DR KELLY HILL

"The results of sewage surveillance must be considered in the context of epidemiological surveillance"

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Academics and authorities across the world are looking into wastewater based epidemiology as a tool to monitor the prevalence of COVID-19 in the population and inform health measures to manage the pandemic.

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Wastewater monitoring research applied to the detection of SARS-CoV-2 has been underway for months now by research groups in many countries, and the methods have proven useful to detect the presence of infection by the novel coronavirus in the population. Many challenges remain before sewage surveillance can provide population-relevant information that can be interpreted and integrated with other sources of information to inform health policy. Collaboration at all levels is key, and in this regard, the Australian "ColoSSoS" project has made great progress to track and monitor the presence of the virus that causes COVID-19 and its persistence in that country's sewerage network. We talked with Dr Kelly Hill from Water Research Australia to learn about their latest developments and the way forward in sewage surveillance.

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Firstly, we would like to know briefly your career path and your current role in Water Research Australia.

After completing my Honours Bachelor of Science at The University of Northampton in England, I was sponsored by the Scottish Environmental Protection Agency to conduct a Master of Science (MSc) in Sustainable Catchment Management at the University of Dundee in Scotland. In 2011 I was awarded a Scholarship from the International Centre of Excellence for Water and Resource Management (ICE WaRM) to do my MSc Research in South Australia. I have lived in Australia now for 9 years, and am Research Manager at Water Research Australia, where I have managed a portfolio of national water quality and wastewater projects for over 3 years. I am currently the Project Director for the national Collaboration on Sewage Surveillance for SARS-CoV-2 "ColoSSoS" Project.

Can you tell us a bit about the current status and future plans of the ColoSSoS (Collaboration on Sewage Surveillance of SARS-CoV-2) project? Can you tell us about any preliminary findings?

The Collaboration on Sewage Surveillance of SARS-CoV-2 (ColoSSoS) program is an accelerated research program,

with four expert task groups at its core covering the key elements needed in this type of research. These four expert groups are sampling, molecular analysis, data integration and interpretation and communication. The task groups contain experts nationally and internationally across water, health, research and consultancy. They feed into the state nodes, which were set up by Water Research Australia. The program has been set up in a State-based way to efficiently and effectively sample and test. The ColoSSoS methods, whilst novel with respect to SARS-CoV-2, have built on extensive experience with sewage surveillance for other viruses, such as norovirus, adenovirus and poliovirus. The methods are now considered sufficiently specific and robust that they can be used to detect the presence of SARS-CoV-2 RNA fragments (used as markers) in raw sewage and for ongoing sewage surveillance. The methods will continue to be refined with an aim to improve sensitivity and if possible to explore quantification of the virus in the longer term. Appropriate normative controls have been established to help provide information on result reliability. The controls are aligned with those used in clinical test settings. Inter-laboratory trials have taken place on multiple groups of samples and results are sufficiently consistent that they mutually support one another.

During those trials, independent methods were used by different laboratories and this has included using three distinct WHO-recognised clinical primer/probe sets (US CDC, China CDC and Hong Kong University). There has been evidence such as amplicon size and sequencing to confirm the reliability of the results. The results of sewage surveillance must be considered in the context of epidemiological surveillance and therefore must belong to the jurisdictional health departments to avoid any misinterpretation or premature announcements out of context by academics or the media resulting in misplacement of public health response efforts. However, there are lots of excellent learnings from the project that can be shared, such as 'how to sample', the findings of various molecular analysis method investigations,

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the interpretation of data and the key to understanding what it all means in terms of communications guidance. This is all being brought together in the soon-to-be-released Good Practices Guide for Sewage Surveillance of SARS- CoV-2 for members of Water Research Australia.

You have been involved in the international initiative for SARS-CoV-2 monitoring employing sewers. Can you tell us about this collaboration?

The ColoSSoS program is well underway, and a global first for leading the sewage surveillance initiative in close collaboration with health departments. This program is one-of-a-kind as it is driven and informed by jurisdictional health departments every step of the way. Its development has involved collaboration between leading experts in the different aspects of the work, necessary to have the quality outcomes we need. For example, the optimal location for sampling is determined by several factors and groups. It is led by Health departments who have the information of clinical case numbers, and expert knowledge of at-risk locations/communities to test. This is combined with water agencies who have expert knowledge of the sewer network and 'peak' timings for collection of samples. This use of expertise, networking and relationships flow right through the core of this project using the most experienced laboratories and researchers who have been sampling at wastewater locations for decades, such as Australian Laboratory Services (ALS), those who have been analysing sewage for viruses and pathogens for decades, such as the Australian Water Quality Centre (AWQC) and Sydney Water, and those who are nationally responsible for virus analysis and standard development, such as VIDRL and NMI, and the highly specialised Next Generation Sequencing for the confirmation of RNA fragment detection at the Walter and Eliza Hall Institute for Medical Research (WEHI). The collaboration extends nationally and internationally, with organisations and health departments coming together to discuss and peer review at every step. An example of which is the collaboration with the Canadian Water Network (CWN), who are undertaking a similar program. We have developed our guiding principles of collaboration with CWN, as well as with the CWN Public Health Advisory Group who have been reviewing our data integration, and interpretation studies that have been developed by health departments.

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What are the uncertainties involved in establishing a relationship between viral detection in wastewater and population-relevant information? How are they being addressed?

The uncertainties of the relationship between viral detection in wastewater and population-relevant information are significant, and situation and context-dependent, and therefore we have been extremely careful in the engagement of experts for each step of the process. Understanding this relationship is complex, and the expert task group for data interpretation and integration relies on those expert epidemiologists, both environmental and clinical to understand and interpret the data. There are still many questions about the potential utility of wastewater surveillance for early detection of the fragments, including the assessment of how well sewage surveillance can accurately identify the pres-

ence or absence of infectious cases in a catchment, and over what period since infection or onset of symptoms and the distance from the sampling site.

This is not the end of the story and by no means the full picture. A key challenge is how to interpret sewage sampling results, for example considering variations in faecal shedding, viral degradation within sewage systems and related transit times, temperature and other variables. The data will be analysed in connection with other sources of information, as you mention. The sources of information include swab testing, serology, molecular epidemiology, contact tracing (identifying contacts), distancing information (lockdown measures, physical distancing requirements), and even border controls (international, interstate, intrastate), to name just a few! Therefore, the core group analysing the results and making sense of them are the only ones who should be attempting to do this, and that is the jurisdictional health representatives and their COVID task force colleagues.

Recently wastewater samples from the Paris and Montpellier sewage systems showed increases in SARS-CoV-2 RNA after the end of the lockdown in France. The increase does not correlate with infection rates. Do you think wastewater surveillance efforts are ready to predict a comeback of the disease?

It is hard for me to comment on the wastewater sample monitoring results coming out of Paris and Montpellier, without an understanding of the research, how it has been conducted or used. To attempt to understand if these findings correlate to infection rates or not would be speculation at this stage. Some studies, like those in the Netherlands, have shown that fragments of the virus have been found before known clinical cases arise. I think we are many years from being able to rely solely on the surveillance efforts of wastewater as an indicator of the presence of infection in the community, as I mentioned, the data really needs to be understood in the full context of what we are dealing with; it is a hugely complex environment and we should be commending our health departments for seeking every avenue possible to understand the spread of the virus for the protection of public health. However, it is possible. The use of sewage

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surveillance for detection of Polio identified the transmission of the virus in the community as recently as 2013 in Israel, through a sewage monitoring protocol which was created in 1989.

Proof of concept studies have provided estimates of the prevalence of infection using modelling approaches. Local news (for example, in Yosemite, California) have reported such estimates of prevalence. Do you think these data are currently accurate enough to be communicated to the public and health officials?
I think my previous explanations answer this. The significance of fragment detection in sewage should be determined by the health department specialists who have the greatest understanding of the whole suite of interactivity going on, and caution should certainly be exercised on any result not driven by, or informed by the health departments. There is hope for the future of sewage surveillance for the detection of SARS-CoV-2, as we currently use it for polio and other viruses. The hope is that we develop a system of rapid mobilisation for any future outbreaks of novel viruses by conducting these proof of concept and integrated research studies properly, with caution and expertise.

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What is your assessment of the potential cost and effectiveness of a wastewater surveillance system versus extensive individual testing to estimate disease prevalence in a community?
The cost is high for the initial development of a wastewater surveillance system, largely due to the high cost of consumables that are needed to undertake the analysis required to detect the fragments of virus in sewage. It is useful to note that one sewage sample can cost 10-100x that of one clinical sample, however, taking one test at a wastewater treatment plant could cover 200,000 people. The cost-benefit is complex to understand as it is entirely dependent on the situation, the interpretation and integration of the result with clinical, health and population relevant data. We must not, however, disregard the potential for wastewater-based epidemiology. The cost may be high now, but, if done correctly, could be hugely valuable with the potential for early detection of cases, which could prevent outbreaks and spread of illness, both in real-time during this pandemic, and looking into the future. The thing to remember is not, what is the most costly, or inexpensive solution, but what tests can we use, and how can we use them, to provide the greatest value, so that we can continue to provide the most appropriate and careful attention to public health protection and safety.

When do you think there might be widely available standardised protocols for wastewater monitoring to relate results to the burden of disease in a wastewater catchment?
Specific to SARS-CoV-2 virus, and the applicable COVID disease in the community, the Water Research Australia project partners work based on the information provided by the expert task groups that is being developed into the current 'best practices' guidance.

There are common protocols used among ColoSSoS partners for sample collection and storage, and common methods, primers, and reagents being used for molecular analysis. The key part of the project, the data interpretation and integration is still underway. It is a hugely valuable and important task and the expert epidemiologists are undertaking it with care and caution.

In general terms, the relationship of wastewater monitoring to the burden of disease is not a new phenomenon and has been used worldwide to monitor the eradication of poliovirus. There are over 100 types of pathogenic viruses from human and animals that end up in sewage, and so there are many expert virologists and molecular biologists who have been detecting and monitoring viruses and pathogens in

wastewater for decades. The task for Australia, and indeed, the world, is to ensure that what we do now, is well considered, driven and understood by the end-users (health), and well informed, through integration with data from other sources. The risks are high, for those who are not experts conducting these tests and publicly releasing results that are not appropriately validated and not presented in the context of the response deemed by health officials to best protect public health. We acknowledge that it is common practice in the research community to race for answers in the face of such a devastating new disease, however, we are confident that the robust, comprehensive and collaborative approach taken in the ColoSSoS project will provide profound and long-term benefits to the Australian community.

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