The Game Changing Coronavirus Early Warning System

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Executive Summary

In the fight against Coronavirus, scientists and engineers globally have adapted and innovated, developing novel methods to safely restart economies and maintain business continuity by getting ahead of the SARS-CoV-2 Coronavirus.

By sampling and analysing wastewater directly from sewers, Arcadis is providing an early warning system detecting SARS-CoV-2 infections within a workforce or population. Molecular biological tools can amplify and enumerate genetic material specifically from the SARS-CoV-2 virus allowing detection and quantification of the viral load. Assessing the number of SARS-CoV-2 virus particle (virions) in wastewater can identify whether asymptomatic or presymptomatic individuals are unwittingly transmitting infections within a facility, city, or region, before a COVID-19 outbreak is discovered. This approach has been proven to assess levels of infections within a community well ahead of reported COVID-19 cases, with Arcadis data showing 6-14 days advanced warning.

With this method it is possible to identify and isolate infected individuals, before COVID-19 cases manifest and impinge on business operations. If increases of detectable virions in wastewater are reported, a rapid response can be mobilized, in order to maintain workplace safety and business continuity, rather than closing down entire facilities. Tracking upstream of an initial sampling point – in a wastewater system – can identify the sources of the virus within a facility, campus, city or region. Within buildings, infected individuals can be rapidly identified by environmental monitoring of their surroundings, by swabbing surfaces and using molecular biology tools to identify the virus on surfaces such as doors, desks and ventilation filters.

The Sentinel early warning system has been described as the "*canary in the coal mine*" to get ahead of the virus and potentially plan targeted lockdowns before COVID-19 outbreaks take hold, allowing faster economic recovery. This simple and cost-effective monitoring of wastewater can keep facilities operating by rapidly detecting the virus before it gets a chance to transmit amongst colleagues. Further targeted sampling can identify carriers allowing them to be isolated to maintain COVID-secure operations. In the Netherlands the Mayors of Amsterdam and Rotterdam have already used data from monitoring SARS-CoV-2 prevalence in wastewater to strengthen lockdown measures in advance of COVID-19 outbreaks to keep their cities safe. Surveillance of wastewater is faster and has been calculated to be orders of magnitude cheaper than clinical screening yet cannot fully replace it. This approach guides the use of clinical screening, identifying where to apply it. Effective surveillance for SARS-CoV-2 infections may be envisioned as a two-step process in which a wastewater based Sentinel approach serves to identify and enumerate infected cases, where after targeted clinical human testing then serves to identify infected individuals in the hotspots revealed by the pooled wastewater survey Arcadis is assisting clients to stay operating and cities to stay open by providing a Sentinel service, bringing back control and confidence, as we work to overcome this virus.

Introduction

Many organisations in both the public and private sectors are seeking cost-effective early warning-based approaches to provide reliable data regarding the presence and prevalence of the SARS-CoV-2 virus in their facilities and communities. With transmission of the virus via individuals – who may be carriers and exhibit no symptoms – temperature monitoring is ineffective, so more advanced methods to detect the virus within a facility are required. Testing wastewater to quantify the unique genetic signature material (ribonucleic acid (RNA)) only associated with the SARS-CoV-2 virus has emerged as an approach which provides a scientifically proven and reliable early warning system.

Measuring the amount of SARS-CoV-2 virus (number of virions) in wastewater identifies whether individuals contributing to the system are infected with the virus. Increasing trends in detections indicate that the viral infections are increasing within that population, and the virus is potentially spreading. However, as individuals begin shedding virus to the wastewater system before they display symptoms of infection, they can be potentially be identified and isolated before they can infect others. This provides an early warning system as the virus can be detected within a community before it starts to spread.

Human Coronaviruses, including the first SARS-CoV virus which caused Severe Acute Respiratory Syndrome (SARS) in 2003 and the MERS-CoV virus which caused Middle East Respiratory Syndrome (MERS) in 2012, are also known to cause gastrointestinal symptoms in addition to respiratory symptoms [1, 2]. The SARS-CoV-2 virus has been shown to infect human digestive system as it can attach to cells in the ileum and colon [3] with previous studies demonstrating that Coronaviruses can replicate in the gastrointestinal tract [1, 4].

Detection of non-infectious genetic material from the SARS-CoV-2 virus in untreated wastewater has been reported in Italy, Spain, Australia, Turkey, Israel, Pakistan the Netherlands, France and USA with researchers demonstrated a correlation between wastewater SARS-CoV-2 RNA concentrations and COVID-19 clinical cases [5]. Several of these studies report advanced notice ahead of COVID-19 confirmed cases, with data from Arcadis projects demonstrating 6-14 days advanced notice.

The Netherlands, there are plans to incorporate daily sewage surveillance into its national COVID-19 monitoring program [5] with 355 wastewater treatment plants currently monitored. The use of genetic testing of wastewater for pathogens using molecular biology tool is commonplace in Dutch cities, so it was easy to adapt to detect the SARS-CoV-2 virus. The Mayors of Amsterdam and Rotterdam have already used data from monitoring SARS-CoV-2 prevalence in wastewater to inform decision to strengthen lockdown measures in advance of COVID-19 outbreaks to keep their cities safe. Assessment of the SARS-CoV-2 virus in stored frozen wastewater samples from Barcelona identified that the virus was detected some 41 days before the first reported COVID-19 cases [6].

Assessment of SARS-CoV-2 virus loading in wastewater reflects the proportion of infections present within the population contributing to the sewer system and includes individuals who may be asymptomatic or presymptomatic. This confers some major advantages over other testing methods. First, it is a cost-effective method to determine whether the virus is present or increasing amongst populations of potentially thousands of individuals, as just one aggregated test is needed to cover everyone and increasing or decreasing trends can be identified. Second, and maybe most

importantly, these data reflect real time advances of infections which tracks ahead of reported COVID-19 case numbers, assessed by the other standard testing means within a population i.e. people individually get tested only when they show symptoms.

The wastewater Sentinel system can capture data from individuals who have just contracted the infection but have not developed symptoms of disease – which can take 5 or more days – and carriers who are asymptomatic and infectious with no symptoms. This means there is potentially time to isolate them or instigate localised community lockdowns in advance of reported COVID-19 cases. Using this approach there is time to get ahead of the virus several days before it has a chance to spread and take hold among unknowing communities, as we can detect and snuff out its burning embers, thus avoiding national lockdowns and keeping business running.

Wastewater Sentinel monitoring is supported by the World Health Organisation (WHO) who have identified that there is potential to use it for early warning, particularly of clusters or outbreaks in countries that have already contained viral transmission and are easing public health and social measures, or in the event of seasonality [5].

With survival of the SARS-CoV-2 virus on outdoor surfaces estimated to rise in London from around 30 minutes in mid-summer to 300 minutes in winter [7] this means that the risk of outdoor fomite transmission (and re-aerosolisation) could be elevated under UK winter conditions, as the virus survives on outdoor surfaces significantly longer [8]. With increases in seasonal flu viruses also expected as the UK moves into winter, it becomes more important to determine whether the SARS-CoV-2 virus is circulating rather than seasonal flu or the common cold, which both exhibit similar symptoms.

The WHO highlight that environmental surveillance can be used for pooled testing of high-risk settings where response can be quickly implemented, such as closed residential settings (e.g. nursing homes, prisons, worker dormitories, university campuses), large crowded workplaces or in the context of mass gatherings. However, as the UK returns to work, universities and schools, traveling via public transport and beginning increased social interaction, the need for an early warning system is clear – to protect communities and businesses alike as the SARS-CoV-2 virus seizes these opportunities for increased transmission. Using the wastewater Sentinel surveillance to get ahead of the virus and snuff out outbreaks early, before they take hold could help provide an exit route from this Pandemic.

The Challenge

Monitoring for the SARS-CoV-2 Coronavirus, as the infectious agent that causes COVID-19 diseases, is critical to controlling virus spread in communities and restarting the economy. However, sampling individuals one by one, potentially on multiple occasions to identify cases of infection is challenging, expensive and requires significant resources. Sufficient and widespread oral/nasal testing is unable to be implemented in many places and may not be practicable as a standalone testing strategy.

The challenge of identifying and isolating those infected with the SARS-CoV-2 virus is compounded as many infected individuals can exhibit no or mild symptoms. Viral transmission via asymptomatic and presymptomatic cases is considered widespread [9], with viral shedding and hence transmission reported to occur 5 days before symptoms appear, as shown in Figure 1. Symptom driven testing

misses these carriers of COVID-19 disease and detects spread of the virus after it has impacted a workforce or community.

For businesses, the major challenge can be maintaining operations in a COVID-secure manner while there is huge uncertainty regarding spread of the virus within a facility and the only method to discover infections is once a major outbreak has already occurred.

For communities in villages, town and cities, lockdowns tend to occur as a reaction to an outbreak of COVID-19, which after there is a substantial amount of pre-symptomatic transmission that occurs before diagnosis of an incident case [10] i.e. after the horse has bolted.

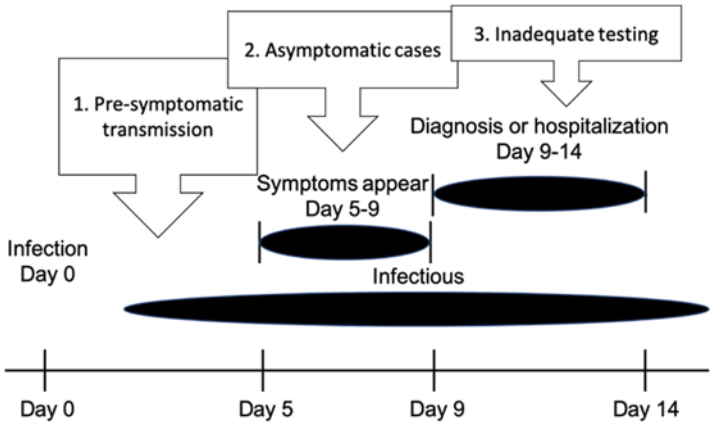

Figure 1. Leakages in the surveillance system that can lead to missing SARS-CoV-2 infections and failing to control transmission [10].

<u>The Solution</u>

Effective surveillance for SARS-CoV-2 infections may be envisioned as a two-step process in which a wastewater based Sentinel approach serves to identify and enumerate infected cases, where after targeted clinical human testing then serves to identify infected individuals in the hotspots revealed by the pooled wastewater survey [11].

Surveillance of populations using wastewater has been calculated to be faster and orders of magnitude cheaper than clinical screening yet cannot fully replace it. The data from testing wastewater is used to guide where to use clinical screening and identify infections. For resource-poor regions and nations, it has been put forward as the only viable means of effective surveillance [11]. Using the wastewater networks as a means of zeroing in on the locations of infections to pinpoint their specific locations represents a method whereby outbreaks can be identified, and contained.

Wastewater monitoring for the virus provides advance notice of symptomatic and presymptomatic cases, with up to 6 to 14 days before a case presents, meaning there is advanced warning of “hot spots” for community transmission or that the virus is present within a facility. This enables rapid health decision making, with near real-time SARS-CoV-2 transmission rate estimates. The data can also be normalized to the population sampled and be used to confirm the absence of transmission in

areas with zero cases, to keep a watching brief on populations ensuring the virus is detected if there are localised resurgences.

The iterative approach, shown below in Figure 2, can be adapted as data is received and protective measures are increased or relaxed, based on a real time assessment of community or facility infection levels.

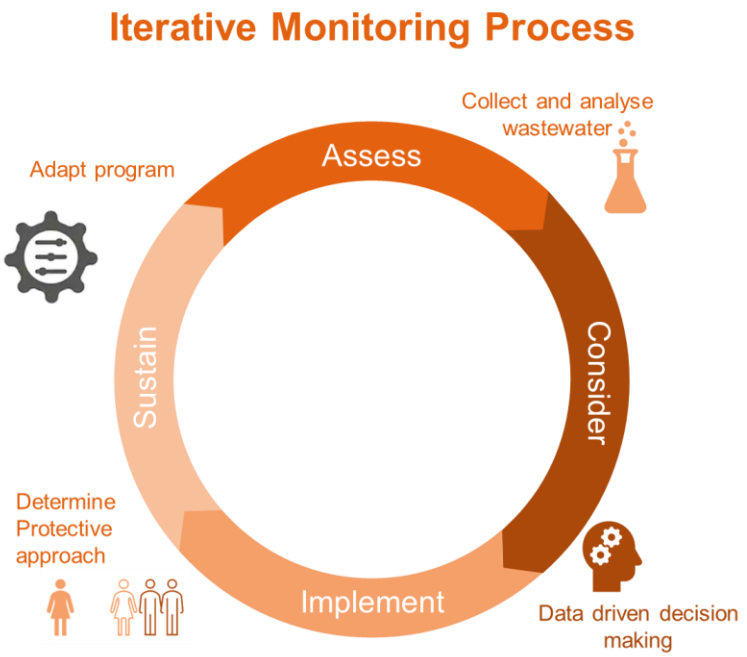

Figure 2. The iterative monitoring process applied for surveillance and management of the SARS-CoV-2 virus.

Wastewater analysis in a public sewer system cost-effectively supplements human testing at approximately ~£0.8/person/yr with a large population anonymously sampled using a few strategic testing points.

<u>The Process</u>

The potential to use the outfall of a wastewater system – for example, from a large site or the inlet from a town to a wastewater treatment plant – for monitoring appears to be most effective place to start. If detections of virions start to rise, then the major and minor branches of a wastewater system can be rapidly tested to establish the source of the infections. Narrowing down the location of the infections within facilities can also be accomplished by swabbing environmental surfaces to detect genetic material from the SARS-CoV-2 virus. This allows rapid identification of infected individuals so they can be isolated.

Rapid Information is imperative as sample analysis turnaround times can eat into the advanced notice conferred by the monitoring system and will be critical to the success of any wastewater

surveillance program. It is possible to achieve fast turnaround on wastewater data in the UK to help stakeholders make informed decisions about appropriate responses as detections of the SARS-CoV-2 virus rise or fall.

The approach is to monitor wastewater systems for the presence and concentration of SARS-CoV-2 virus. Regular monitoring requires taking periodic grab samples or proportional composite samples using autosamplers at specific locations within a sewer system (Figure 3). Actionable data is provided by following trends in enumerating SARS-CoV-2 genetic material at multiple intervals.

Figure 3. Arcadis locating an autosampler in a manhole chamber

The frequency of sampling may be adjusted based on the occurrence of the virus in the wastewater system and the location of sampling. In some instances, we are regularly monitoring the sewer outfall fed from as few as 35 individuals to determine whether the SARS-CoV-2 virus is present. Larger scale projects include monitoring wastewater entering several treatment works and evaluating the flow from multiple major branches within sewersheds to assess the location of the transmission within specific areas. We can then home in on the location of the transmission within an area using a combination of timed sampling at targeted locations within the wastewater system to facilitate discovery of those who are infected, before individuals are aware that they are shedding virus.

For analysis we employ reverse transcriptase-digital polymerase chain reaction (RT-dPCR) for detecting SARS-CoV-2 in sewage and environmental samples. The analysis reduces the potential for false positives by detecting and amplifying multiple unique SARS-CoV-2 genes on the viral RNA. Positive and negative controls, as well as internal amplification controls, ensure each analysis is accurate and will yield a positive result if the viral RNA is present. The analytical approach is highly sensitive with the detection limits resolving 1 COVID-19 case in 25,000 people. The samples are safe

to collect with risk of infection to field sampling personnel is no different than sampling for other micro-organisms. The method uses a reliable clinical methodology that has been adapted for environmental testing using widely accepted RT-dPCR technology that provides accurate quantitation over a concentration range of 5 orders of magnitude.

Using the epidemiology results requires data to be correlated and normalized to the sampled population, wastewater flow, time of travel, and RNA degradation. Upstream sampling in the sewershed can be done to better target geographic areas where virus is prevalent. Data trends are established over time and space to produce a dashboard showing key indicators and trends. Data can then be used by health agencies and individual clients to assess the effectiveness of current control measures, guide implementation of next steps in community reopening/closing and provide additional focused human testing in high potential transmittance areas (e.g., nursing homes, high density housing).

Figure 4 shows the lead time that wastewater-based surveillance has provided vs known community cases. This indicates that wastewater surveillance provides an advanced warning of both community increases and decreases in infections from SARS-CoV-2.

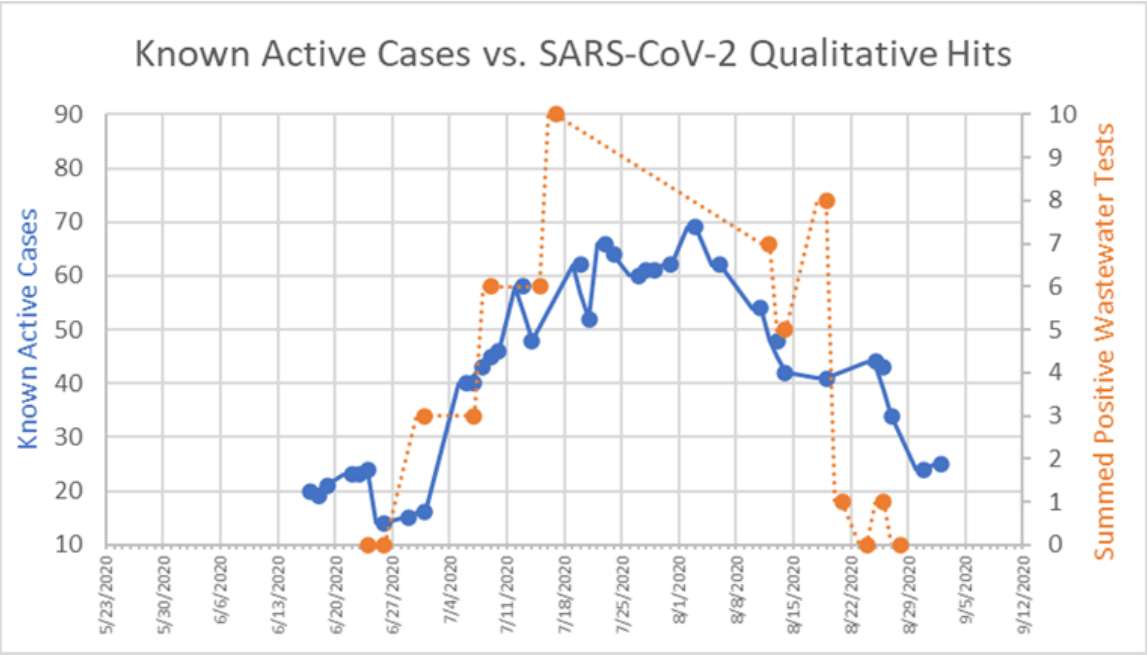

Figure 4 Arcadis data from use of wastewater sentinel surveillance at wastewater treatment plants

This environmental surveillance could be implemented by municipalities right away as a tool, designed to help authorities to coordinate the exit strategy to gradually lift its coronavirus lockdown [12].

Next Steps

The wastewater Sentinel surveillance system is scientifically proven and can enumerate genetic material from the SARS-CoV-2 virus to identify the presence of infections, some 6-14 days prior to COVID-19 cases being reported. Depending on the sampling location this can allow monitoring of everyone in a whole facility, campus a town using a single non-invasive test, sensitive enough to detect 1 case in 25,000 people. Arcadis is assisting clients to apply this approach to maintain business

continuity, protect communities, and assist with governmental exit strategies for the COVID-19 Pandemic. For further information please contact Dr. Ian Ross ian.ross@arcadis.com

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