Australian Government

Chief Scientist

21 April 2020

The Hon Greg Hunt MP
Minister for Health
Parliament House
CANBERRA ACT 2600

CC:
The Hon Karen Andrews MP, Minister for Industry, Science and Technology
Dr Brendan Murphy, Chief Medical Officer

Dear Minister

Please find attached a response to your request for advice on the feasibility of monitoring wastewater for early detection and monitoring of COVID-19 in the population.

This rapid response has been prepared by the Rapid Research Information Forum that I Chair. The report synthesises the evidence base on this matter and has been informed by relevant experts and has been peer reviewed. Details of the authors and peer reviewers can be found in the Appendix.

I hope this document proves useful to you and your colleagues.

Yours sincerely,

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This rapid research brief responds to the request for advice on the feasibility of monitoring wastewater for early detection and monitoring of COVID-19 in the population.

- Wastewater-based epidemiology (WBE) techniques are used in routine surveillance for human pathogens and have provided valuable public health data. Developing similar WBE techniques for detection of SARS-CoV-2 is an active area of research and rapid improvements can be expected.
- Further understanding of SARS-CoV-2 infection biology and standardisation of WBE methods, along with improvements in their sensitivity and specificity, will enhance use of WBE tools to inform public health authorities of the prevalence of COVID-19 and management of its spread.
- Given the resolution of WBE techniques can facilitate the identification of communities in a given geographic location, there are concerns of stigmatisation of communities resulting from WBE. Careful thought must be given to research design and public release of data.

Since COVID-19 emerged as a "pneumonia of unknown cause" in December 2019,[1] it has since spread from Wuhan, China around the world.[2] Without a vaccine or clear treatment options,[3,4] there is a need to develop robust monitoring strategies for infection surveillance and control.[5]

Established techniques in wastewater-based epidemiology (WBE) have shown promise overseas and in Australia. Here, the term 'wastewater' means sewage and is distinct from stormwater. Wastewater refers to both greywater and blackwater; the former is used water from baths, showers and washing machines, and the latter from toilets.

Tools to monitor and predict the spread of SARS-CoV-2 in the population, particularly with the prospect of a second wave of infection, can improve understanding of the presence and prevalence of SARS-CoV-2 at the population level. Rapid advancement in WBE technologies, complemented by clinical surveillance methods, which are restricted to specific people, could provide estimates on the scale of SARS-CoV-2 prevalence or carriage in the population. Further development of the sensitivity and specificity of WBE techniques could contribute to information about the population that has not been tested and add strong support to the target of 'no undetected community transmission'. Once clinical testing has eased, WBE could also be used as an on-going monitoring system or to evaluate the effectiveness of a future vaccine. When WBE development has reached a higher level of sensitivity and specificity, it may be a preferred mechanism for ongoing monitoring as it is less intrusive in people's lives and poses less threat to privacy than other approaches. As such, WBE could be used as a tool to support public health authorities in easing physical distancing measures for regions identified as COVID-19-negative or to direct more intensive testing of particular communities.

Wastewater-based epidemiology

The detection of viruses or fragments of their genetic material (DNA or RNA) via WBE techniques is possible due to the process of viral shedding – the mechanism by which a virus releases its progeny following infection of a host cell.

WBE techniques are widely used as early warning and monitoring systems for the spatial and temporal trends of diseases. WBE is primarily based on the extraction, detection and subsequent analysis and interpretation of chemical or biological compounds.[6] Viral examples include polio,[7,8] SARS-CoV,[9,10] influenza,[11] hepatitis A and norovirus.[12–14] In addition to pathogen detection, the use of illicit drugs, pharmaceuticals, food consumption and industrial chemicals can also be monitored in wastewater.[15–22] Importantly, the timing of sampling wastewater is critical as the components of interest may have been subjected to varying degrees of degradation or transformation. In Australia, although the time from 'flush' to wastewater treatment plant can vary, on average it is between 1 and 8 hours.

The performance of WBE assays are based on two primary metrics: sensitivity and specificity.[23] The sensitivity of an assay reflects the percentage of correctly identified positive samples (true positives), and specificity refers to the percentage of correctly identified negative samples (true negatives). An assay is considered 'well performing' if it demonstrates 80% in both metrics.[23,24] Inherent biological differences between different pathogens mean that different WBE techniques are used for the detection and monitoring of each virus, and that each virus and technique have different sensitivity and specificity.

Wastewater samples taken from pumping stations and wastewater treatment plants can be traced to specific urban catchment areas, and when combined with Census data, can provide population-scale information within the catchment area boundaries.[20] In Australia, the population serviced by a wastewater treatment plant ranges from fewer than 5,000 to over 500,000 people.[25,26] Some areas with localised catchments, such as airports, hospitals, aged-care facilities and prisons, allow for more targeted WBE analysis. WBE has the potential for significant coverage of the Australian population, as 93% of Australian households are connected to a public sewerage system.[27] It has been demonstrated that 56% of the Australian population is covered by surveying just 58 of 1,234[28] wastewater treatment plants.[25]

Routine surveillance for human pathogens in wastewater has provided valuable public health data since 1849 – when faecal-oral transmission of cholera was first described.[29,30]

Wastewater-based epidemiology for the monitoring of SARS-CoV-2

Whilst COVID-19 is primarily a respiratory disease, numerous reports have confirmed detection of SARS-COV-2 RNA in the faeces of both symptomatic and asymptomatic COVID-19 patients.[31–42] The virus can also be shed and transferred to wastewater via other bodily secretions including sputum.[43]

Once faeces enter the wastewater system, the associated viral RNA can be detected by WBE techniques. Importantly, the RNA of viruses is fragile and timely sampling may be required before it is degraded. The stability and duration of possible detection of SARS-CoV-2 RNA in wastewater has not yet been determined.

A proof-of-concept study by Ahmed *et al*. from the University of Queensland and CSIRO was the first to successfully detect SARS-CoV-2 in Australian wastewater representing catchments in south-east Queensland.[44,45] The researchers combined standard WBE techniques with genetic sequencing and were able to match their estimated number of cases with clinical observations. The ability to detect SARS-CoV-2 in wastewater has been confirmed by other research groups in the Netherlands and the USA.[46,47]

Researchers at the Australian National University are partnering with Icon Water to sample wastewater in Canberra for the next 12 months.[48] And an Australia-wide investigation, Collaboration on Sewage Surveillance of SARS-CoV-2 (ColoSSoS Project), led by Water Research Australia, will monitor the presence of the virus in the nation’s wastewater network and explore ways to combine this with population health data to aid in future COVID-19 responses.[49]

WBE tools can be combined with other techniques to help refine estimates of the prevalence of SARS-CoV-2. For instance, Brouwer *et al*. demonstrated the possibility of combining environmental data collected by WBE techniques and public health tools to intervene in the management of a polio outbreak.[50] In China, Li and colleagues used WBE data in combination with the number of COVID-19 patients tested, and their results, to infer the number of undocumented cases of COVID-19 and their level of contagiousness.[51]

Encouragingly, WBE techniques to monitor other viral pathogens demonstrate that it is possible to develop methods for the early detection of outbreaks. For example, Hellmér *et al*. from Sweden, could detect the outbreak of hepatitis A and E in wastewater seven weeks before clinical diagnosis, as pre-symptomatic patients shed the virus.[12] To strengthen the accuracy of using WBE methods for the early detection of COVID-19, it must be determined if pre-symptomatic patients shed SARS-CoV-2 – an area of ongoing investigation.

Limitations of wastewater-based epidemiology for monitoring SARS-CoV-2

Although current laboratory methods to detect SARS-CoV-2 have been developed,[52,53] they are only adequately specific and sensitive to samples obtained from clinical testing. Due to the complex nature of wastewater, Ahmed *et al*. noted that when virus concentrations are too low, in the vicinity of fewer than 1,500 viral RNA copies per litre of wastewater, the ability to differentiate between true negatives and positives is compromised.[44] Furthermore, the researchers also experienced inconsistencies between different techniques applied.

These limitations were highlighted in the discrepancies observed between different studies using WBE analysis of SARS-CoV-2. In the Netherlands, wastewater surveillance of SARS-CoV-2 was estimated to detect 3.5 cases of COVID-19 per 100,000 people in the catchment area.[46] Notably, false negatives were identified in this study — that is, negative results were indicated in samples taken from catchments with known COVID-19 cases. Another study in the USA estimated COVID-19 prevalence to be between 4 and 200 times the number of confirmed cases within the catchment.[47] These discrepancies highlight the need for standardised wastewater sampling and analysis methods. The ColoSSoS Project aims to release national protocols for sampling and virus analysis that are being developed in collaboration with international experts.[49]

Several studies demonstrated that recovered COVID-19 patients continue to shed viral RNA fragments in their faeces for nearly five weeks following negative nose throat swab clinical test results.[31,35–37,40] While the viral shed rate remains uncertain and information on the decay of SARS-CoV-2 in wastewater systems remains unknown, the absolute number of COVID-19 patients in the community cannot be calculated.

In addition to the discrepancies of WBE sampling and methodology, there are limitations in our understanding of SARS-CoV-2 infection biology. For WBE detection of SARS-CoV-2 to be informative of the epidemiology of COVID-19, accurate values for the rates at which patients shed virus are required. COVID-19 patients do not shed virus equally. We have limited understanding of the duration and amount of virus shed by different people and by people at different stages of infection, and how long the wastewater-borne virus remains detectable.[54–56] However, as WBE looks at the catchment population as a whole, and not individually, this is a less relevant issue, because it applies more to the single infection level and not the population level.

WBE for precise and timely detection of SARS-CoV-2 in the population is an area of active research and we can expect to see rapid improvements. As this area of research matures, it is possible that monitoring wastewater could serve as a useful surveillance tool for early detection of COVID-19 in the population, to manage its spread, or to provide evidence supporting its absence.

Ethical considerations for wastewater-based epidemiology

Potential ethical harms of WBE include stigmatisation and the potential for severe public policy responses. For example, WBE testing for COVID-19 could lead to heightened stigmatisation of a particular community or ethnic group residing in a given geographic area. This is possible, especially if stigma already exist.[57–59]

Generally, the risk of harmful consequences resulting from WBE is considered low as samples are collected from composite sites and individual participants cannot be identified. However, more stringent oversight may be required for highly localised catchments, especially those with vulnerable residents such as in prison facilities. Relatively consistent sampling across the whole of the community will reduce risks of excessive surveillance of already stigmatised localised communities.

Researchers and policy makers appear to be aware of potential harms. In one example, care was taken to maintain the confidentiality of individual wastewater treatment plants to reduce the possibility of stigmatising specific communities.[25]

Mitigating the risk is possible with careful planning of research methodology; managing relationships with research partners such as local government and communities; managing how information is communicated, particularly to media; and regular evaluation and amendment of WBE practices.[60–63] Risks must be assessed in relation to the dangers of the virus, including its infection fatality rate and the likelihood of its reoccurrence.

An important note on available COVID-19 research

Although current COVID-19 research is available through pre-print servers, many of these articles have not yet been peer reviewed (an imperative pillar of the scientific method) and the relatively short time length of the current outbreak has resulted in variable testing and reporting practices in different countries. As such, conclusions drawn need to be interpreted with caution.

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RAPID RESEARCH INFORMATION FORUM

Wastewater monitoring for COVID-19 detection

The Rapid Research Information Forum (RRIF), convened by Australia's Chief Scientist, Dr Alan Finkel AO, is a forum for rapid information sharing and collaboration within the Australian research and innovation sector. It provides a mechanism to rapidly bring together relevant multidisciplinary expertise to address pressing questions about Australia's response to COVID-19, as they emerge. RRIF enables timely responses to be provided to governments based on the best available evidence. RRIF also informs the Chief Scientist's interactions and collaboration with other national chief scientific advisers. RRIF demonstrates the critical value of research and innovation in driving societal as well as economic progress now and into the future.

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