# Wastewater and Environmental Surveillance Summary for SARS-CoV-2

Pilot version 6 Dec 2024

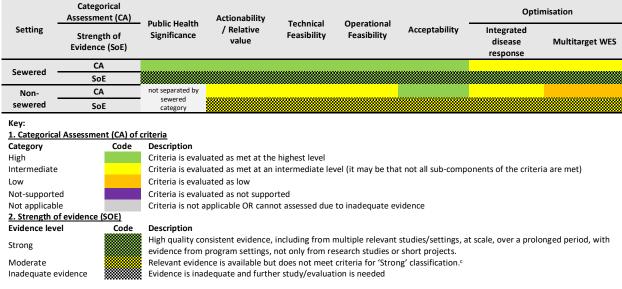


This document provides information on wastewater and environmental surveillance (WES) for SARS-CoV-2. It should be used together with the accompanying WES Guidance for one or more pathogens, which includes general and cross-cutting information (available <a href="here">here</a>). Except where cited otherwise, information has been drawn from existing World Health Organization (WHO) and United States Centers for Disease Control and Prevention (US-CDC) publicly-available sources, current at the time of writing 1-4.

# WES for SARS-CoV-2 at a glance

- SARS-CoV-2 remains of high public health significance, including as a pandemic threat.
- In sewered settings, there is strong evidence that SARS-CoV-2 WES provides actionable information, with high relative value, technical and operational feasibility and acceptability.
- However, with a few notable exceptions, integration as part of COVID-19 and respiratory disease surveillance and response, as well as with multi-target WES is not widely operationalized.
- In non-sewered settings, based on limited evidence, WES for SARS-CoV-2 has moderate potential.
- Ongoing innovation and improvements in sampling and multi-target laboratory and analytic pipelines will improve cost-effectiveness and applications for diverse settings.

Table 1 : At a glance assessment of key WES criteria for SARS-CoV-2 (sewered and non-sewered)<sup>a,b</sup>



<sup>&</sup>lt;sup>a</sup> Further description of the criteria used to assess the applicability of WES for a specific pathogen, as well as the methods used to evaluate them, is included in WES Guidance for one or more pathogens. The assessment in Table 1 provides a snapshot at the global level, but country level assessment may differ.

<sup>&</sup>lt;sup>b</sup> Sewered settings refers to closed reticulated sewage systems. Non-sewered settings refers to the diverse settings which are not 'sewered', including open drains and community sampling points. Individual small septic tanks at residential or building level are not viable to sample individually and are not considered here separately. Most WES evidence to date is reported from reticulated sewered settings, often from high-income settings. Yet much of the global population is on heterogenous non-sewered systems and this has implications for assessment of various WES categories.

<sup>&</sup>lt;sup>c</sup>-Evidence classified as 'Moderate' meets one or more of the following criteria: not from numerous settings, for a short period, without program-level evidence, and/or where findings are not consistent or of high quality.

# Summary

- SARS-CoV-2 is a pathogen of high global human health importance, including as a pandemic threat. Animal reservoirs and potential hosts have also been identified.
- Global surveillance networks include the expanded Global Influenza Surveillance and Response System (eGISRS) with integrated surveillance of respiratory pathogens and the WHO Coronavirus Laboratory Network (CoViNet).
- WES provides actionable information for emerging SARS-CoV-2 variant trends to public health authorities. It has been used alongside available clinical genomic surveillance (if any) to inform healthcare policies and guide public health action. Population infection trends have also been useful and actionable in some contexts.
- It is **technically feasible** to monitor SARS-CoV-2 quantitative and genomic trends by WES. There is evidence of strong correlation between WES and clinical data in sewered settings.
- It is **operationally feasible** to meet specific COVID-related surveillance objectives as part of routine and agile WES programs, and there is considerable global, at scale experience of this.
- Population-level surveillance of SARS-CoV-2 appears to have high acceptability and rates positively
  on key ethical considerations. These include respect, transparency, justice and equity, populationlevel benefit and lack of harm. WES surveillance costs are relatively low compared to alternatives.
- Integrated surveillance opportunities:
  - WES should be planned together with event-based and other SARS-CoV-2 multi-modal surveillance, with information visualized in integrated dashboards to aid timely decision making.
  - Multi-target WES implementation, including SARS-CoV-2, provides opportunities for costefficient surveillance if workflows align. WES of multiple respiratory pathogens (such as influenza and respiratory syncytial virus) can provide integrated respiratory surveillance.
  - A multi-target approach may be implemented as part of routine or agile WES, and to enhance local epidemic/pandemic preparedness and response capability.
  - WES sequencing information can be integrated with results derived from individual clinical sequences for combined intelligence.
- Most at-scale published evidence comes from middle to high-income country settings with high
  population coverage of reticulated sewage systems. There is limited evidence from non-sewered
  sentinel sites in lower-income countries.
- Key knowledge gaps that merit further applied research include:
  - Description and costing of the context-specific value-add of WES to current eGISRS integrated sentinel surveillance priorities, including as part of pandemic preparedness
  - Feasibility and public health applications in contexts that are not well studied; in particular, in lower-income countries, non-temperate climates and a range of unsewered settings.
  - Resource requirements for initiation and maintenance of routine and agile WES, including for SARS-CoV-2, and as part of multi-target WES.

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# 1. General information

#### 1.1. The virus, associated disease and risk factors

SARS-CoV-2 is an enveloped RNA virus within the family *Coronavirida*e. COVID-19, short for 'Coronavirus Disease 2019' is caused by SARS-CoV-2 infection. The virus emerged as a novel human pathogen in late 2019 in China, with rapid global spread. WHO declared a Public Health Emergency of International Concern (PHEIC) on 30 January 2020, lasting until 5 May 2023. In the post-emergency phase, it continues to be an important cause of morbidity and mortality in all regions and remains a global pandemic threat.

The time from viral exposure to when symptoms begin in symptomatic persons can range from one to 14 days, with a shorter incubation period reported for Omicron variants compared to earlier SARS-CoV-2 variants. The clinical presentation of COVID-19 ranges from asymptomatic to severe illness. COVID-19 illness can be similar to those of other common respiratory illnesses such as those caused by influenza (flu) and respiratory syncytial virus (RSV).

Symptomatic persons with COVID-19 may experience one or more of the following: fever or chills, cough, shortness of breath or difficulty breathing, fatigue, myalgia (muscle or body aches), headache, new loss of taste or smell, sore throat, congestion or runny nose, nausea or vomiting and diarrhoea (non-exhaustive list). In severe cases, COVID-19 can lead to pneumonia, acute respiratory distress syndrome (ARDS), organ failure, and death, particularly in older adults and those with underlying health conditions. SARS-CoV-2 infection can lead to a rare but serious condition such as multi-system inflammatory syndrome which occurs in both children (MIS-C) and adults (MIS-A). SARS-CoV-2 also results in persistent multi-system symptoms in a subset of those infected, known as post-COVID-19 conditions (PCC) or Long COVID. The possible very long-term sequalae are not yet known due to its recent emergence.

If infected, the risk of severe outcomes, including hospitalization, admission to intensive care, and death, increases as people age. People with underlying medical conditions, including but not limited to heart disease, diabetes, lung disease, or who are immunocompromised, are at increased risk of severe illness compared to those without these conditions. Access to COVID-19-related health information, vaccinations, COVID-19 antivirals and supportive health care varies between and within countries. The risk of severe outcomes is greatly reduced by vaccination, timely uptake of antivirals (if eligible) and access to supportive care.

# 1.2. Global burden, geographic distribution and seasonality

COVID-19 is distributed globally and presents a major disease burden. As of October 2024, there were more than 776 million confirmed cases of COVID-19 and 7 million deaths reported to WHO<sup>5</sup>. However, due to various causes of under-reporting, the true number of cases and deaths is much higher. Specifically, most of the global population is thought to have been infected with SARS-CoV-2 at least once, albeit most cases are not reported. This widespread infection, along with global vaccination programs, mean that most of the global population are likely to have been infected and/or vaccinated at least once. However, immunity wanes over time, and is less effective against new variants. Excess morbidity and mortality also arise due to the indirect effects of COVID-19 on the health system and on access to, and uptake of, health services.

In the post-emergency phase, SARS-CoV-2 continues to circulate globally in all WHO regions. The current circulating variants are genetically distant from the ancestor Wuhan strain, as SARS-CoV-2 continues to evolve, with associated changes in transmissibility, immune escape and disease manifestation. Virologic, host and environmental factors interact together resulting in recurrent waves of infections which have not yet become predictable nor with clear seasonal patterns. There remains a risk that future variants may cause more severe or widespread disease than current variants.

In summary, SARS-CoV-2 is globally circulating and will continue to spread, genetically evolve, and cause persistent disease with morbidity, and in some cases deaths, for the foreseeable future. Surveillance for SARS-CoV-2 remains globally relevant; particularly genomic surveillance to monitor emergence and spread of genetic mutations and variants.

# 1.3. Routes of transmission<sup>4</sup>

In humans, SARS-CoV-2 is primarily transmitted from person-to-person through infectious respiratory particles. Exposure occurs through:

- Inhalation of very fine respiratory droplets or aerosol particles.
- Deposition of infectious respiratory particles in a wide range of sizes on mucous membranes in the mouth, nose, or eye especially through splashes and sprays like a cough or sneeze.
- Touching mucous membranes with hands or other objects that have SARS-CoV-2 virus particles on them.

In the absence of properly-fitted P2/N95 masks, or similar, any person in contact with an infected host is at risk. Peak transmissibility appears to occur early during the infectious period (prior to symptom onset and until a few days after), but infected persons can shed significant levels of infectious virus up to 10 days following infection. People infected with SARS-CoV-2 can transmit the virus even when asymptomatic or pre-symptomatic.

Transmission via drinking water and food is not significant, and risks from fomite transmission are low.

#### 1.4. Zoonotic hosts and potential reservoirs

The risk of zoonotic transmission of SARS-CoV-2 to humans is considered low. In some situations, mostly during close contact, people have spread SARS-CoV-2 to certain types of animals, including companion animals (cats and dogs), animals in zoos and aquaria (big cats, great apes, mustelids), farmed mink, and wildlife. There are various infected animal reservoirs such as mink, hamsters, and deer, with reports of zoonotic transmission to people when in close contact, but this is rare<sup>6</sup>. Of relevance to WES, the sewer rat (*Rattus Norvegicus*) is reported to be an animal reservoir <sup>7–11</sup>

# 1.5. Human pandemic potential

Multiple coronaviruses, including SARS-CoV-2 and Middle East Respiratory Syndrome coronavirus (MERS-CoV), are considered a high threat for a future human pandemic <sup>12</sup>.

# 2. Information related to SARS-CoV-2 and wastewater and environmental waters

# 2.1. Potential inputs to wastewater and environmental waters

**Human shedding:** While patterns of individual shedding following acute infection vary widely, multiple studies have demonstrated high correlations between reported case data and quantitative wastewater levels and between the proportion of variants in clinical surveillance and wastewater at a population level <sup>13</sup>. Both asymptomatic and symptomatic people infected with SARS-CoV-2 can shed virions and viral RNA in feces, and respiratory secretions like sputum and saliva and at lower levels in urine <sup>13,14</sup>. Respiratory and nasopharyngeal secretions may be direct inputs to wastewater or via swallowed saliva and sputum. An early (2020) pandemic meta-analysis found positive SARS-CoV-2 stool or anal swab samples in 52% of 2,149 patients, with stool samples testing positive for a mean of 12.5 days (van Doorn et al. 2020). This is similar to the meta-analysis pooled prevalence of 46.8% (95% Ci 38.3 – 55.4%) of fecal RNA from 2,352 hospitalized COVID-19 patients <sup>15</sup>. Stools appear to be the major contributor to community-level wastewater samples <sup>16</sup>.

Individual shedding levels and duration are also influenced by SARS-CoV-2 variant type, age, disease status and vaccination status (Cevik et al. 2021; Prasek et al. 2023). These in turn influence community-level specific shedding patterns  $^{17}$ . A meta-analysis of 79 shedding studies in the early pandemic phase to mid-2020 reported a similar mean RNA-shedding duration for the upper respiratory tract and stool; 17.0 (95% CI 15·5–18·6) and 17.2 (14.4 – 20.1) days respectively, with maximum duration of 83 and 126 days  $^{18}$ . The Delta variant was associated with more severe disease and higher levels of viral shedding  $^{19}$ . Later meta-analyses of 29 studies and 230,227 patients with the Omicron variant found a shorter pooled duration of shedding for the upper respiratory tract of 10.8 (10.2 – 11.4%), longer than the period of viable virus shedding of 5.1 days (4.2-6.1)  $^{20}$ .

Post COVID conditions with persistent multisystem symptoms are not associated with shedding. However, there are rare cases of prolonged shedding after acute infection including among immunocompromised individuals.

**Zoonotic shedding**: As described above there are potential animal hosts and reservoirs (including sewer rats) which may contribute to wastewater. These require consideration as they may give rise to WES detections of variants with unusual mutations not seen in human samples, referred to as cryptic lineages <sup>21</sup>.

# 2.2. SARS-CoV-2 target persistence, degradation and risk of infectious virus

To detect SARS-CoV-2 in wastewater and interpret quantitative RNA levels it is important to consider numerous factors in relation to the sanitation or sewage system. These include: the amount of virus shed into the system at various points; its relative partitioning within wastewater components; the transit time within the wastewater system; the degradation rate to the sampling point; the potential role of biofilms; any inhibitory factors present; and methodological approaches and limitations to adjust for these variables.

A key factor influencing the rate of degradation is temperature; degradation rates increase as wastewater temperature increases; infectious SARS-CoV-2 virus decays rapidly at ambient temperatures with much higher stability and slower decay over days to weeks observed for viral RNA <sup>22–24</sup>. The relative stability and persistence of viral RNA over a wide range of temperatures make it a suitable candidate for wastewater surveillance in most settings.

SARS-CoV-2 also interacts dynamically with biofilms in sewers, which influences degradation as well as persistence through reservoir formation <sup>25</sup>.

While replication-competent virus is detected at low levels in PCR positive fecal samples, there is no evidence that infectious, replication-capable SARS-CoV-2 is present in wastewater or human-contaminated environmental waters. Well-documented epidemiological evidence of COVID-19 infection has never been attributed to these exposure media <sup>26,27</sup>. However, standard protections are recommended for those with occupational exposure given the known infectious hazards.

# 2.3. SARS-CoV-2 WES experience

Since 2020, there has been wide at-scale experience of WES for SARS-CoV-2 in varied global settings. This, coupled with extensive applied research to address key knowledge gaps, has demonstrated the correlation between WES results and relevant clinical results <sup>28</sup>. SARS-CoV-2 WES demonstrates well-established technical and analytical feasibility for quantitative results (including adjustment for population, dilution and other confounders) and relative proportion of variants with genomic characterization. This means WES results can be analyzed, interpreted and combined with other available data and actioned in relation to public health surveillance objectives with considerable confidence. There are also extensive use cases from countries with a prolonged early period of low or no COVID-19 community transmission <sup>29–31</sup>. While most at-scale published evidence comes from higher income country settings with extensive reticulated sewage systems, there is also substantial experience in a variety of settings including in lower- and middle-income countries with varied sanitations systems.

WES surveillance costs are much lower than alternative forms of surveillance based on individual samples. However, there is limited published evidence of the costs to establish and maintain SARS-CoV-2 WES programs in various settings, their cost-benefit or cost-effectiveness for different use cases <sup>39–41</sup>.

# 3. COVID-19 surveillance

# 3.1. Overall SARS-CoV-2/COVID-19 surveillance and response

In the post PHEIC emergency phase, SARS-CoV-2 remains the most significant respiratory pathogen globally (due to morbidity and mortality of acute as well as post-COVID-19 conditions), with unpredictable infection waves and ongoing genetic evolution. It and other specific members of the *Coronoviridae* family remain a threat for future pandemics <sup>12</sup>. Timely intelligence on SARS-CoV-2 circulation intensity, severe disease and circulating viral variants are needed, with attention to global equity.

Many resource-intensive SARS-CoV-2 and COVID-19 specific surveillance systems established during the emergency phase have been stood down, including those related to confirmed case reporting and clinical genomic surveillance. There is an ongoing shift to integration as part of routine communicable disease surveillance and response systems including as part of pandemic preparedness and integrated disease surveillance.

The shift from emergency response to integrated surveillance and response approaches is occurring at a global as well as national levels; there are two complementary WHO-led global programs that include a broader focus on coronaviruses and integrated respiratory surveillance, including but not limited to SARS-CoV-2:

- The WHO Coronavirus Network (CoViNet) aims to bring together surveillance programs and reference laboratories to support enhanced epidemiological monitoring and laboratory (phenotypic and genotypic) assessment of SARS-CoV-2, MERS-CoV and novel coronaviruses of public health importance. This is done through a One Health approach that encompasses human, animal and environmental surveillance, including wastewater surveillance. CoViNet will facilitate detection and characterization of new variants and support identification of novel coronaviruses posing public health threats <sup>42</sup>.
- The longstanding WHO-led GISRS includes laboratory, epidemiologic, and surveillance teams that
  routinely conduct facility-based, integrated, surveillance for influenza. This has been expanded to
  other respiratory viruses as part of expanded GISRS (eGISRS), including respiratory syncytial virus
  (RSV) and SARS-CoV-2. E-GISRS is expected to be the anchor for reliable and consistent global SARSCoV-2 sentinel surveillance for the foreseeable future, with data submitted to a global data platform
  called RespiMart <sup>43</sup>.

#### 3.2. COVID-19-related surveillance systems and data sources

COVID-19 surveillance systems vary widely between countries. Available data is country (and locally)-specific and changes over time. It may include data such as:

COVID-19/SARS-CoV-2 specific data:

- Wastewater surveillance data (described further below).
- Reported cases, hospitalizations, Intensive Care Unit (ICU) admissions and deaths in relation to SARS-CoV-2/COVID-19 diagnosis (age disaggregated when available).

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- Number of specimens tested and positivity rate (disaggregated by primary and secondary care centers when available).
- Variant information from clinical specimens from cases with relevant metadata.
- Emergency department visits due to COVID-19.
- Vaccination coverage (age-disaggregated when available).
- Seroprevalence level (nationwide, for example among blood donors).
- Antiviral treatment uptake (if locally available).

#### Non-specific data:

- Syndromic diagnosis (Influenza-like illness (ILI)/Severe acute respiratory infection (SARI)): cases, hospitalisations, ICU admissions.
- Excess mortality.
- Health system data: hospitalization and ICU bed occupancy and capacity.
- Absenteeism.
- Population mobility data.
- Rare insights from social media/news.
- Expert opinion (e.g. unusual symptoms or presentations from medical and veterinary communities).

Table A.1.1 (Appendix 1) summarizes some existing surveillance systems and reporting dashboards that can be used in conjunction with wastewater surveillance. Some of these dashboards also include wastewater surveillance data. They provide background information that may be useful to inform wastewater surveillance programs as part of system design for collaborative surveillance.

# 4. WES objectives and related public health actions

WES forms one part of multi-modal surveillance so results should be integrated with other information data to provide actionable intelligence (not stand alone). WES must have potential to provide additional value in the local context to be considered for implementation.

#### 4.1. Routine WES for SARS CoV-2

Wastewater surveillance objectives for SARS-CoV-2 (when widely prevalent) are to:

- Provide timely assessment of quantitative infection trends including the timing of local increases, peaks and declines.
- Provide timely identification of circulating SARS-CoV-2 variants and mutations of interest.
- Provide relevant data that can be integrated with clinical, environmental and other information to:
  - inform short-term forecasting of cases and health system burden as an early warning for potential surges and when peak is reached;
  - o provide additional evidence and insights on evolving SARS-CoV-2 and COVID-19 epidemiological patterns (as well as in multi-target WES, other respiratory pathogens).

# 4.2. Agile (or responsive) WES for SARS-CoV-2 and pandemic risk of beta *Coronaviridae*

Early detection may (again) become relevant if SARS-CoV-2 stops circulating in an area or community, or a more severe or transmissible variant emerges. In these cases, WES objectives are to:

- Provide early detection of SARS-CoV-2 (or a specific strain of concern) incursion, facilitating public health action.
- Provide additional reassurance of the absence of significant SARS-CoV-2 community transmission (noting that WES alone cannot exclude presence of a single or few cases)

Agile (non-routine) use of WES could also be considered where additional results would inform specific actions; for example, to characterize geographic and temporal spread of a variant associated with more severe clinical outcomes or to assist the containment of an outbreak in highly vulnerable settings.

Countries and subnational actors may have additional secondary surveillance objectives depending on local priorities.

Agile WES means that it is time-limited surveillance with a specific trigger to initiate. Agile WES involves establishing new time-limited activities or purposive changes in the existing WES program. E.g. sampling more frequently or in different locations, reducing the turn-around time to results, and/or performing new or different analyses.

**Routine WES involves** 

consistent sampling at

the same sites using

consistent methods.

Other potential use cases for hyper-localized settings exist. Examples include residential aged care facilities, correctional facilities, and other populations that are at heightened risk and to whom benefits can accrue through targeted interventions. These use cases are considered less as surveillance and more as part of a mixed screening and testing model to spare diagnostic capacity. Such use cases are not considered further here.

# 4.3. Potential public health actions arising from the addition of WES for SARS-CoV-2

WES results can be used in combination with other available surveillance data, to identify geographic areas where trends in SARS-CoV-2 concentrations are changing, where new variant subtypes and mutations are appearing and their trends. These can be identified at various levels, including community, national and regional. If increased circulation is detected, health authorities can consider:

- Public communications to promote individual preventive behaviors (social distancing, wearing a
  mask), mitigation (staying home when unwell) and health-seeking actions (vaccine uptake, use of
  diagnostic tests, health services access, uptake of antivirals).
- Public health preparedness including targeted testing, vaccination and other population-level interventions.
- Clinical health system preparedness including diagnostic and antiviral, oxygen and other health care logistics, human resource and hospital bed capacity planning.
- Additional agile WES and/or other enhanced surveillance activities.

Conversely, as community levels decline, decisions can be made to allocate scarce resources elsewhere, plan human resources effectively, and inform the community of the lower risk levels. There are several communication toolkits for health departments to communicate messages to different target audiences including pregnant people and new parents<sup>44,45</sup>.

# 5. WES additional methodological considerations for SARS-CoV-2

This section should be read in conjunction with general methodological consideration in Section 5 of Wastewater and environmental surveillance for one or more pathogens: Guidance on prioritization, implementation and integration (available <a href="https://example.com/here">here</a>).

# 5.1. Sampling methods

When SARS-CoV-2 is widely prevalent with unpredictable patterns and ongoing genomic changes, the focus of routine sampling is stable catchment sampling to establish trends. The choice of sampling locations requires local knowledge of population movements between residence, work, health facilities and for leisure. Sentinel site selection within reticulated sewage systems generally prioritizes high population coverage in urban centers, considerations around local and international mobility, other population level risk and vulnerability and equity. In the case of non-reticulated sewage systems, sentinel locations may be selected where the catchment population is likely to be representative of the surrounding community and results can reasonably be generalized to the broader at-risk population. Sampling choices should also consider equity aspects especially for disadvantaged populations with a disproportionate burden of disease or for whom surveillance coverage is poor, including those not covered by sewered systems <sup>13</sup>. Consideration should also be given to monitoring at strategic sites, including transport hubs such as large airports, which represent both local populations and incoming travelers. This helps to provide timely detection of emerging variants and enables participation in relevant global sentinel surveillance networks.

Sampling frequency and timeliness can be modified to meet surveillance objectives while minimizing costs and resource requirements. For example, increased frequency may be relevant for detecting the timing of a peak or characterizing the rate of spread of a new variant, but may otherwise be too costly, and should be reduced to baseline frequency at other times. SARS-CoV-2 is the pathogen for which much of the relevant comparative studies were undertaken. There is a need to assess, monitor and evaluate the various sampling methods including their related costs and public health value.

# 5.2. Laboratory methods and interpretation

Widely used and validated laboratory methods are able to detect the presence of SARS-CoV-2, normalize quantitative results to adjust for population, dilution and other confounders, and identify variants present <sup>13,32</sup>. SARS-CoV-2 variants and specific mutations are identified using targeted primer-probe combinations and/or sequencing against global classification databases. CDC provides one widely used reference for primer-probe sequence<sup>46</sup>. The performance of primer-probe kits must be monitored, updated, validated and optimized as variants evolve. There is a critical dependency on the completeness and timing of updates of these global SARS-CoV-2 genomic databases and associated software which are much reduced and less frequent compared to the PHEIC emergency phase.

Priorities for strengthening SARS-CoV-2 laboratory methods in this emerging field include harmonization and standardization of methods, accreditation of tests and external quality assurance. Improvements in these areas will enable inter-laboratory comparison of results and scalability. In addition, the use of multiplex rather than singleplex PCR methods can be strengthened. These methods aim to integrate multiple targets and improve cost-efficiency without compromising sensitivity or other key parameters.

# 5.3. Reporting and communications

Globally, the WHO Coronavirus Dashboard tracks and reports COVID-19 cases and deaths by WHO region<sup>5</sup>. There are several country and location-specific dashboards that include WES results and visualizations for multiple pathogens, sometimes together with other COVID indicators. There are several global repositories with links to available WES dashboards<sup>47,48</sup>. The European Union Wastewater Observatory for Public Health is one resource. It provides monthly reports summarizing available global WES activity, including SARS-CoV-2, influenza, RSV, and links to country and subnational dashboards (European Union October Bulletin, 2024). WES data reporting is not yet integrated into the RespiMart as part of e-GISRS. While there is increasing alignment, a wide diversity of analytic and reporting approaches remains, which limits comparisons and scalability.

It is best practice to visualize and report on WES data alongside other surveillance data for SARS-CoV-2 and other respiratory pathogens. These other data provide additional context to the WES data and improve integration of relevant surveillance for accessible combined intelligence and response. This is illustrated by the Swiss infectious diseases dashboard (Switzerland Federal Office of Public Health, 2024). The United States also provides a number of emerging best practices for bioinformatics and public-facing reporting. COVID Data Tracker is CDC's home for COVID-19 data. It provides surveillance data from across the response, including hospitalizations, vaccinations, demographic information, and daily and cumulative case and death counts reported to CDC since January 21, 2020. COVID Data Tracker is updated frequently. Timing depends on the availability of data provided by jurisdictions<sup>49</sup>. The US CDC presents standardized wastewater data showing the percent change in virus levels alongside other data, such as: the overall level of the virus in wastewater as a ratio against historical wastewater data for that location; the geographical context (for example, whether areas have high tourism or neighboring communities with increasing cases)l and clinical cases. Communities may see change in the virus wastewater levels as prevention strategies in their areas change<sup>2</sup>.

Communication to relevant stakeholders must be tailored according to the surveillance objective and context including health departments, health system administrators, clinicians, the general public and any specific communities. For the majority of users, the most useful data is likely to be that which enables integrated information about risk levels of exposure and disease severity.

# 5.4. Acceptability of WES for SARS-CoV-2

There is very limited direct qualitative and quantitative evidence from the general public and community groups; a repeat survey shows sustained high acceptability of WES for larger populations in the United States of America <sup>50,51</sup>. There do not appear to be any specific acceptability or ethical concerns raised by large population-level WES for SARS-CoV-2 other than the opportunity cost involved in allocating scarce resources common to all resource allocation decisions. As a pooled population sample, individuals are not identified in WES. The use and strengths of population-level WES of SARS-CoV-2 appear to align with key ethical considerations of respect, justice, and population level benefit and lack of harm including equity considerations <sup>13,52</sup>. More targeted localized sampling from individual facilities, airplanes or other smaller populations do raise specific ethical considerations including in relation to privacy and potential for both benefits and harms which are different to WES at the population level. These are not the focus of the population level WES discussed in this summary.

# 6. Integrated surveillance and multitarget WES considerations

# 6.1. Integration of SARS-CoV-2 WES into existing COVID-19 surveillance and response

- COVID surveillance overall is dynamic due to the transition from the emergency pandemic phase to more sustainable and integrated surveillance within national and global systems.
- In settings which have ongoing SARS-CoV-2 WES, since the end of mandatory case reporting, WES
  often provides the principal, timely information about local infection and variant trends and is
  triangulated against non-specific and the more delayed COVID-specific case-based data. In these
  settings WES appears relatively well integrated within the local COVID surveillance and response
  systems, albeit with a wide variety of coordination and governance as well as data and reporting
  practices.
- There are opportunities in many countries to strengthen WES plans, as planning and implementation of eGISRS matures, and with support from CoViNet and other collaborative surveillance activities more broadly.
- A key area of focus for improved integration is data management, sharing and bioinformatics. This
  can enable timely access and ease of interpretation for WES data together with other relevant
  information for public health action.

# 6.2. Integration of multi-target WES surveillance together with SARS-CoV-2

- Leveraging existing SARS-CoV-2 WES activities has allowed the cost-efficient integration of other
  targets, noting substantial alignment with many of the specific work processes from sampling,
  various laboratory processes, through to reporting.
- In some high-income settings, integrated WES surveillance already combines multiple respiratory
  pathogen targets from the same samples with multiplex or other approaches including, for example
  influenza viruses, RSV and SARS-CoV-2 combined contributing to integrated respiratory
  surveillance.
- Likewise, routine WES activities for SARS-CoV-2 provide local capacity and capability to which agile
  WES can be initiated, enhancing local epidemic/pandemic preparedness and response capability
  for a more severe coronavirus as well as for other pathogens.

# 7. Key knowledge gaps and applied research priorities

There are several applied research priorities to advance and optimize actionable application of WES for SARS-CoV-2. Key knowledge gaps and recommended areas of applied research include:

- Context-specific value addition of routine and agile WES to current eGISRS integrated surveillance priorities including consideration of pandemic preparedness.
- Resource requirements for initiation and maintenance of routine and agile WES as a single pathogen or integrated as part of multitarget WES.
- Feasibility and public health applications in contexts not well studied, including in countries of
  varying income and resource levels and diverse public health governance approaches, nontemperate climates, various unsewered settings, and in emergency situations and at major events.
- Ongoing innovation and improvements in sampling and multitarget laboratory and analytic pipelines for improved cost-effectiveness and applications for diverse settings.

In addition, maturation of implementation at scale requires additional:

- Standardization and harmonization of methods adapted to diverse global settings, albeit noting that numerous factors influence the local choice of method (and a single set of methods is unlikely emerge).
- External quality assurance and proficiency programs to support laboratories.
- Evidence in relation to public health value given the costs and benefits to help assess costeffectiveness.
- Ongoing monitoring and evaluation with harmonized key performance indicators and periodic assessment of program value including for preparedness

# Annex 1. Existing surveillance systems for SARS-CoV-2

Table A1.1. Global or multi-country examples of existing surveillance systems for SARS-CoV-2

Surveillance System	Outcome(s)	System type	Freque ncy	Geographic resolution
WHO Global COVID-19 data repository and the dashboard (WHO). <sup>5</sup> Source: WES public dashboards from 30 countries. Data is as reported to WHO by each country, with metrics often differing between countries.	<ul> <li>Confirmed COVID-19 cases</li> <li>Deaths</li> <li>Vaccinations</li> <li>Variants in circulation</li> </ul>	Passive reporting of collated country data.	Weekly	Country, region, and global
Expanded Global Influenza Surveillance and Response System (GISRS). <sup>53</sup> Source: Sentinel sites from GISRS member countries.  *multiple respiratory pathogens including SARS-CoV-2, influenza and other viruses	<ul> <li>Number of specimens tested for SARS-CoV-2</li> <li>Test positivity rate</li> <li>COVID-19 related ARI/ILI and SARI cases</li> </ul>	Active sentinel surveillance	Weekly	Country, region, and global
Global Initiative on Sharing All Influenza Data (GISAID) Data Science Initiative. <sup>54</sup> Source: genomic sequence from participating country laboratories (open source).  *multiple pathogens including SARS-CoV-2, influenza, other respiratory pathogens and arboviruses	<ul> <li>Number of specimens sequenced for pathogen</li> <li>Sequence information with clinical and epidemiological information</li> <li>SARS-CoV-2 sequence relative abundance</li> <li>Species-specific data (avian and other animal source viruses)</li> </ul>	Passive reporting of collated country data.	Near real- time	Country, region, and global
European Respiratory Virus Surveillance Summary (ERVISS) (European Centre for Disease Prevention and Control (ECDC) and WHO Regional Office for Europe). <sup>55</sup> *multiple respiratory pathogens	Confirmed COVID-19 cases     COVID-19 variants (sequenced cases)	Syndromic surveillance, laboratory confirmed - passive reporting of country data.	Weekly	Country, European Union, European Economic Area, and WHO European Region
World Organization for Animal Health. <sup>56</sup>	<ul> <li>Ad hoc as per pathogen with laboratory, clinical and epidemiological information</li> <li>Number of countries reported</li> </ul>	Outcomes of investigations into animal infections and outbreaks	Ad hoc	Country, region, and global

Table A1.2. Illustrative country examples of existing surveillance systems for SARS-CoV-2

Surveillance System	Outcome(s)	System type	Frequency	Geographic resolution
United States of America				
Respiratory Virus Hospitalization Surveillance Network (RESP-NET). <sup>57</sup>	Hospitalizations associated with COVID-19, influenza, RSV with laboratory confirmation (among children and adults)	Sentinel case- based surveillance	Weekly	Sentinel sites cover ~10% of population; site and national estimates
National Syndromic Surveillance Program (NSSP). <sup>58</sup>	Patient clinical encounter (from emergency departments, urgent and ambulatory care centers, inpatient healthcare settings, and laboratories)	Syndromic surveillance; electronic patient encounter data	Daily	Regional estimates
National Vital Statistics System (NVSS). <sup>59</sup>	Mortality data	Electronic death reporting system;		Jurisdiction level
New Vaccine Surveillance Network (NVSN). <sup>60</sup>	Hospitalizations and outpatient visits	Active sentinel surveillance		7 selected sites
National Healthcare Safety Network (NHSN). <sup>61</sup>	Healthcare-associated infections (at medical facilities including acute care hospitals, ambulatory surgery centers and dialysis centers)	Active sentinel surveillance		Facility- level
Traveler-based Genomic Surveillance (TGS). <sup>62</sup>	Genomic sequencing for confirmed COVID-19 cases	Active surveillance	Weekly	Country
Brazil			JI.	l .
National surveillance System for cases of Severe Acute Respiratory Syndrome. <sup>63</sup>	Reported cases of Severe Acute Respiratory Syndrome reported in the SINAN (Notifiable Diseases Information System <sup>64</sup>	Active surveillance from reported cases of Sars- Cov-2, INF-A and INF-B, RSV, Rhino, Adeno, among others based on reported cases in SINAN.	Weekly	Country

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