WASTEWATER SCAN
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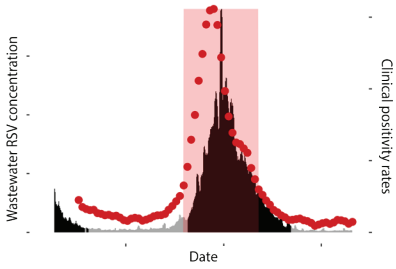
Establishing a correlation between wastewater data and clinical data for RSV infections in the U.S.

The national-scale study paves the way for public health agencies to begin using wastewater as a routine RSV surveillance tool

Before public health agencies can begin using wastewater data as a routine tool for monitoring any disease, they need to know that the wastewater data they are generating reflect disease trends in the underlying population. Scientists investigate this question by conducting **correlation studies**—first, at relatively small geographic scales and, once a correlation is established, at larger geographic scales and broader timescales. The correlation studies help public health agencies understand the relationship between insights generated via wastewater data and clinical insights generated via established surveillance methods. The ultimate goal is to give agencies confidence about using wastewater as a monitoring and decision-making tool.

Different diseases can follow very different trajectories during outbreaks, so scientists perform correlation analyses for each disease that public health agencies are interested in tracking via wastewater. To date, large-scale correlation studies have been completed for **SARS-CoV-2** (Duvallet et al. 2022) and **influenza A** (Schoen et al. 2023), paving the way for public health agencies to implement routine wastewater monitoring programs for these disease targets. The latest large-scale correlation study—the focus of this fact sheet—is for respiratory syncytial virus (RSV), a leading cause of pediatric pneumonia and bronchitis that is responsible for more than 100,000 deaths each year among children and up to 10,000 deaths among adults 65 and older.



Correlation studies help public health agencies understand the relationship between insights generated via wastewater data and clinical insights generated via established surveillance methods. In the example graph above, a strong correlation between RSV wastewater concentrations (gray and black bars) and RSV clinical cases (red dots and red shading) gives public health agencies confidence about using wastewater as an RSV monitoring and decision-making tool.

Overview of the science

A handful of studies at smaller geographic scales have previously established that RSV wastewater data correlate with RSV disease occurrence in the community contributing to the sewershed, including Hughes et al. 2022.

Zulli et al. 2024—the newest RSV correlation paper and the focus of this fact sheet—builds on the smaller studies by establishing a broad-scale correlation across 14 different states over a 17-month period that, in some states, encompassed multiple seasonal RSV outbreaks.

- The spatial and temporal scales at which the correlation analysis was performed provide confidence that RSV wastewater data can be relied upon as a tool for routine RSV monitoring across the U.S.

Read the full paper:

Observations of Respiratory Syncytial Virus (RSV) Nucleic Acids in Wastewater Solids Across the United States in the 2022–2023 Season: Relationships with RSV Infection Positivity and Hospitalization Rates

Key Takeaways

RSV wastewater concentrations correlated significantly with RSV clinical surveillance data

- The correlation gives public health agencies confidence about using wastewater as a monitoring and decision-making tool.
- The national-scale analysis was completed using wide-ranging data sets encompassing urban and rural settings, tropical to continental climates, and population ranges of 3,000 to 4 million, covering 0.05% to 59.5% of a state's population.

RSV wastewater data can augment traditional clinical indicators during RSV season

- RSV hospitalization peaks largely matched wastewater peaks over time, consistently falling within an eight-day range of each other.
- Wastewater data are available in as little as 24 hours after sample collection, and are not subject to clinical testing biases (e.g., socioeconomic factors, testing availability).

Although the study did not always match between wastewater and clinical data for dates of RSV onset, offset, and peak, the differences are a result of inherent differences and biases in the two analysis methods used

- The two surveillance sources capture insights about different populations (i.e., those who are sick and being tested vs. those who are shedding RSV RNA).
- RSV clinical testing is limited in many areas, and testing rates fluctuate based on clinicians' awareness of RSV circulation.
- If the thresholds used in the wastewater and clinical algorithms for RSV were to be changed, it could affect the level of concordance in the RSV season dates between the two methods.

What the Zulli et al. 2024 paper found

Researchers established a **significant positive correlation** between RSV wastewater data and RSV clinical data.

- Nationally aggregated RSV wastewater data were positively correlated with clinical data reflecting positivity and hospitalization rates.
- The same strong positive correlation was found for each of the individual states for which wastewater data were available.

Researchers found **strong concordance** between RSV season onset, offset, and peak as derived from each of the two analysis methods.

- The analysis was limited to 14 states in which wastewater data was available before season onset.
- RSV onset, offset, and peak dates were not always perfectly aligned—an outcome that researchers expected.

4 of 14 states
Wastewater-derived onset occurred **the same week as** clinical onset.

3 of 14 states
Waterwater-derived onset occurred **2-4 weeks prior** to clinical onset.

7 of 14 states
Wastewater-derived onset occurred **2-7 weeks after** clinical onset.

Multiple reasons explain the **lack of perfect alignment** between RSV season dates as derived via the two methods.

- The two surveillance sources capture information about different populations: those who are sick and receive testing, and those who are shedding RSV RNA.
- The majority of RSV infections are unrecognized and are not captured by clinical surveillance—a consequence of low testing and RSV diagnosis rates.

The lack of perfect alignment is a direct consequence of the **specific algorithms** that researchers selected for analyzing both wastewater and clinical data.

- The algorithm for identifying RSV season onset based on clinical data is commonly used by public health agencies.
- The wastewater algorithm that researchers developed for this study uses a threshold for RSV RNA concentrations that is equal to or greater than twice the detection limit for RSV in wastewater—a relatively conservative threshold. The wastewater algorithm was developed independently of the clinical algorithm.

Public health agencies have the option to develop and use more **purpose-fit algorithms** for their wastewater analyses.

- If the thresholds used in the wastewater and clinical algorithms for RSV were to be changed, the level of concordance in the RSV season dates between the two methods also would be affected.
- Public health agencies interested in using wastewater data to predict RSV clinical onset could develop an algorithm that incorporates statistical or machine learning approaches.

Considerations when tracking RSV in wastewater

Benefits

- Many RSV infections are not captured in clinical surveillance data because RSV goes unrecognized by clinicians and/or testing is not done.
- Wastewater has the potential to offer earlier warnings for hospitals and clinical sites to prepare for surges in RSV-infected patients.
- Wastewater has the potential to offer earlier warnings for public health agencies to launch vaccination campaigns to combat RSV outbreaks; RSV vaccines first became publicly available in fall 2023.

Limitations

- Infants in diapers—among the most vulnerable to RSV—are less likely to contribute to wastewater streams.
- Researchers have not yet quantified the timing of RSV shedding in sewersheds relative to when individuals experience symptoms from RSV infections; for example, researchers don't yet know if prolonged shedding occurs after individuals have recovered from RSV.
- Without data on shedding, a given concentration of RSV RNA in wastewater cannot yet be linked to a population-level RSV incidence or prevalence rate.

More reading

- Zulli, A., M.R.J. Varkila, J. Parsonnet, M.K. Wolfe, and A.B. Boehm. Observations of Respiratory Syncytial Virus (RSV) Nucleic Acids in Wastewater Solids Across the United States in the 2022–2023 Season: Relationships with RSV Infection Positivity and Hospitalization Rates. Environmental Science & Technology DOI: 10.1021/acsestwater.3c00725.
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- Schoen, M.E., A.L. Bidwell, M.K. Wolfe, and A.B. Boehm. 2023. United States Influenza 2022–2023 Season Characteristics as Inferred from Wastewater Solids, Influenza Hospitalization, and Syndromic Data. Environmental Science & Technology 57 (49), 20542-20550. DOI: 10.1021/acs.est.3c07526.
- Hughes, B., Duong, D., White, B.J., Wigginton, K.R., Chan, E.M.G., Wolfe, M.K., Boehm, A.B. Respiratory Syncytial Virus (RSV) RNA in Wastewater Settled Solids Reflects RSV Clinical Positivity Rates. 2022 Environ. Sci. Technol. Lett. , 9 (2), 173–178. https://doi.org/10.1021/acs.estlett.1c00963.