Review

How has the COVID-19 pandemic impacted wastewater-based epidemiology?

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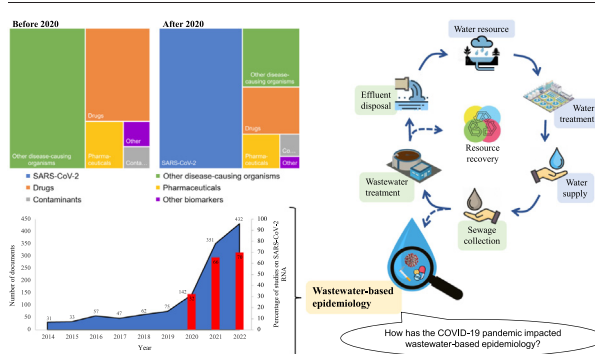[c] Graduate Program on Water Resources and Environmental Engineering, Department of Hydraulics and Sanitation, Federal University of Paraná, Curitiba, Brazil

HIGHLIGHTS

- COVID-19 pandemic made the diversity of research objects in WBE decrease.
- With COVID-19 pandemic, the participation of developing countries in WBE increased.
- COVID-19 reduced international cooperation in WBE and strengthened local networks.
- The pandemic has increased the diversity of stakeholders involved in WBE research.
- The global coronavirus pandemic has changed the research funding profile at WBE.

GRAPHICAL ABSTRACT

ARTICLE INFO

ABSTRACT

Wastewater-based epidemiology (WBE) was one of the areas of scientific knowledge that developed significantly with the COVID-19 pandemic, with robust worldwide application to monitor the circulation of the SARS-CoV-2 virus in urban communities at different scales and levels. This mini-review assesses how the COVID-19 pandemic may have influenced the WBE based on the investigation of 1305 scientific reports published (research, review, and conference papers) up to the end of 2022, considering the research objects, funding sources, actors, and countries involved. As a result, 71 % of all WBE-based publications occurred since the beginning of the pandemic, with 62 % addressing SARS-CoV-2, demonstrating the migration of WBE's relative importance in studies on drug abuse, pharmaceuticals consumption, and other disease-causing organisms to the constitution of a tool to support the monitoring of the coronavirus. Before the pandemic, WBE was a tool used for epidemiological surveillance of several diseases (54 % of studies), drug abuse (30 %), and pharmaceutical consumption (9 %). With the pandemic, these research topics lost to space, constituting only 37 % of the area's studies, and SARS-CoV-2 became the central object of studies. In addition, there has been a 4.7 % expansion of developing country participation in sewage surveillance publications and greater diversification of collaborators and funders, especially from government, businesses, and the water industry. International research partnerships had a reduction of 8 %, consequently, there was an increase in local and regional partnerships. With the COVID-19 pandemic, funding for research in WBE became approximately 6.5 % less dependent on traditional research funds. The future of WBE involves different approaches, including different focuses of research and technological advancements to improve the sensitivity, precision, and applicability of these investigations. The new WBE research arrangements are promising, although the post-pandemic challenges are likely to be in maintaining them and overcoming the trend toward a lack of diversity in study subjects.

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Contents

1. Introduction

Historically, the London cholera outbreak of 1854 was a crisis moment that transformed modern science and showed the inextricable link between epidemiology and sewage. The mapping of the location of deaths, known as the "ghost map," changed the concept of public health and was probably the first scientifically documented case of sewage depicting epidemiological information on the population. This "ghost map" made it possible to discover the location and period of infection of the original victim, patient zero, of the cholera outbreak in that city (Johnson, 2007). Despite this evidence on the scope and informational richness derived from sewage, it was only in the 2000s that an approach dedicated to studying this functional component of cities emerged as a basis for understanding the epidemiological profile of the population.

The significant advances in analytical methodologies that have occurred since the mid-1990s (Santos et al., 2010; Barcellos et al., 2022) allowed Daughton (2001) to propose wastewater-based epidemiology (WBE) to identify and determine collective parameters on the use of drugs in the community. This environmental or epidemiological surveillance of wastewater, which had already been applied since the 1990s to understand the circulation of disease-causing organisms (e.g., Marques et al., 1993; Yano 1993; Grabow et al. 1999), began to be applied a few years later to understand drug abuse and pharmaceutical consumption on a residue basis (e.g., Zuccato et al., 2005; Lindberg et al., 2005; Heberer and Feldmann, 2005). Since then, the application of WBE has gained a worldwide scale, expanding its scope, e.g., to early warning of infectious disease outbreaks, to understanding city metabolism, the use of pesticides, food, and chemical consumption (Mao et al., 2020; Kasprzyk-Hordern et al., 2022) and constituting informational foundations to guide public policies (Cyranoski, 2018). Although the WBE has already achieved the status of a powerful complementary tool for examining the profile of waste generated by an entire population or community and thus contributing to determining the effectiveness and direction of government health actions (Rice et al., 2020), the crisis caused by the COVID-19 pandemic increased the visibility of this approach.

In this mini-review, based on scientific reports from the Web of Science (WoS), we seek to assess how the COVID-19 pandemic may have changed WBE. The database was searched by "topic" up to 2022 using the terms "wastewater-based epidemiology" OR "sewage-based epidemiology" OR "wastewater surveillance" OR ("epidemiological surveillance" OR "environmental surveillance") AND (sewage OR sewer OR wastewater)), considering research, reviews, and conference papers (Fig. 1). The first part of the review presents the state of the art of WBE research, emphasizing the objects of study and the annual behavior of scientific production. The second part identifies and discusses the profile of the WBE research during the COVID-19 pandemic (funding sources, stakeholders, and countries involved), looking for evidence of changes. The third part of the manuscript discusses future perspectives of the WEB.

2. State of the art of wastewater-based epidemiology research

The first articles on epidemiological surveillance of wastewater appeared in 1993 in the WoS database, focusing on virus detection (Marques et al., 1993; Yano 1993). The polio virus was the first challenge of sewage surveillance epidemiological and environmental. Since the 1990s, sewage has been used as an important source of information to understand the circulation of this virus. From the end of the 1990s, studies on this topic intensified and became recurrent (e.g., Grabow et al. 1999; Manor et al., 1999). Until 2010, the polio virus was the main subject of studies on environmental and epidemiological surveillance of sewage (e.g., Horie et al., 2002; Dedepsidis et al., 2007). However, scientific reports addressing other diseases in wastewater were also published during this period, e.g., on vibrio cholera and enteric viruses (e.g., Tamrakar et al., 2006; Blinkova et al., 2009). In these first studies retrieved from the WoS database, something that draws attention is the representativeness of developing countries,[1] e.g., South Africa, Brazil, Cuba, Egypt, and India, which were pioneers in conducting these studies. As a tool to understand the circulation of diseases in communities, sewage surveillance is strategic. However, for many developing countries with insufficient epidemiological surveillance systems, it may be the most efficient and feasible strategy to understand the circulation of diseases.

Despite the environmental and epidemiological surveillance of sewage being a field of investigation since the mid-1990s, in the 2000s, a new terminology emerged that opened new areas of investigation for the surveillance of wastewater. The terminology "wastewater-based epidemiology" has appeared in the WoS database since 2009 (Van Nuijs et al., 2009), with investigations based on this perspective emerging as an alternative to understanding mainly drug abuse and the use of illicit substances (Van Nuijs et al., 2009; Been et al., 2014; Lai et al., 2015). These advances have made this field more multidisciplinary and dependent on entirely different analytical methodologies, not only from the biology field but also from chemistry. The WBE has played an essential role in investigations to quantify the consumption of drugs because their use is beyond formal controls, practically making the use of other methods unfeasible.

From 2014 the number of studies on sewage surveillance has its highest annual increase, increasing 182 %, from this year onwards, the number of articles published per year was always greater than 30 (Fig. 2). In these first years of use of the WBE terminology, there is an evident cleavage in sewage surveillance studies. The terminology "environmental or epidemiological surveillance of sewage" is used for studies to monitor disease-causing organisms (e.g., Ahmad et al., 2015; Tao et al., 2015; Ferreyra et al., 2015). On the other hand, the WBE terminology for studies on illicit and licit drugs (e.g., Been et al., 2014; Been et al., 2015; Senta et al., 2015) and pharmaceutical substances (Lai et al., 2015; Chen et al., 2015). This innovation in using sewage surveillance to understand drug and pharmaceutical consumption patterns held promise for public health management and as a strategic basis for urban environmental policies. For example, in several developing countries, such as Brazil (Barcellos et al., 2019), well-structured systems to identify, quantify and report pharmaceutical consumption do not exist or are highly precarious. In these countries with high social inequality, the WBE can reveal essential information from the consumption

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[1] We consider developing countries to be those classified as such in the most recent list of the International Monetary Fund's (International Monetary Fund. 2017. Seeking Sustainable Growth: Short-Term Recovery, Long-Term Challenges. Washington, DC, October).
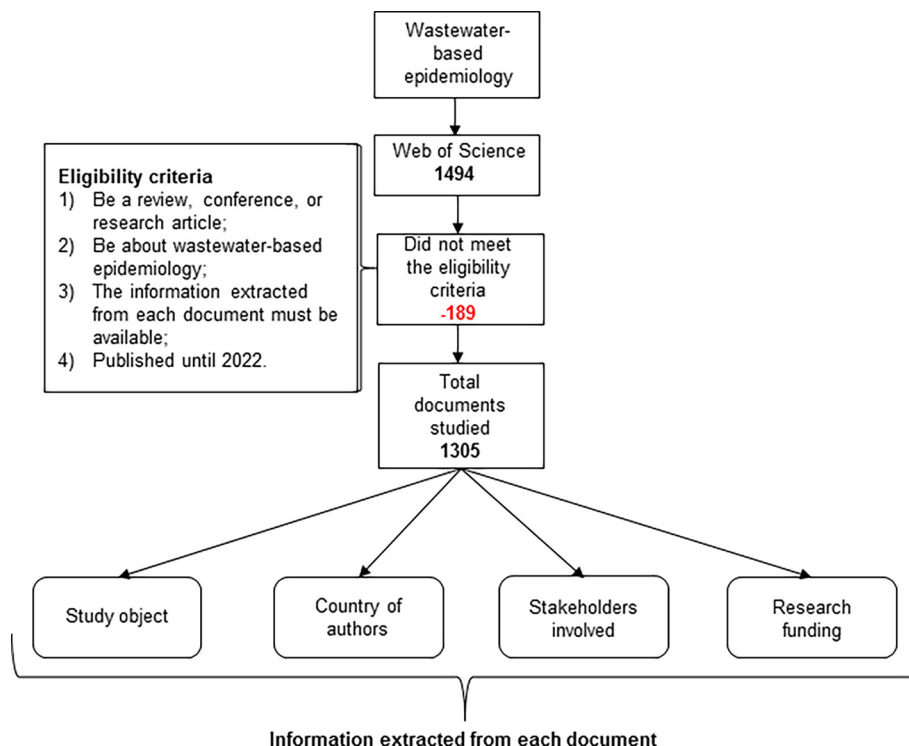
Fig. 1. Sequential diagram of research.

profile of the socially excluded population, which is outside the prescription pharmaceutical controls based on access to health services. Paradoxically, the WBE approach may have disadvantages in locations with low basic sanitation, e.g., being less effective because part of the sewage does not enter the collection network or is more diluted by rainwater.

In 2016, the number of published scientific reports had a relevant increased compared to the previous year, increasing by 73 % (Fig. 2). The content of these reports brought innovations in the exposure of the population to pesticides (Rousis et al., 2016) and the consumption of licit drugs (Baz-Lomba et al., 2016). Most studies focused on illicit drug use (e.g., McCall et al., 2016; Yang et al., 2016; Lai et al., 2016), and disease-causing organisms (e.g., Ram et al., 2016; Muluh et al., 2016; Furtak et al., 2016) with a small group advanced to the assessment of pharmaceutical substance use (Gao et al., 2016; Baz-Lomba et al., 2016; Fattore et al., 2016). About 46 % of sewage surveillance studies conducted this year were on disease-causing organisms, 44 % on drugs, and 16 % on pharmaceuticals (Table 1). The predominant origin of these studies is from developed countries, about 67 %.
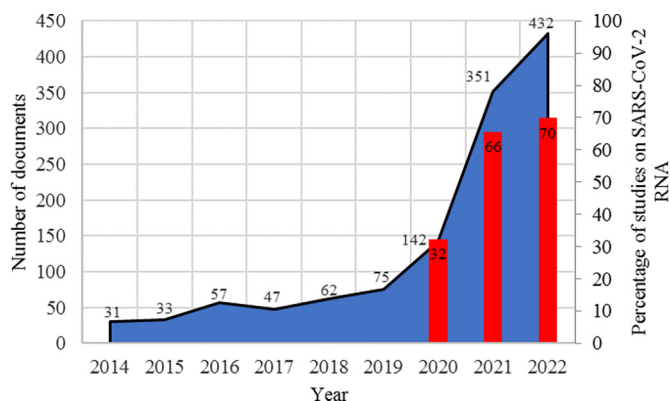
The number of reports using sewer surveillance was reduced by 18 % in 2017 and increased by 32 % in 2018 and 21 % in 2019. Investigations focused mainly on disease-causing organisms (2017:34 %; 2018:48 %; 2019:37 %), the consumption of drugs (2017:45 %; 2018:47 %; 2019:47 %), and, to a lesser extent, the consumption of pharmaceutical substances (2017:15 %; 2018:6 %; 2019:17 %) (Table 1). Furthermore, research in developing countries remained relatively infrequent (e.g., Gao et al., 2017; Castrignanò et al., 2018; Yan et al., 2019). The approach remained discreet during this period to address pesticide exposure (e.g., Rousis et al., 2017) and licit drug use (Banks et al., 2018). The first studies on the consumption of drugs of abuse were published in Brazil, South Africa, and Turkey. In 2017, 2018, and 2019, developed countries were responsible for 83 %, 65 %, and 56 % of scientific production on sewage surveillance. The inaugural studies of new WBE areas were published in 2017, emphasizing the monitoring of biomarkers (Rico et al., 2017), anabolic steroid consumption (Causanilles et al., 2018), and bisphenol exposure (Lopardo et al., 2018).

In 2020, there was a drastic increase of 89 % in the number of reports published compared to 2019 (Fig. 2). In addition to research on disease-causing organisms, drugs, and pharmaceuticals, WBE-based advances have occurred in research on antibiotic-resistant genes in aquatic environments (Castrignanò et al., 2020; Eramo et al., 2020), dietary habits (Li

Fig. 2. Annual studies (research, reviews, and conference papers) in WoS on wastewater-based epidemiology since 2014.

Table 1
Main subjects of study in WBE from 2016 to 2022 in publications in WoS database.

Year	Total number/(%) of studies	Number/(%) of studies on disease-causing organisms[a]	Number/(%) of studies on drugs	Number/(%) of studies on pharmaceuticals
2022	432(33.10)	380(87.96)	38(8.80)	22(5.09)
2021	351(26.90)	280(79.77)	52(14.81)	27(7.69)
2020	142(10.88)	87(61.27)	43(30.28)	15(10.56)
2019	75(5.75)	28(37.33)	35(46.67)	13(17.33)
2018	62(4.75)	30(48.39)	29(46.77)	4(6.45)
2017	47(3.60)	16(34.04)	21(44.68)	7(14.89)
2016	57(4.37)	26(45.61)	25(43.86)	9(15.79)

[a] Includes studies on SARS-CoV-2.

et al., 2020; Gracia-Lor et al., 2020; Choi et al., 2020), and the concentration of bisphenol in sewage (Tang et al., 2020; Wang et al., 2020). In that year, 61 % of the publications were on disease-causing agents in sewage (e.g., Farkas et al., 2020; McCall et al., 2020; Diemert and Yan, 2020), with 32 % investigating the RNA of SARS-CoV-2. Therefore, 53 % of the studies dealt with the RNA of the SARS-CoV-2 virus (e.g., Ahmed et al., 2020; Daughton, 2020; Sherchan et al., 2020), mainly in developed countries, with 60 % of studies. Although the COVID-19 pandemic influenced the increase in research publications based on the WBE that year, an essential part followed the same trend as in previous years, dealing with the consumption of pharmaceuticals (11 %) and illicit drugs in sewage (30 %).

The number of scientific publications on WBE published in 2021 was even more drastic, with an increase of 147 % compared to the previous year (Fig. 2). The content of these documents included classical investigations about disease-causing organisms (e.g., Faleye et al., 2021; Lizasoain et al., 2021; Ahmed et al., 2021), illicit drug use (e.g., Bijlsma et al., 2021; Bade et al., 2021; Asicioglu et al., 2021) and pharmaceutical substances (e.g., Escolà Casas et al., 2021; Bodík et al., 2021; Yan et al., 2021). Investigations extended diversity to address antimicrobial-resistant bacteria (Spänig et al., 2021; Kumar et al., 2021a, 2021b; Gumede et al., 2021), disease biomarker proteins (Mohapatra et al., 2021), pesticide exposure (Rousis et al., 2021; Vera-Herrera et al., 2021) and plasticizers (Estévez-Danta et al., 2021a, 2021b), and consumption of sweeteners (Li et al., 2021a, 2021b). Of these reports, 80 % dealt with disease-causing organisms identified in sewage (Table 1) and 66 % with SARS-CoV-2 RNA (e.g., Hillary et al., 2021; Agrawal et al., 2021; Mota et al., 2021). The volume of research on disease-causing organisms corresponded to 82 % focused on the RNA of SARS-CoV-2. This year's research focused on developed countries, with 62 % of studies, but addressed some developing countries like Brazil, South Africa, China, India, Argentina, Chile, and Mexico. This general increase in publications based on the WBE was mainly the impact of the COVID-19 pandemic, with a small part of the studies dealing with other subjects, such as pharmaceuticals (8 %) and drugs of abuse (15 %).

In 2022, despite being numerically expressive, the percentage increase in scientific documents on the WBE was much smaller than in the previous two years. The 23 % increase compared to 2021 (Fig. 2) returned to pre-pandemic growth levels (2017–2019), situated in the range of normal growth in an emerging field of research. In the last year, little news appeared in the themes of the published investigations. There was a continuity of classic studies on disease-causing organisms (e.g., Dai et al., 2022; de Araújo et al., 2022; Mercier et al., 2022), pharmaceutical use (e.g., Duan et al., 2022; Gao et al., 2022a; Tomsone et al., 2022), of illicit and licit drugs (e.g., Wang et al., 2022; Chappell et al., 2022; Zheng et al., 2022), antibiotic-resistant bacteria (e.g., Cai et al., 2022; Steenbeek et al., 2022; Holton et al., 2022), and consumption of sweeteners and steroids (Li et al., 2022; Shimko et al., 2022). The novelties were, e.g., the study of the biochemical load in an urban system via WBE, which allowed a holistic understanding of the city's metabolism (Kasprzyk-Hordern et al., 2022). The 88 % share of WBE studies deal with disease-causing organisms (e.g., Dzinamarira et al., 2022; Faleye et al., 2022; Johnson et al., 2022), and 70 % deal with SARS-CoV-2 RNA. The volume of research on disease-causing organisms corresponded to 79 % focused on the RNA of SARS-CoV-2 (e.g., Johnson et al., 2022; de Araújo et al., 2022; Masachessi et al., 2022). Other WBE areas of study, such as pharmaceutical use (5 %) and drug abuse (9 %), were poorly addressed in studies that year. In the same direction as the previous year, in 2022, many developing countries published research based on the WBE, especially on the RNA of SARS-CoV-2, such as Kenya, Turkey, Uruguay, Peru, Nepal, and Morocco, but 68 % of studies were from developed countries.

3. Changes in wastewater-based epidemiology with the COVID-19 pandemic

The first report using the WBE terminology in the WoS database appeared in 2009, but since the mid-1990s, epidemiological and

environmental surveillance of sewage has already been carried out to learn about the circulation of diseases. Until 2019, before the COVID-19 pandemic, only 29.1 % of the 1305 documents were published in such article base. Therefore, 70,9 % of reports on WBE were published after the start of the COVID-19 pandemic, i.e., these publications occurred in the last three years. Additionally, 62,5 % of those reports dealt with SARS-CoV-2. These percentages show that the health crisis caused by the COVID-19 pandemic was crucial for the spread of WBE. The WBE terminology arises to characterize the consumption of drugs of abuse (Daughton, 2001) and is practically co-opted by studies of this field before the pandemic (Escolà Casas et al., 2021), with 46 % of studies in this entire area about drug use, in the last three years before the pandemic, and 40 % about disease biomarkers (Table 1). Nevertheless, the WBE terminology has become more common than environmental and epidemiological sewage surveillance with the pandemic for reporting disease biomarkers. Before the pandemic, 40 % of the studies in our sample used the WBE terminology, and 60 % used environmental or epidemiological sewage surveillance. With the pandemic, 70 % of the studies addressed began to use the WBE terminology, and only 30 % continued to use environmental or epidemiological surveillance.[2] In addition to this terminology migration, the WBE has become a fundamental approach to understanding the circulation of the SARS-CoV-2 virus in real-time in urban communities during the pandemic of COVID-19 (e.g., Prado et al., 2021; Masachessi et al., 2022; de Araújo et al., 2022). In practical terms, the WBE approach has taken on a strategic role during the pandemic because it is efficient and relatively inexpensive, especially for countries with low testing capacity.

Documents with studies based on the WBE showed that the COVID-19 pandemic increased by 4.7 % of publications from research in developing countries. From 2020, 36.8 % of WBE-based investigations involved collaborators from these countries. Before 2020, in the three years before the pandemic (2017, 2018, and 2019), 32.2 % of publications had participants from that context. Historically, the lead in publications on the WEB has been interspersed between developed and developing countries. However, from 2014 onwards, when the number of annual publications had its most significant rise, the participation of developed countries became dominant. With the pandemic, the United States, China, and Australia maintained their leadership as countries with the highest number of studies on WBE (Table 2). Spain tied in the number of studies with the United Kingdom, and India surpassed Italy. In this period, India, South Africa, Turkey, and Mexico also significantly increased scientific production based on the WBE (Table 2). Mexico, in particular, started publishing on this topic only after the onset of the pandemic. This movement also happened in numerous other countries (28 out of 75 with WBE-based publications), mainly in developing countries. The following countries started publishing WBE-based reports only after the start of the COVID-19 pandemic: Mexico, Austria, United Arab Emirates, Slovakia, Hungary, Ireland, Latvia, Qatar, Slovenia, Czech Republic, Luxembourg, Romania, Bangladesh, Costa Rica, Cuba, Ethiopia, Philippines, Ghana, Indonesia, Iraq, Malaysia, Mozambique, Nepal, Peru, Senegal, Serbia, Vietnam, and Zimbabwe. Therefore, one of the consequences of the global health crisis caused by SARS-CoV-2 was the strengthening of the WBE approach worldwide, expanding possibilities for the development of this field of scientific knowledge, especially in developing countries.

Current advances in knowledge in science commonly occur through international cooperation between countries with expertise and others seeking such development. However, this does not appear to have been the case with recent advances at the WBE. The investigations based on this approach showed a significant reduction in international cooperation after the start of the pandemic, around 8.3 %. Before the pandemic, 36.6 % of research was part of international cooperation. After the pandemic's start, only 28.3 % of investigations involved these cooperations. This behavior may reflect the pandemic period in which WBE was used as a local and regional tool to support the health crisis, despite the existing international

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[2] These proportions refer to the use of terminologies in titles, abstracts and keywords.

Table 2
Documents published by the twenty countries with more studies on the WBE in WoS database.

Corresponding author country	Total number/(%) of studies	Number/(%) of studies before 2020	Number/(%) of studies from 2020	Percentage of studies published after 2020 compared to the total
United States	272(20.84)	46(12.07)	226(24.46)	83.09
China	122(9.35)	37(9.71)	85(9.20)	69.67
Australia	106(8.12)	30(7.87)	76(8.23)	71.70
United Kingdom	66(5.06)	18(4.72)	48(5.19)	72.73
Spain	61(4.67)	13(3.41)	48(5.19)	78.69
Italy	58(4.44)	26(6.82)	32(3.46)	55.17
India	54(4.14)	8(2.10)	46(4.98)	85.19
Brazil	50(3.83)	19(4.99)	31(3.35)	62.00
Japan	42(3.22)	17(4.46)	25(2.71)	59.52
Canada	35(2.68)	2(0.52)	33(3.57)	94.29
France	29(2.22)	7(1.84)	22(2.38)	75.86
Israel	29(2.22)	19(4.99)	10(1.08)	34.48
South Africa	26(1.99)	5(1.31)	21(2.27)	80.77
Belgium	24(1.84)	12(3.15)	12(1.30)	50.00
Greece	24(1.84)	13(3.41)	11(1.19)	45.83
Netherlands	23(1.76)	10(2.62)	13(1.41)	56.52
Germany	22(1.69)	5(1.31)	17(1.84)	77.27
Switzerland	16(1.23)	9(2.36)	7(0.76)	43.75
Argentina	14(1.07)	7(1.84)	7(0.76)	50.00
Mexico	13(1.00)	0(0.00)	13(1.41)	100.00

exchange of techniques and methods (e.g., Mota et al., 2021; Masachessi et al., 2022; Ali et al., 2022). Therefore, the involvement of local and regional actors from different sectors of society seems to have been the main driver of the development of the WBE during the COVID-19 pandemic crisis.

The COVID-19 pandemic has promoted an increase in local and regional multi-stakeholder networks in the field of the WBE. These networks usually remained led by universities and research institutes, but with the pandemic, the participation of other stakeholders increased significantly (Table 3). Some institutions began to participate in research on WBE only after the start of the pandemic, such as police, and associations. These studies have not always been about SARS-CoV-2 (e.g., Bijlsma et al., 2021; Estévez-Danta et al., 2021a, 2021b; Wang et al., 2022), which indicates that part of this increase is not directly related to the pandemic but with a natural increase process of an emerging field of scientific knowledge. Before the pandemic, participation in WBE-based research by research institutes, international agencies, and non-governmental organizations (NGOs) was higher. The pandemic's beginning was reflected in the increased participation of all other institutions in research, emphasizing governments, companies, hospital centers, and the water sector.

The intensity of the increased participation of different organizations in scientific research based on the WBE seems to indicate that the involvement of these stakeholders was more dependent on the pandemic than the result

Table 3
Stakeholders involved in WBE publications in WoS database.

Study authors institutions[a]	Total number/(%) of studies	Number/(%) of studies before 2020	Number/(%) of studies from 2020	Percentage of studies published after 2020 compared to the total
Company	85(3.65)	6(0.9)	79(4.7)	92.94
Government	293(12.59)	82(12.4)	211(12.7)	72.01
Research institute	606(26.04)	217(32.8)	389(23.3)	64.19
University	1128(48.47)	302(45.7)	826(49.6)	73.23
Police	4(0.17)	0(0.0)	4(0.2)	100.00
Hospital center	67(2.88)	17(2.6)	50(3.0)	74.63
International agency	33(1.42)	21(3.2)	12(0.7)	36.36
NGO	10(0.43)	6(0.9)	4(0.2)	40.00
Water industry	99(4.25)	10(1.5)	89(5.3)	89.90
Association	2(0.09)	0(0.0)	2(0.1)	100.00

[a] Institutions of all authors were considered.

of a natural increase process in this field (Table 3). The involvement of police and associations in research after 2020 slightly increased, with a relevant part of research not related to SARS-CoV-2, 50 % of police and 100 % of associations (e.g., Bijlsma et al., 2021; Estévez-Danta et al., 2021a, 2021b; Wang et al., 2022). Businesses, hospitals, government, and the water industry collaborate heavily on investigations based on the WBE after 2020, mainly with investigations related to the new coronavirus (e.g., Prado et al., 2021; Kumar et al., 2021a, 2021b; Ali et al., 2022). For these stakeholders, interest in WBE has emerged with the health crisis, likely to address it as a decision support tool for government and public health (e.g., Mota et al., 2021; Guerrero-Latorre et al., 2022; Ali et al. 2021; Ali et al., 2022). Changes in the profile of stakeholder participation in WBE-based research have also reflected in fundamental changes in the funding of these studies (Table 4). In the post-COVID-19 period, there was a reduction of around 6.5 % in research funding by research funds (public or private), which were the primary funding sources, and greater diversification in funding institutions. The direct participation of companies, governments, universities, research institutes, and the water industry in research funding has increased significantly, as has the number of studies without funding.

Participation, support, and research funding naturally involve sectoral and corporate interests. The WBE was one of the scientific approaches used to face the coronavirus pandemic, gaining a lot of repercussions and visibility for its funders and participants. When science gains prominence as a solution to a health crisis, participation, and institutional investment bring visibility to organizations and become an important marketing strategy. Often, what is proposed by science and researchers as applicable for decision support, including justifying the importance of research for its funders, is not effectively considered in government decisions but is saleable by collaborators and funders.

4. The future of wastewater-based epidemiology

The future perspectives of WBE in developed and developing countries are likely to differ. In developed countries, WBE is already being used to monitor community health and identify hotspots of drug use and other risky behaviors. In the future, WBE is likely to become more widespread in developing countries as the technology becomes more sophisticated and the testing costs continue to decrease.

In less developed countries, the use of this tool may be slower due to limited resources and infrastructure for wastewater management. However, WBE could be particularly valuable in developing countries where traditional disease surveillance systems are weak or non-existent. In such contexts, WBE could provide an affordable and scalable means of monitoring population health and detecting outbreaks of infectious diseases.

Table 4
Financing of WBE research in WoS database.

Financing	Total number/(%) of studies	Number/(%) of studies before 2020	Number/(%) of studies from 2020	Percentage of studies published after 2020 compared to the total
Company	12(0.67)	1(0.19)	11(0.87)	91.67
Research fund[a]	843(47.20)	271(51.82)	572(45.29)	67.85
Government	345(19.32)	90(17.21)	255(20.19)	73.91
University	196(10.97)	41(7.84)	155(12.27)	79.08
International agency	21(1.18)	14(2.68)	7(0.55)	33.33
Research institute	60(3.36)	15(2.87)	45(3.56)	75.00
Water industry	33(1.85)	6(1.15)	27(2.14)	81.82
No funding	269(15.06)	85(16.25)	184(14.57)	68.40
Association	1(0.06)	0(0.00)	1(0.08)	100.00
Hospital Center	6(0.34)	0(0.00)	6(0.48)	100.00
NGOs	1(0.06)	1(0.19)	0(0.00)	0.00
Police	1(0.06)	0(0.00)	1(0.08)	100

[a] A public or private "research fund" was considered when only grants were mentioned. When. e.g., companies, universities, and government institutions are mentioned, funding has been attributed to these institutions.

The first challenge for the WBE in developing countries is their small sewage system coverage. WBE relies on collecting and analyzing wastewater samples, which can provide important information on the health and behavior of the population. However, the lack of adequate sewage systems means that a significant proportion of the population cannot access safe sanitation facilities, and untreated wastewater is often discharged directly into the environment, leading to public health risks and environmental pollution. In addition, there would be social exclusion since the sewage system does not serve the most vulnerable population. The low coverage of sewage systems in developing countries underscores the urgent need for investments in sanitation infrastructure and the development of innovative approaches to improve access to safe and sustainable sanitation services. Undoubtedly, WBE would benefit from this eventual improvement in sewage infrastructure.

The data presented in this study shows that the COVID-19 pandemic has been the focus of studies conducted in the last three years. However, the future of WBE includes different approaches, such as:

- Biomarkers of disease, such as viral RNA, can be detected in wastewater to provide valuable information on the population's prevalence and spread of diseases. In addition to COVID-19, other disease biomarkers include enteric viruses (Guo et al., 2022; Salvo et al., 2022), arbovirus (Lee et al., 2022), oncogenic viruses (Hou et al., 2020), and chronic diseases (Amin et al., 2023; Shao et al., 2023). Monitoring these biomarkers allows identifying and preventing potential outbreaks and can provide information on the prevalence of the disease in the population.
- Antimicrobial-resistant microorganisms (ARMs) pose a risk to the effectiveness of preventing and treating a range of infections caused by viruses, bacteria, fungi, and protozoa. Traditionally, ARM surveillance focuses on laboratory-generated report-based monitoring, where specific pathogens are identified that are isolated from human clinical infections. However, WBE may be a potential alternative for ARM surveillance, including information from large populations and healthy individuals who are not typically monitored when surveillance is conducted on clinical samples (Hendriksen et al., 2019; Aarestrup and Woolhouse, 2020). Monitoring for ARMs can provide important information for health authorities in controlling the spread of resistant strains.
- Illicit drugs, such as opioids (Gushgari et al., 2019), cocaine (da Silva et al., 2018), amphetamines (Gao et al., 2022b), cannabis (Causanilles et al., 2017), and their metabolites, can be analyzed in wastewater. Monitoring for illicit drugs can provide information on drug use patterns in a given population, guide public health responses, and the presence of new or emerging drugs. Global campaigns for monitoring illicit substances in sewage can be warning systems for these drugs' prevalence and support public health and safety policies (Bade et al., 2023).
- Pharmaceuticals and their metabolites can also be detected in wastewater, providing insights into medication use and adherence, including antidepressants, antipsychotics, benzodiazepines (Laimou-Geraniou et al., 2023), antibiotics (Han et al., 2022), and antiviral drugs (Galani et al., 2021). Monitoring these substances allows for estimating the level of use, the prevalence of modern diseases, and tracking the spread of epidemics. In addition, pharmaceutical substances can also be useful for estimating the size of the population with chronic diseases, such as diabetes (Zheng et al., 2023) and hypertension (Hou et al., 2023).
- Dietary biomarkers can be used to estimate population-level dietary intake and monitor changes in dietary habits. In addition, this information can be used in public health policies to guide the population in improving their diet and reducing the risk of chronic diseases. Dietary biomarkers include caffeine, alcohol, nicotine (Driver et al., 2020; Shao et al., 2023), and artificial sweeteners (Li et al., 2021a, 2021b).
- Environmental contaminants, including metals (Markosian and Mirzoyan, 2019) and emerging pollutants (Gracia-Lor et al., 2018), can also be monitored in wastewater to provide insights into environmental exposure and potential health risks.

In addition to the target substances monitored in sewage, there are technological approaches to improve WBE's sensitivity, accuracy, and applicability. Machine learning and artificial intelligence algorithms can analyze large amounts of WBE data and identify patterns or anomalies indicative of disease outbreaks or other health risks (Abdeldayem et al. 2022). Spatial analysis techniques can be used to map the distribution of biological markers in wastewater and identify hotspots of drug use or other risky behaviors (Shao et al., 2023). Advances in metagenomics can provide a more comprehensive view of the microbial communities present in wastewater, including emerging pathogens or antibiotic-resistant strains (Riquelme et al., 2022). Microfluidics technologies can miniaturize and automate the sample processing and analysis steps in WBE, making it faster and more efficient (Ou et al., 2021). Finally, online monitoring systems can continuously monitor wastewater in real-time and provide early warning of emerging health risks (Köke et al., 2022).

Overall, the future perspectives of WBE in both developed and developing countries are promising and these approaches and techniques have the potential to become an important tool for public health surveillance and disease control.

5. Conclusion

The COVID-19 pandemic is the most significant health crisis of the century thus far and consequently has transformed the WBE's approach. WBE-based research has expanded into developing countries, broadened the diversity of contributors from different sectors of society (mainly business, government, and the water sector), and has seen fundamental changes in the dynamics of research funding, making it more varied. Research in this field has expanded local and regional knowledge exchange, strengthening national networks and reducing international cooperation. The WBE became less used for evaluating drug abuse, pharmaceutical consumption, and other disease-causing organisms and developed into a complementary and essential strategy to understand the circulation of SARS-CoV-2 in real-time, mainly from the sewers of large urban centers.

The limited diversity of study objects continues to be a cause for concern for advancing the scientific development of WBE, especially in 2022 where 70 % of the studies were on SARS-CoV-2, even considering the atypical pandemic period. On the other hand, multi-stakeholder networks, the participation of developing countries, and the great recognition that WBE achieved during the pandemic, even outside research institutes and universities, are the legacies that can contribute to its continuity by expanding and diversification of study objects in the coming years. However, it is essential to create mechanisms to make the new WBE-based research arrangements permanent by establishing national epidemiological surveillance programs and public policies based on wastewater. Stakeholder networks and a funding model less dependent on traditional research funds are fundamental advances that need continuity.

The suggestion is for future investigations to critically assess whether the information produced by WBE-based research during the pandemic has been integrated into management practice in different countries or is ad hoc utilitarian interests based on market logic.

CRediT authorship contribution statement

Demian S. Barcellos: Conceptualization, Methodology, Formal analysis, Investigation, Data curation, Visualization, Validation, Writing – original draft, Writing – review & editing. **Carlos E.R. Barquilha:** Conceptualization, Investigation, Supervision, Validation, Visualization, Writing – review & editing. **Pâmela E. Oliveira:** Investigation, Data curation, Writing – review & editing. **Mario Prokopiuk:** Conceptualization, Validation, Funding acquisition, Project administration, Writing – review & editing. **Ramiro G. Etchepare:** Conceptualization, Validation, Funding acquisition, Project administration, Writing – review & editing.

Data availability

No data was used for the research described in the article.

Declaration of competing interest

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