CD Summary
January 2023 | Volume 72 Number 1
Contact: 971-673-1111 | cd.summary@state.or.us | www.healthoregon.org/cdsummary

NOT LETTING A USEFUL DATA SOURCE GO TO WASTE: Wastewater surveillance for SARS-COV-2 in Oregon

AN INTRODUCTION TO WASTEWATER SURVEILLANCE

Wastewater-based surveillance (WBS) has been used for the surveillance of infectious diseases since the 1940s. Its earliest application was in monitoring poliovirus circulation.[1,2] The COVID-19 pandemic has underscored the benefits of WBS as a complement to case-based surveillance. Data from clinical surveillance, which are contingent upon patients seeking care and being tested, have underestimated the true burden of COVID-19 infection in the general population. Early seroprevalence data from Oregon demonstrated a ten-fold difference in measured versus reported SARS-CoV-2 infections.[3] As vaccination and infection-induced immunity have led to more asymptomatic and milder cases, and the usage of at-home rapid antigen tests has dramatically expanded, case-based surveillance data for SARS-CoV-2 have become unreliable in reflecting the incidence of infection.[4,5]

Given the limitations of case-based surveillance, epidemiologists are increasingly turning to community-level surveillance methods such as WBS. WBS for COVID-19 offers several advantages over traditional surveillance methods. WBS allows the rapid detection of community disease spread, captures mild and sub-clinical infections that would be missed by clinical surveillance efforts and functions independently of healthcare-seeking behavior and testing access.[6-9]

ADOPTION IN OREGON

Through a collaboration between the Oregon Health Authority (OHA), Oregon State University (OSU) and wastewater treatment facilities statewide, Oregon became an early adopter of COVID-19 wastewater surveillance, and today, >40 municipalities participate by collecting 24-hr composite samples of their influent wastewater 1–2 times weekly. Following RNA extraction, pathogen sequence is quantified using reverse transcriptase droplet digital PCR (dd-PCR). Additionally, samples with a SARS-CoV-2 concentration >$10^{3.5}$ genome copies per liter* undergo amplicon-based sequencing and variant identification through multi-locus sequence typing.[10] OSU tests all samples and reports results to OHA weekly.

DATA AVAILABILITY

SARS-CoV-2 wastewater surveillance data have been publicly available since October 2020. The current SARS-CoV-2 wastewater dashboard displays three primary data sources: flow- and population-adjusted SARS-CoV-2 viral concentration data (log copies per person per day); incident daily cases per 100,000 from the corresponding wastewater treatment facility's service area; and sequencing data including variants detected in wastewater and the level at which they were detected (low, medium, or high†). A trend regression produces five categorical trend classifications: sustained decrease, decrease, plateau, increase, or sustained increase based on a two-sided p-value = 0.10 significance level for the regression coefficient. The three and five most recent measurements define "short-term" and "sustained" trends, respectively.

* $10^{3.5} \approx 3{,}162$

† Low: variant comprises 10–24% of all variants circulating. Medium: 25–49%. High: > 50%.

PUTTING THE DATA TO GOOD USE

Wastewater surveillance data in Oregon are currently being used to better understand community transmission of SARS-CoV-2 over time and to monitor for the emergence of new COVID-19 variants. Given the shortcomings of case-based surveillance, an important objective of the program is the evaluation of the ability of wastewater surveillance data to provide independent, quantitative estimates of incident cases.

The following analysis of data from Bend, Oregon demonstrates the correlation between SARS-CoV-2 viral concentration in wastewater and COVID-19 case counts within the corresponding wasteshed. Bend was chosen because it has participated in wastewater surveillance since the program's inception.

A CLOSER LOOK AT WASTEWATER SURVEILLANCE DATA FROM BEND, OREGON

The accompanying Figure, (*supra*) shows daily COVID-19 cases per 100,000 persons (histogram) along with the 174 wastewater virus concentrations (scatter plot) measured in Bend during September 4, 2020–May 27, 2022. Trend regressions of the SARS-CoV-2 wastewater concentration data are color-coded to indicate a sustained decrease (blue), decrease (light blue), plateau (yellow), increase (pink), or sustained increase (red). A visual inspection of the overlay reveals corresponding peaks and troughs. The peaks in case surveillance data clearly correlate with the red (sustained increase) scatter points.

The association between viral concentrations and 7-day rolling averages of daily incident cases was statistically significant (Spearman correlation coefficient r=0.67, p<0.0001). When repeated with variable lead and lag times between wastewater and case-based surveil-

Figure. Detection and quantification of SARS-CoV-2 in wastewater and in the Bend community from September 4, 2020–May 27, 2022.

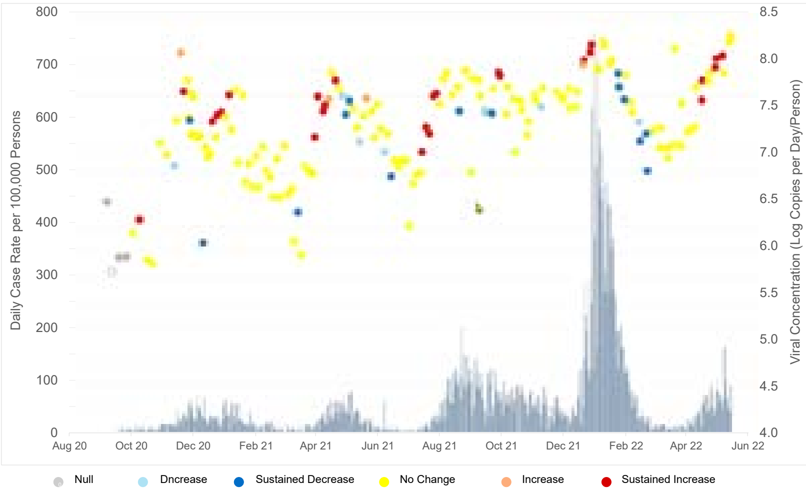

Table. Correlation between viral concentration in wastewater (log copies per person per day) and 7-day rolling average case counts per 100,000 persons. Analysis performed with variable lead and lag times (wastewater data to case data).

Lead or Lag Time (Days)	Spearman Correlation Coefficient	P Value
8 (lag)	0.46	< 0.0001
6 (lag)	0.57	< 0.0001
4 (lag)	0.57	< 0.0001
2 (lag)	0.52	< 0.0001
0	0.67	< 0.0001
2 (lead)	0.70	< 0.0001
4 (lead)	0.72	< 0.0001
6 (lead)	0.72	< 0.0001
8 (lead)	0.78	< 0.0001
10 (lead)	0.77	< 0.0001
12 (lead)	0.76	< 0.0001

lance, the correlation was greatest when wastewater data preceded case data by 8 days (r=0.78, p<0.0001; Table).

DISCUSSION

Wastewater surveillance data have the potential both to confirm case-based surveillance trends and to function as leading indicators of community-level COVID-19 disease transmission. Many infected individuals may shed the virus in stool before any develop symptoms and seek medical care.[8] Additionally, case-based surveillance relies on testing access and acceptance, while wastewater surveillance leverages pooled community samples and so operates independently of healthcare-seeking behavior and testing access. In short: the sewer collects samples from a higher percentage of persons than does the nasopharyngeal swabber.

The results of this analysis are consistent with those of previous studies, which have wastewater concentrations of SARS-CoV-2 and reported COVID-19 cases are maximally correlated when wastewater surveillance data preceded case-surveillance data by 2–8 days.[11-14] These findings may inform both individual-level and community-level public-health interventions such as masking and avoiding social gatherings. Active surveillance of SARS-CoV-2 RNA in wastewater up to twice weekly in more than 40 communities gives an accurate picture of Oregon's COVID-19 case and variant trends, which can be viewed on the publicly available wastewater dashboard. The brief analysis of Bend's wastewater data highlights the potential of WBS to provide an early warning of emerging outbreaks.

WBS has some limitations. Due to unknown parameters regarding fecal shedding of the SARS-CoV-2 virus and population movement, wastewater surveillance cannot be used to estimate the true number of cases in a population. Additionally, wastewater surveillance excludes populations without access to municipal sewer service (i.e., those with septic systems). Lastly, the lead time demonstrated in this analysis may not be generalizable to all populations or all variants. The disease time course of the current variant, testing access, availability and turnaround time and the use of at-home testing may delay or change the relationship between case counts and wastewater virus quantification. Despite these limitations, WBS complements and strengthens case-based surveillance systems and fills in important gaps.

FUTURE DIRECTIONS

The successful collaboration of OHA with OSU and our partners in public works has also facilitated the expansion of wastewater surveillance in Oregon to pathogens beyond SARS-CoV-2. Oregon is currently piloting wastewater surveillance for influenza, respiratory syncytial virus (RSV) and *Cryptosporidium*. With the success of wastewater surveillance of SARS-CoV-2, and the expansion of the program to other important pathogens, WBS is expected to become an intrinsic component of Oregon's communicable disease surveillance efforts in the future.

REFERENCES

1. Schmidt C. Watcher in the wastewater. Nature Biotechnology. 2020;38:917–21.
2. Metcalf T, Melnick J, Estes M. Environmental virology: from detection of virus in sewage and water by isolation to identification by molecular biology-a trip of over 50 years. Annual review of microbiology. 1995;49:461–88.
3. Sutton M, Cieslak P, Linder M. Notes from the field: seroprevalence estimates of SARS-CoV-2 infection in convenience sample—Oregon, May 11–June 15, 2020. Morbidity and Mortality Weekly Report. 2020;69:1100.
4. Bergwerk M, Gonen T, Lustig Y, et al. Covid-19 breakthrough infections in vaccinated health care workers. New England Journal of Medicine. 2021;385:1474–84.
5. Rader B, Gertz A, Iuliano AD, et al. Use of At-Home COVID-19 Tests—United States, August 23, 2021–March 12, 2022. Morbidity and Mortality Weekly Report. 2022;71:489.
6. Thompson JR, Nancharaiah YV, Gu X, et al. Making waves: wastewater surveillance of SARS-CoV-2 for population-based health management. Water Research. 2020;184:116181.
7. Medema G, Heijnen L, Elsinga G, Italiaander R, Brouwer A. Presence of SARS-Coronavirus-2 RNA in sewage and

correlation with reported COVID-19 prevalence in the early stage of the epidemic in the Netherlands. Environmental Science & Technology Letters. 2020;7:511–16.
8. Daughton CG. Wastewater surveillance for population-wide Covid-19: The present and future. Science of the Total Environment. 2020;736:139631.
9. Mao K, Zhang K, Du W, Ali W, Feng X, Zhang H. The potential of wastewater-based epidemiology as surveillance and early warning of infectious disease outbreaks. Current Opinion in Environmental Science & Health. 2020;17:1–7.
10. Sutton M, Radniecki TS, Kaya D, et al. Detection of SARS-CoV-2 B. 1.351 (Beta) variant through wastewater surveillance before case detection in a community, Oregon, USA. Emerging Infectious Diseases. 2022;28:1101.
11. D'Aoust PM, Graber TE, Mercier E, et al. Catching a resurgence: Increase in SARS-CoV-2 viral RNA identified in wastewater 48 h before COVID-19 clinical tests and 96 h before hospitalizations. Science of The Total Environment. 2021;770:145319.
12. Feng S, Roguet A, McClary-Gutierrez JS, et al. Evaluation of sampling frequency and normalization of SARS-CoV-2 wastewater concentrations for capturing COVID-19 burdens in the community. medrxiv. 2021.
13. Nemudryi A, Nemudraia A, Wiegand T, et al. Temporal detection and phylogenetic assessment of SARS-CoV-2 in municipal wastewater. Cell Reports Medicine. 2020;1:100098.
14. Peccia J, Zulli A, Brackney DE, et al. Measurement of SARS-CoV-2 RNA in wastewater tracks community infection dynamics. Nature Biotechnology. 2020;38:1164–67.

FOR MORE INFORMATION

- Oregon's SARS-CoV-2 Wastewater Monitoring Dashboard: https://public.tableau.com/app/profile/oregon.health.authority.covid.19/viz/OregonsSARS-CoV-2WastewaterMonitoring/WastewaterDashboard\

A New MMR Vaccine

Friday, December 31, 1999. It was the dedication of the National Millennium Time Capsule on a brisk, windy, winter day in Washington, D.C. America was choosing gifts to be preserved for the future. Among the items to be sealed in the capsule housed in the National Archives, were Ray Charles's sunglasses, a piece of the Berlin Wall, Cherokee alphabet, diploma of a brave African American student from a hither-to all-white public school, and a replica of six vaccines (MMR, varicella, hepatitis A, hepatitis B, pneumococcal, and *Haemophilus influenzae* type b vaccines) submitted by the 80-year-old father of modern vaccines.[1]

Hilleman's iconic MMR (Merck) vaccine was licensed by the U.S. Food and Drug Administration (FDA) in 1971 and has been enormously successful in moving us toward measles and rubella elimination and in decreasing the burden of mumps in the United States.[2]

Until this year, only one MMR vaccine, M-M-R II (Merck), has been available in the U.S. (A combination MMR/varicella vaccine has also been available.) On June 6, 2022, FDA approved a second MMR vaccine—PRIORIX (GlaxoSmithKline Biologicals)—for the prevention of measles, mumps, and rubella in persons aged ≥12 months.

GSK's MMR vaccine was first licensed in Germany in 1997. It is approved in >100 countries outside the U.S. (including all European countries, Canada, Australia), and more than 400 million doses have been distributed worldwide. PRIORIX is considered fully interchangeable with M-M-R II in a number of countries.[3]

And on June 23, 2022, the Advisory Committee on Immunization Practices endorsed PRIORIX as safe, immunogenic, and noninferior to M-M-R II. The two vaccines are fully interchangeable for all indications for which MMR vaccination is recommended. As a reminder, current MMR vaccination recommendations include:

FDA-approved use:

- Prevention of measles, mumps, and rubella in individuals ≥12 months of age. For routine vaccination, two doses are recommended, the first at age 12–15 months, and the second at age 4–6 years.
- Off-label use:
  - Children aged 6–11 months who are planning to travel or live abroad; or during outbreaks
  - As a 3rd dose during mumps outbreaks
  - For measles post-exposure prophylaxis

PRIORIX may be administered concomitantly, at different anatomic sites, and with other routine childhood vaccines. It is supplied as a single-dose vial of lyophilized antigen to be reconstituted with the accompanying prefilled syringe of sterile water diluent. Vials must be refrigerated at 36°–46°F (2°–8°C) and protected from light. The prefilled diluent syringes can be refrigerated or kept at room temperature. The route of administration (subcutaneous) and contraindications are the same as those for M-M-R II. Adverse events following administration of any vaccine should be reported to the Vaccine Adverse Event Reporting System.[4]

Seventy-seven years from now, our children will open the National Millennium Time Capsule and find, *inter alia,* Maurice Hilleman's MMR vaccine. The newly approved MMR vaccine will keep the Hilleman dream alive: protecting children from measles, mumps, and rubella with a single vaccine.

RESOURCES:

- Model Immunization Protocols- www.oregon.gov/oha/ph/preventionwellness/vaccinesimmunization/immunizationproviderresources/pages/stdgordr.aspx
- Measles www.oregon.gov/oha/PH/DISEASESCONDITIONS/DISEASESAZ/Pages/measles.aspx

REFERENCES

1. Offit PA. Vaccinated: *One Man's Quest to Defeat the World's Deadliest Diseases*. New York: Harper Collins; 2008.
2. Tulchinsky TH. Maurice Hilleman: Creator of vaccines that changed the world. Case studies in public health. 2018:443–70. doi: 10.1016/B978-0-12-804571-8.00003-2
3. Krow-Lucal E. EtR and proposed recommendations. ACIP Presentation Slides: June 22–23, 2022 Meeting. Available at www.cdc.gov/vaccines/acip/meetings/downloads/slides-2022-06-22-23/02-MMR-Krow-Lucal-508.pdf. Accessed 17 Jan 2023.
4. Krow-Lucal Marin M, Shepersky L, Bahta L, Loehr J, Dooling K. Measles, Mumps, Rubella Vaccine (PRIORIX): Recommendations of the Advisory Committee on Immunization Practices—United States, 2022. MMWR;71:1465–70.

Oregon Health Authority
PUBLIC HEALTH DIVISION

Providence Portland Medical Center designates this enduring material for a maximum of .5 *AMA PRA Category 1 credit*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity. Portland Providence Medical Center is accredited by the Oregon Medical Association to sponsor continuing medical education of physicians.

You can get this document in other languages, large print, braille or a format you prefer. Contact the Public Health Division at 971-673-1222. We accept all relay calls or you can dial 711. for TTY.