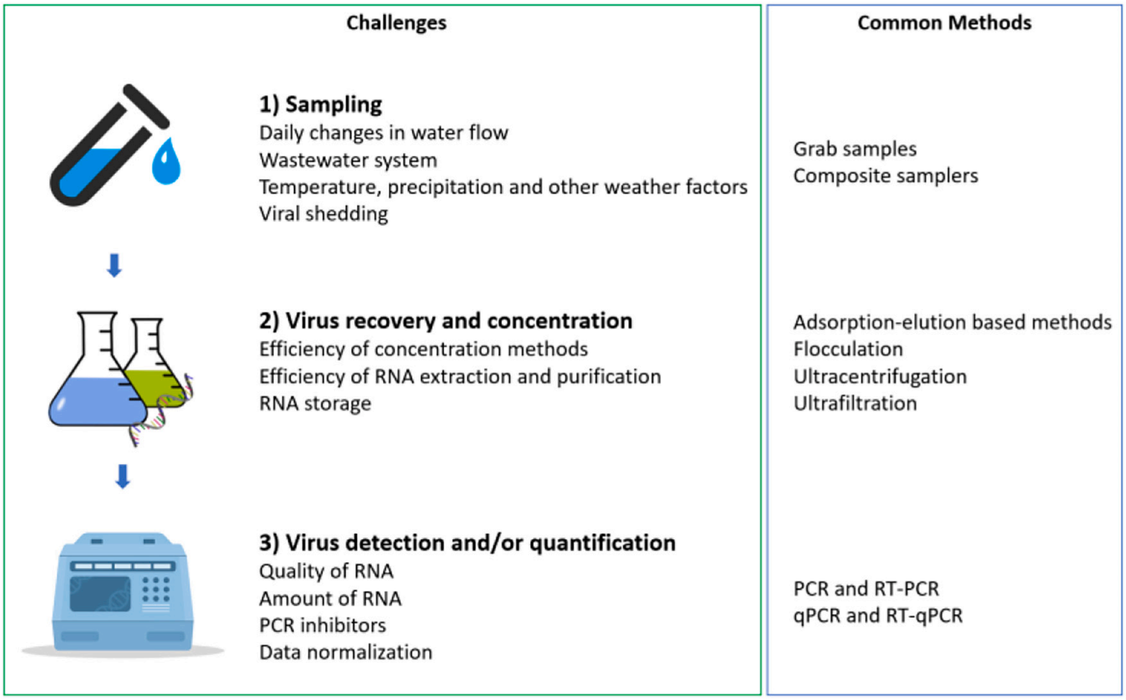

Fig. 1. Main steps of a WBE approach with their main challenges (green box) and common methods (blue box). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

load in the population. Furthermore, watershed modelling and microbial source tracking should be incorporated into the development of WBE strategies to assess wastewater transport and disposal and to determine where sampling should be performed [28]. The speed at which viruses are released from the body is also a challenge for the implementation of WBE systems, and some work has attempted to estimate shedding rates in faeces, which in turn are affected by viremia, duration and severity of the disease, and age [29]. Another factor that is important for the implementation of WBE is the estimation of the population's contribution to wastewater samples. The normalization of the population requires the use of both census and biomarker data. Normalization is essential to allow comparisons between cities and to guarantee that a significant rise in viral concentrations in a sample is not related with an increase in the population in the catchment area [29,30].

The use of WBE allows a near real-time picture of the viral load within a community. Viruses are released into waste streams through a variety of pathways, including urine, stool, skin, saliva, and blood [6]. Previous studies have demonstrated the benefits and potential of wastewater monitoring systems. WBE was used as part of the Global Polio Eradication Programme as a tool to assess the prevalence of polio in the population and to evaluate the effectiveness of immunization against the poliovirus [31–33]. It has also been used retrospectively to predict outbreaks of hepatitis A and norovirus-associated gastroenteritis [34]. WBE is predominantly relevant for early warning of disease outbreaks and to provide information on the effectiveness of public health measures. The advantages of WBE have already been demonstrated for enteric viruses such as rotavirus, norovirus, hepatitis A virus and poliovirus [34–36]. WBE can play an essential role in optimizing decision making and minimizing the incidence of severe cases that can overwhelm the capacity of intensive care hospitals [37,38].

3. Wastewater-based epidemiology for COVID-19

In December 2019, a new coronavirus belonging to the genus *Betacoronavirus* was isolated for the first time in the city of Wuhan, China, from a group of patients with unrecognizable acute pneumonia [39]. The ongoing coronavirus disease 2019 (COVID-19) pandemic has created a huge burden on public health and diagnostic laboratories worldwide due to the demand for mass testing for SARS-CoV-2 [37]. One way to minimize the COVID-19 burden is to use novel rapid diagnostic tests. However, these are not widely available and present challenges in terms of reliability and quality control. Mass testing is therefore hampered and difficult to implement in several countries, specially those from developing regions, due to huge costs and constraints in the production and supply chain [6].

In 2020, viable SARS-CoV-2 has been detected in stools of COVID-19 patients [39,40] and later viral RNA has been found in sewage [16,23,41–43]. This resulted in the use of WBE as surveillance and early warning tool to aid the current COVID-19 pandemic, with several important studies being done worldwide. Previous studies have shown that WBE is a scalable and cost-effective tool that can deliver rapid results, detect a wide range of emerging and re-emerging viral diseases and facilitate community-wide analysis [6,15,16,23]. At the beginning of the use of WBE to track SARS-CoV-2, the prevailing scientific opinion was that the virus might enter wastewater at too low concentrations and that both the virus particles and its RNA might be too unstable to be detected in wastewater [42].

Concentration of SARS-CoV-2 from wastewater samples has been conducted using a wise range of methods, such as PEG precipitation [44], electronegative filters, ultracentrifugal membrane filters [42,45], ultracentrifugation [46], $Al(OH)_3$ adsorption-precipitation [43], Mg_2Cl adsorption-extraction at acidic conditions [47] and by adapting the standard WHO protocol for the surveillance of poliovirus [48,49]. Low recovery rates and time-consuming handling times are some drawbacks of these concentration methods [50–52].

At the moment of submitting the manuscript, more than 500 studies successfully report the detection of SARS-CoV-2 RNA in wastewater. Table 1 summarizes initial reports on the detection of SARS-CoV-2 in wastewater samples. The first studies have shown that SARS-CoV-2 RNA can be detected in wastewater using a wide range of concentration and detection methods and highlighted the viability of WBE for viral surveillance and early-warning system (Table 1).

As seen in Table 1, initial reports were published in the first months of 2020. Rimoldi et al. reported the detection of SARS-CoV-2 RNA in raw and treated samples from a WWTP and river samples in metropolitan area of the city of Milan Area [41,53]. These early studies were not aimed at estimating the prevalence of COVID-19 in the population based on WBE but suggested the possibility of a more quantitative approach. Further studies explored associations between RT-qPCR target gene concentrations (namely N1 and N2) and number of active cases [23,41–44,46,54,55]. Medema et al. suggested that viral loads obtained by multiplying gene concentrations by flow rates measured at the time of sampling should be used to compensate the high variability of gene concentrations [42]. WBE has a great potential for surveillance of COVID-19 as a city zonation tool through comprehensively monitoring sewers and WWTPs [47], which is of high relevance mainly in poor urban areas where massive testing is not available [56]. An example of a national-scale surveillance system is the website VATar COVID-19 (Spain) (https://www.miteco.gob.es/es/agua/temas/concesiones-y-autorizaciones/vertidos-de-aguas-residuales/alerta-temprana-covid19/VATAR-COVID19-Informes-actualizados.aspx), which reports global trends in terms of increases, stability or decreases in SARS-CoV-2 concentrations in the influent wastewater of the main Spanish cities [57].

With the emergence of new SARS-CoV-2 variants, studies attempted to detect and quantify the mutations characteristic of each variant in wastewater. One of the first studies to follow this approach has shown that the SARS-CoV-2 mutations found in wastewater were closely related to the lineages circulating within the community [58]. In a similar study, [59] identified in the city of Nice (France), during October 2020–March 2021, the variants B.1.160, B.1.177, B.1.367, B.1.474, and B.1.221 and the emergence of a variant (Spike:A522S) of the B.1.1.7 lineage, which became dominant in the city [59]. The B.1.1.7 variant was also identified in wastewater analysis in December 2020 in several locations of Israel. However, at the time of the studies, these regions did not have sufficient clinical sampling available to compare mutations found in clinical settings with wastewater surveillance [60].

4. Detection of SARS-CoV-2 RNA in surface waters

WBE has been assessed mostly in high-resource countries, however in lower-resource settings a substantial portion of residents are not connected to a centralized treatment plant. The use of pit toilets, septic tanks or open defecation are still common practices in some countries [61–64]. Discharges of untreated wastewater into the environment and the use of waterways as open sewers are a usual practice. The detection and quantification of SARS-CoV-2 in polluted surface waters contaminated with sewage could represent an complementary epidemiological tool for viral surveillance [63–65]. Studies have been made accessing the concentrations of SARS-CoV-2 RNA in decentralized sewer networks, rivers and sewer interceptors and are summarized in Table 2 [47,53,66–70]. [47], suggests that decentralized sewage monitoring could identify hotspots in a city and help major cities in dealing with the current pandemic [47]. Another study in Quito, Ecuador was performed during the local peak of COVID-19. RNA of SARS-CoV-2 was detected in three points of an urban river that receives untreated sewage from 3 million inhabitants. Interestingly, the viral loads clearly matched with the numbers of reported cases in the collection area [67]. On the contrary, a study conducted in Japan reported that SARS-CoV-2 RNA was not detected in any of the studied influent wastewater and river samples [68]. (See Table 3.)

The findings of these studies show the potential of monitoring SARS-CoV-2 in polluted rivers and surface waters as a feasible complement to

Table 1
Some of the first studies where SARS-CoV-2 was detected in raw wastewater. The table shows the sampling period and location, number of samples, concentration method used and the main highlights of each study.

Location	Period of sampling	Sampling location	Number of samples	Concentration method	Highlights	Reference
Massachusetts, USA	March 25th to April 18th, 2020	WWTP	14	PEG 8000 precipitation	• The concentrations of SARS-CoV-2 in wastewater imply a higher prevalence of COVID-19in the population (0.1%–5%) than the prevalence reported by clinical testing (0.026%) • High uncertainty in estimating number of active COVID cases from viral concentrations in WW	[39]
South-East Queensland, Australia	March 20th to April 1st, 2020	One Suburban pumping station and two WWTPs	2	Electronegative membranes Ultrafiltration	• WBE is viable to monitor infectious diseases, such as COVID-19, at the population level.	[54]
Amsterdam, Netherlands	February 7th to March 25th, 2020	WWTPs of six cities and sewage of Amsterdam Schiphol Airport	24	Ultrafiltration	• SARS-CoV-2 RNA concentrations at the WWTP inlet over time might act as a sensitive tool for early warning of increasing virus circulation in the population.	[42]
Paris, France	March 5th to April 4th, 2020	Three WWTPs	23	Ultracentrifugation	• Surveillance of SARS-CoV-2 genomes in wastewater can produce valuable additional information at local or regional levels	[46]
Milan and Rome, Italy	February 3rd to April 2nd’ 2020	Three WWTPs	12	Modified PEG-dextran precipitation	• Temporal and spatial trends of COVID-19 prevalence in the population can be assessed by measuring concentrations of SARS-CoV-2 RNA in wastewater.	[41]
Murcia, Spain	March 12th to April 14th’ 2020	Six WWTPs	42	$Al(OH)_3$ adsorption-precipitation	• WBE can be used to provide an early warning of the status of COVID-19 infection within a community.	[43]
Ljubljana, Slovenia	June 1st to 15th’ 2020	Hospital sewage	15	Centrifugal filtration	• WBE for SARS-CoV-2 provides a valuable epidemiological tool to monitor COVID-19 prevalence and thus to strengthen public health measures in the ongoing pandemic. • WBE is a useful approach for early warning in risk communities such as hospitals	[23]
Louisiana, USA	January 13th to April 29th, 2020	Two WWTPs	15	Ultrafiltration Adsorption-elution	• First study to report the presence of SARS-CoV-2 RNA in wastewater in North America. • Protocols to detect SARS-CoV-2 RNA in wastewater should be refined and validated in order to increase its sensitivity, including the concentration step and molecular detection.	[45]

Table 2
Examples of studies where SARS-CoV-2 was detected in surface waters and decentralized sewage systems. The table shows the sampling period and location, number of samples and the main highlights of each study.

Location	Period of sampling	Sampling location	Number of samples	Highlights	References
Niterói, Brazil	April 15th, 2020	Wastewater treatment plant; hospital wastewater; sewer network	12; (5 from sewer network)	• 41.6% positive samples. • 3 out 5 positive samples were from sewer network. • Estimation of viral loads in sewers network in various areas of the city will support information for health surveillance.	[70]
Quito, Ecuador	June 5th, 2020	River	3	• 100% positive samples. • The detection of SARS-CoV-2 RNA in wastewater as an early warning system using main sewage discharges along the city is an efficient tool.	[67]
Milano and Moza, Italy	April 14th and 22nd 2020	WWTP; River	18 (3 from river)	• SARS-CoV-2 RNA was detected in the raw WW from all the WWTPs on April 14th and only in the raw WW of the WWTP-B plant on April 22nd. • SARS-CoV-2 RNA was found in all receptors water bodies on April 14th, 2020, but only in the Lambro River on April 22nd, which followed the decrease in community prevalence.	[53]
Yamanashi Prefecture, Japan	March 17th to May 6th, 2020	WWTP; River	13 (3 from river)	• SARS-CoV-2 RNA has been detected in a secondary-treated wastewater sample. • SARS-CoV-2 RNA has not been detected in influent ($n = 5$) and river water samples ($n = 3$).	[68]
Belgrade, Serbia	December 7th to 13th, 2020	River	8	• Upstream and downstream of WWTP input samples were negative. • Next to WWTP input, all samples were positive. • The study reports the first detection of SARS-CoV-2 RNA in surface water of the Danube River.	[69]
Minas Gerais, Brazil	August 2020	Prison and rural area sewage; River	25 (15 from river)	• 80% positive samples. • SARS-CoV-2 RNA was not found in upstream river water from the rural community but has been detected in two downstream river waters. • In the rural area assessed, human sewage is released directly to the river waters and basic sanitation systems are not available.	[66]
Belo Horizonte, Brazil	May 10th to August 1st, 2020	WWTP; Sewer interceptors	204	• COVID-cases hotspots need to be identified based on data generated by decentralized sewage monitoring, instead of clinal data.	[47]

Table 3
Examples of studies where SARS-CoV-2 was detected in wastewater of targeted communities. The table shows the sampling period and location, number of samples and the main highlighs of each study.

Location	Period of sampling	Sampling location	Number of samples	Highlights	References
Ljubljana, Slovenia	June 1st to 15th, 2020	Hospital wastewater	15	• WBE is a useful approach for early warning in risk communities such as hospitals. • RNA increase was followed by an increase in COVID-19 patients.	[23]
Calgary, Canada	August 5th to December 17th, 2020	Hospital wastewater	159	• RNA increase was followed by an increase in COVID-19 patients.	[73]
Virginia, USA	Early 2020	Hospital wastewater; Student dormitories wastewater; WWTP	Not available	• WBE at individual buildings seems to be a feasible tool for SARS-CoV-2 surveillance in occupied congregate living settings.	[74]
Valencia, Spain	October 2020	Nursing homes wastewater	5	• SARS-CoV-2 sewage monitoring in combination with targeted screening of residents and staff can be a powerful tool for early detection of viral transmission and its spread at nursing homes.	[75]
Dubai, UAE	April 22nd to July 7th, 2020	Pumping stations; WWTPs; Aircraft wastewater	27 (Pumping stations); 2940 (WWTPs); 198 (Aircraft wastewater)	• Detection of SARS-CoV-2 in the wastewater of an aircraft may prompt decision-makers in any country to suspend all flights from a particular location.	[77]
Queensland, Australia	April 23th, 2020	Aircraft and cruise ship wastewater	21	• The surveillance of wastewater from large transport vessels containing their own wastewater tanks has the potential to complement and prioritize clinical testing and contact tracing among disembarking passengers.	[76]

WBE, especially in countries or areas with poor sanitation settings and with unequal sewage coverage. A recent review study concludes that there is a lack of WBE programs in African countries to monitor SARS-CoV-2 and that nation-wide WBE programs are difficult to implement in countries with dissimilar sanitary coverage. A decentralized approach can also serve to identify zones with higher viral prevalence, by taking samples in specific points in the sewer system and to promote quick actions in specific population groups [71].

Thus, SARS-CoV-2 a decentralized WBE needs to be further explored and can be applied either in countries with dissimilar sanitary coverage and to target specific population groups. [65,71].

5. Targeted-WBE for SARS-CoV-2

The idea of decentralized sewage monitoring for SARS-CoV-2 can also be applied to target specific groups in a community, in what the authors of the present review call targeted-WBE. Studies have been made accessing the concentrations of SARS-CoV-2 RNA in decentralized and targeted sewage samples, such as hospital wastewater, nursing homes wastewater, among others (Table 2).

Hospitals and medical centres are more likely to systematically monitor and identify COVID-19 cases within their population when compared with entire cities. Nevertheless, COVID-19 outbreaks in hospitals are increasingly being reported and, thus, prevention of outbreaks is urgent and challenging [72]. Plans to understand the epidemiology of SARS-COV-2 in hospitals and to prevent outbreaks are needed. One of the strategies can be targeted-WBE [56,73]. A pilot study concluded that targeted-WBE at individual building level is a feasible approach, where sensitivity is more important that accurate quantification [73].

Targeted-WBE has been applied not only in hospitals, but also in student dormitoriesS [74], nursing homes [75], commercial aircrafts [76,77] and cruise ships [76]. Detection of SARS-CoV-2 in large transportation systems can give critical information to decision makers and minimize the role of a global economy in the spread of infectious diseases [77], as well as facilitate clinical testing and contact tracing among passengers [76].

6. Limitations of WBE

Some limitations of existing surveillance systems were highlighted during the current COVID-19 pandemic and during previous disease surveillance systems. The main limitations are the sensitivity and specificity of surveillance approaches based on clinical symptoms. These approaches heavily depend on clinical symptoms and on the extent of their reporting, as well as how symptoms overlay with existing diseases in the population [4,6–8]. WBE can overcome some of these restrictions, especially for COVID-19. A significant proportion of COVID-19 patients are either asymptomatic, pre-symptomatic or have mild and non-specific symptoms and are therefore not reported. These factors lead to a significant underestimation of infection, and the rate of asymptomatic infection cases has been estimated at 20–45% [5,9,40].

7. Conclusions

The ongoing coronavirus disease 2019 (COVID-19) pandemic created an unprecedented burden on public health and diagnostic laboratories all over the world because of the need for massive laboratory testing. Individual testing in large scale is the most accurate way to measure active transmission and disease prevalence. However, this entails enormous costs with serious economic consequences. Over the last 20 years, environmental scientists have developed and refined Wastewater-Based-Epidemiology. It is still needed to invest in the analytical power of concentration and detection methods and to standardize WBE pipelines to allow data comparison among countries, as previously employed for poliovirus [49].

WBE is an important tool to predict, contain and mitigate viral outbreaks, while minimizing unnecessary restriction policies that pose serious stress to humans and economies. This tool has not yet been widely incorporated by epidemiologists and public health officials. A well-implemented WBE system is imperative for viral surveillance. Governments need to begin evaluating WBE and actively coordinate the development of standardized methodologies that need to be deployed within national public health monitoring programmes. WBE can be extended beyond previous surveillance strategies and circumvent its current limits, which have been established for reasons of privacy, ethics and legal concerns, as in its application for surveillance of illicit drugs [78].

Developing countries often have inadequate wastewater infrastructure, which, among many other problems, can hinder the application of WBE and further stunting monitoring efforts in the very countries that would benefit from this cost-effective surveillance approach. Due to the high proportion of households not connected to the sewage network, poor management of sewage and non-functioning operational facilities, analysis of untreated wastewater from centralized WTTPs in these countries is not representative of disease prevalence in the population [79]. A way to circumvent these limitations is the environmental surveillance of SARS-CoV-2 RNA in polluted waters. Available data suggest that rivers polluted by waste disposal and sewage discharge could be an alternative source for COVID-19 prevalence information [65].

Another application of decentralized WBE is to avoid populations that are likely to be negative and focus the value of diagnostic tests in what we call targeted-WBE. Targeted-WBE can be used to reach populations where diagnostic tests should be strengthened by monitoring smaller and key population groups. Key target populations include hospitals, schools, university dormitories, overcrowded social housing, long-term care facilities such as retirement homes, prisons, airports, and mass entertainment facilities, where outbreaks have been frequently reported. For affordable, sustainable and successful WBE implementation in high-, middle- and low-income countries, a combination of centralized and decentralized WBE should be considered.

8. Future perspectives in WBE

Emerging and reemerging infectious diseases, as well as the rising rates of antimicrobial resistance, demonstrate the importance of developing disease surveillance strategies that follow the One Health approach, where human, animal and environmental health are interlinked [80]. The concept of One Health and WBE are particularly important for antimicrobial resistance. Antibiotic resistance has been historically regarded as a clinical concern and considered to be exclusively related to the excessive use and misuse of antibiotics [81]. In recent years, the fate of antimicrobial resistance genes (ARGs) released to wastewaters has received increasing interest and there is a worldwide consensus that raw municipal wastewater, treated effluent and wastewater sludge are reservoirs of ARGs and crucial hotspots for the evolution and spread of antibiotic resistance [82]. Antibiotics entering water and wastewater are insufficiently removed and/or inactivated in treatment plants, causing a significant fraction being released directly into the environment in effluent waters. A part of these are retained in the sludge, which accumulates these compounds [83]. Direct contact between pathogenic bacteria and environmental ARG carriers, as well as the continuous selective pressure enforced by traces of antibiotics in wastewaters makes WWTPs an ideal hub for the spread of antimicrobial resistance [84]. Centralized and decentralized WBE are crucial to monitor the spread of antimicrobial resistance across hosts and environments. Lessons learned from the COVID-19 pandemic can thus be applied for wider surveillance strategies and the implications of environmental and animal health in human health.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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