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How sewage is helping us to understand the dynamics of Covid-19 infections

David Lloyd Owen
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One of the more encouraging aspects of the Covid-19 Pandemic has been seeing water utilities and academia working together across the world to mine data from our sewerage networks to better appreciate the spread (and retreat) of the disease over time. By measuring the presence (or absence) of RNA (Ribonucleic acid, which carries the virus' genetic code) fragments from the virus in effluents at sewage treatment works, it is possible to get an accurate picture of the presence or absence of the disease in a community served by a treatment works irrespective of any symptoms seen or unseen. This allows for the speedy and targeted implementing of social distancing where and when it is actually needed.

When we flush our loos, we tend to think that what goes down there, once out of sight is also out of mind. It is better to imagine our sewers as conduits of information. Institutions such as Arizona State University's Human Health Observatory (HHO) has been tracking health indicators in sewage since 2008. Sewage monitoring has played a central role in the almost complete elimination of polio worldwide and to alert healthcare workers of any new instances, and has also been used to track Norovirus and Salmonella outbreaks.

Monitoring for Covid-19 in sewage started when KWR Water Research in the Netherlands when the RNA data for SARS-CoV-2 gene sequence became available. They swiftly established a relationship between the RNA in the sewage effluent and infections in the community. People excrete RNA within three days of being infected against 14 days for physical symptoms to be manifested. Travel time from the first flush to the treatment works varies from half a day to three days. Such a 7-10 day time difference can simply be crucial for the effective implementation of containment measures. While testing via sewage sample is inevitably less accurate than direct testing, the differences in cost and timing more than make up for this.

Detection is swift. Sample preparation typically takes from 30-60 minutes, depending on the centrifuging method used. RNA detection is then carried out using well established methods meaning that day on day testing is perfectly feasible, generating near to real-time data where a lab is close to the effluent source.

What is being picked up is not the virus, which rapidly degrades before excretion (Wölfel, R., Corman, V.M., Guggemos, W. et al. (2020) Virological assessment of hospitalized patients with COVID-2019. Nature. <https://doi.org/10.1038/s41586-020-2196-x>), but its genetic material in fragments of SARS-CoV-2 RNA. In Paris, all raw sewage samples tested positive, while 75% of treated effluent samples tested positive. In those cases, the RNA concentration was one hundred times lower. In the Netherlands, no samples were detected in the treated effluent. It is crucial to understand that sewerage networks are not a means of transmitting the infection.

Over the past few weeks, a worrying trend has been the realisation that the proportion of people infected with Covid-19 who are asymptomatic could be very high. This redoubles the need for sewage-based testing.

Over the last month, cooperation between academia and utilities has flourished and this has in turn blossomed between countries. In the Netherlands the initial plan is to expand testing to each of the 12 provincial capitals and a further 12 sites where Covid-19 has not been detected to date. In Australia, Water Research Australia is working with the Water Services Association of Australia to integrate SARS-CoV-2 testing at STWs with public health data on Covid-19 on a national basis. The ColoSSoS Project (Collaboration on Sewage Surveillance of SARS-CoV-2) aims to track the presence of the virus in communities, especially for the extent of asymptomatic infections. In the UK, a team at Bangor University working with Dŵr Cymru Welsh Water is taking weekly samples from 21 sewage treatment works that cover 75% of the Welsh population. A steady decline in RNA concentrations has been noted in the five weeks since the start of April. A similar project run by Newcastle University and Northumbrian Water is covering North East England.

It is already evident that this testing is remarkably powerful and useful. First, it is a means of alerting people about an outbreak in the community before any physical symptoms are manifested. Next, it can inform us when it has stopped in the community using that particular sewerage system. Likewise, it can warn that it is

still prevalent, even in the absence of any positive testing of people. Finally, it can provide an early warning about a secondary or even a tertiary wave of infections.

When it comes to early warnings, we are unfortunately in most cases well past that point. Early warnings about a second or third wave of the Pandemic are another matter altogether.

Two further dimensions of the current research are of particular interest. Firstly, the pay off between ease of sampling and the number of people in any given sample. For example, Thames Water's Beckton plant treats the emissions of 3.5 million Londoners, which makes it easy to monitor this population, but it is rather vague for the population as a whole. However, a team lead by Australia's CSIRO believes testing can be taken 'up-pipe' even to the post code level (Ahmed, W, et al., (2020) First confirmed detection of SARS-CoV-2 in untreated wastewater in Australia: A proof of concept for the wastewater surveillance of COVID-19 in the community, Science of the Total Environment).

In Europe, there were 25,153 sewage treatment works registered under the EU's Urban Wastewater Treatment Directive in 2016 (EU net of Croatia, plus Iceland and the United Kingdom), serving 381 million people, an average of 15,150 per facility. Monitoring these facilities would provide a level of scrutiny that personal testing could not affordably hope to aspire to. Arizona University's HHO believes that by tracking the 15,014 urban wastewater treatment plants in the USA, 70% of the population could be screened for SARS-CoV-2 in a single operation costing \$225,000 in reagents.

The next step could be to turn this into a quantitative test by monitoring the levels of the material in the effluent. This is very much a work in progress. Research in the USA, Netherlands, Australia and France is demonstrating that there is a consistent relationship between the presence of SARS-CoV-2 in sewage effluent and local infection rates (Nature, 3rd April 2020).

A firm idea of the amount of SARS-CoV-2 RNA excreted by an individual each day will be needed, dilution also needs to be factored in, along with other factors such as biomarker degradation rates in the effluent, per-person water consumption and the demographic profile of each community. Next is the need to take into account external factors such as rainfall diluting the effluent and assuring the consistency of sampling and wastewater temperature also affects results.

Researchers at Arizona's HHO believe that they can detect the presence of a single infected individual amongst 2 million people (which would make Beckton a powerful early onset sampler for London). The range at present is between 114 and 2 million individuals based on the amount of viral genomes being excreted and using RNA amplification. Meanwhile, the Paris research (Science, 21st April 2020) noted a rise in the concentration of SARS-CoV-2 RNA ahead of official infection estimates.

Looking at the wider world, the next step is to develop testing for those without easy access to labs. Cranfield University's Cranfield Water Science Institute has developed a simple paper-based test for SARS-COV-2 nucleic acid in effluents. The wastewater-based epidemiology (WBE) test is aimed at being used by non-specialists at a cost of less than £1 per device. This could be a significant resource in developing economies, especially if linked with smartphone enabled reporting systems.

Covid-19 testing has the potential to transform our appreciation about the positive effects of an effectively managed sewerage and sewage treatment system in the delivery of public health services. The more countries and labs sampling, measuring and monitoring the better, as more comparators will be crucial in correlating RNA concentration to infection rates and modelling individual outbreaks. The costs of the current (and future) lockdown, the potential benefits of a timely, efficient and effective sewerage-based monitoring are compelling.