WASTEWATER-BASED SURVEILLANCE FOR PUBLIC HEALTH

KNOWLEDGE TO ACTION SERIES

CASE EXAMPLE

COST-UTILITY ANALYSIS

Wastewater-Based Surveillance of RSV

KEY TAKEAWAYS

1

Accurately identifying the start of RSV season saves children's lives.
Respiratory syncytial virus (RSV) is a major cause of respiratory infections in young children that can result in hospitalization, death or long-term health impacts like asthma. The primary prevention against severe RSV infection in infants and young children is timely immunization just before the RSV season begins. The province of Ontario bases this timing on clinical testing, a lagging indicator compared to wastewater-based surveillance (WBS) data, which capture early community transmission. In 2022 - 2023, WBS identified the start of RSV season 12-36 days earlier than the provincial start date, which was based on clinical testing.

2

Well-designed programs can ensure reliable and timely data.
The University of Ottawa developed and validated representative 24-hour, primary sludge wastewater sampling. Data were rapidly disseminated within 8 hours of sample transport, providing near real-time reporting. They used enrichment methods that directly target the fraction of wastewater where RSV RNA is known to partition and PCR assays with high specificity and sensitivity.

3

Adding wastewater-based surveillance doesn't necessarily cost more.
Cost-utility analysis (CUA) is used to help inform resource allocation decisions across different healthcare settings. A CUA comparing the impact of RSV disease in immunized and non-immunized infants found WBS to be a cost-saving approach over clinical testing. WBS costs can be offset by savings from the reduced need for medical care.

4

Wastewater-based surveillance is a valuable tool.
This RSV case study is an important demonstration of how harmonized sampling strategies, timely data reporting and effective partnerships can enable public health action. By linking early, population-level detection with actionable clinical and policy responses, WBS yields measurable gains in health utility and health outcomes, while enhancing preparedness for future outbreaks.

BACKGROUND

Wastewater-based surveillance (WBS) is the measurement of health targets in wastewater to identify or assess health threats and develop an understanding of disease burden and spread (see Figure 1). During the COVID-19 pandemic, WBS was implemented at more than 260 locations in Canada and more than 4,600 locations in 72 countries internationally as an economical, anonymized, non-invasive surveillance system to monitor pathogen spread, evolution and outbreak risk.[1,2]

Although WBS was rapidly implemented across Canada and around the world, there remains a glaring lack of WBS integration and actionability by Canadian and global public health and policy decision-makers, resulting in only a few instances of WBS findings being used for health interventions around the world.[3,4,5] This lack of WBS actioning is largely attributed to the disconnect between the rapid discovery of new analytical methods to measure disease targets in wastewaters and the comparatively slower development of critical health policy, public health structure and procedures, as well as health decision-making responses necessary to action generated WBS data.[4,5,6] This limited integration resulted in very few economic evaluations of WBS.

In this case study, we describe a cost-utility analysis (CUA) of WBS in Ontario, Canada, applied to the 2022-2023 provincial respiratory syncytial virus (RSV) season — a first in the world.

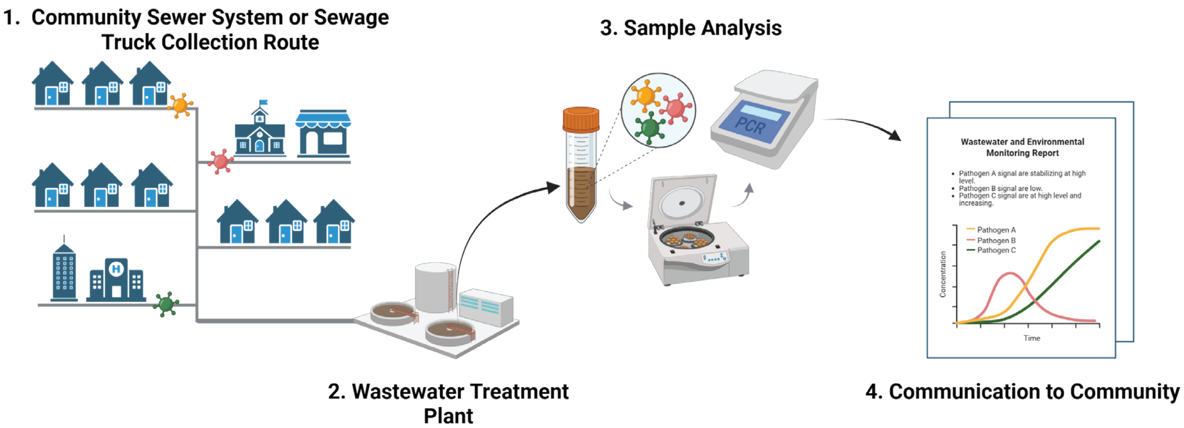


Figure 1. Schematic of WBS sampling, analyses and communication

Reliable and timely WBS-RSV data

The CUA is founded on the City of Ottawa's WBS-RSV data that was collected daily during the 2022-2023 provincial respiratory season for integration in the Ottawa Public Health Respiratory Transmission Risk Assessment tool. The City of Hamilton's 2022-2023 WBS-RSV data was also included in the CUA, leveraging 5-days-per-week sample collection and analyses that were established in 2020.

Two critical aspects of the WBS-RSV dataset used for the CUA are the reliability of the data and the timely dissemination of the dataset to clinicians and public health end users in the two cities to support actioning of the results. To ensure reliability and rapid analytical turnaround times, the University of Ottawa developed and validated:

- Representative 24-hour, primary sludge wastewater sampling in both cities to augment the sensitivity of the disease measurements.
- Enrichment methods that directly target the fraction of wastewater where RSV RNA is known to partition.[7]
- PCR assays that demonstrate high specificity and sensitivity.
- Optimized analytical methods to rapidly disseminate data within 8 hours of sample transport, hence providing near real-time reporting.
- An automated data pipeline to ensure WBS data quality (see Figure 2).

The data quality pipeline shown as the qPCR analyzer in Figure 2 ensures that all WBS-RSV data used for the CUA was subjected to rigorous quality assurance and quality control measures, along with algorithms applying correction factors for identified inhibition effects and large rainfall and snowmelt sewer flushing events that can impact the data.[8,9]

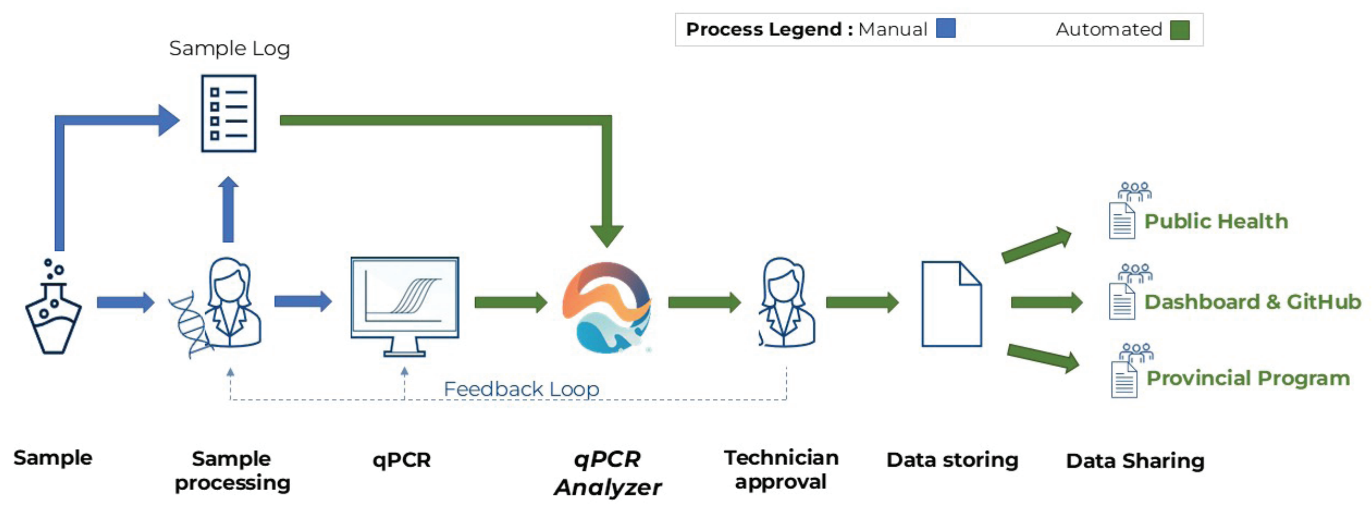


Figure 2. Schematic of WBS sample processing to ensure data reliability and rapid dissemination to health end users

WBS-RSV criteria to establish the start of RSV season

The primary prevention against severe RSV infection in at-risk infants is the timely administration of immunizations just before the RSV season begins. Accordingly, the Ontario Ministry of Health's RSV Advisory Group utilizes clinical surveillance to determine the start date of the RSV season and initiates a provincially funded immunization program for at-risk infants across the province (which has approximately 15 million people). However, clinical metrics are lagging indicators that are biased towards severe cases, as RSV testing is restricted to symptomatic children who present to the emergency room and are likely to require hospitalization.[10]

In this case study, WBS was investigated as an early indicator and novel data source. Retrospective analysis found that it could additionally serve to assist in the timely identification of the RSV season start date. To achieve this, WBS-RSV data was smoothed in real-time using a 7-day endpoint moving average. Subsequently, the season start date was identified using the following criteria: one week of consecutive endpoint averaged RSV measurements above the assay limit of quantification.

WBS identified the RSV season start date 36 days before the clinically determined provincial start date in Ottawa and 12 days earlier in Hamilton, demonstrating WBS's ability to capture the known geospatial variability of RSV transmission.[11] WBS also captured the early peaking of pediatric RSV hospitalization with a 12-day lead time, concurrently documenting the subsequent rise in adult hospitalizations that exemplifies the previously documented shift of infections from the pediatric to the adult population.[12] The finding of WBS's ability to identify the RSV season start was used in the CUA to quantify the cost and health outcomes of investing in WBS to enable a more timely initiation of provincial immunization in Ontario.

Understanding cost-utility analysis

CUA is frequently used to help inform resource allocation decisions across different healthcare settings by providing a standardized method of comparing the costs and benefits of different interventions. CUA is a type of economic evaluation that compares the costs and health outcomes of an intervention by measuring health effects in terms of both extension and quality of life. Each year of life under the intervention regime is weighted to reflect the quality of life in that year, using a scale from 0 (death) to 1 (perfect health). By comparing the costs and quality-adjusted life years (QALYs) gained from different interventions (expressed as cost per QALY), decision-makers can assess which interventions offer the best value for money.

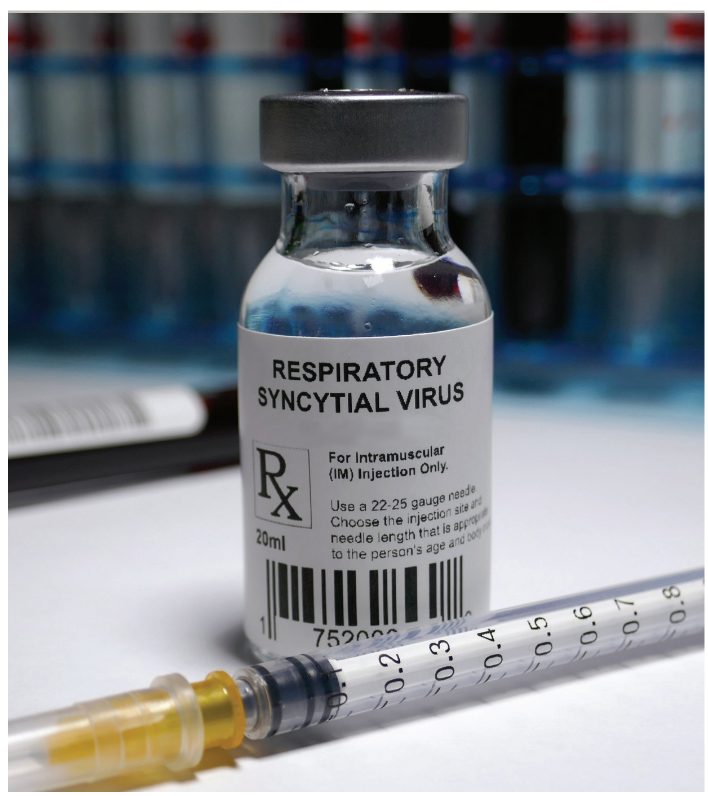
Assessing RSV immunization

RSV is a major cause of respiratory infections in young children, which can result in hospitalization and long-term morbidity (wheezing/asthma). Severe RSV disease during the winter epidemic season can be prevented effectively with immunization using a long-acting monoclonal antibody (nirsevimab). To evaluate the cost versus benefit (cost-effectiveness) of this intervention, a CUA has been developed wherein the impact of RSV disease in immunized and non-immunized infants is compared, taking into consideration emergency room/outpatient attendance, hospitalization, admission to the intensive care unit, mortality and long-term respiratory morbidity for up to 18 years of age, modeled through a decision tree. Costs and QALYs are assessed in the CUA over a lifetime horizon to account fully for the long-term impact of RSV in terms of mortality and respiratory morbidity with 1.5% *per annum* discounting. Discounting accounts for a unit of money (e.g. $1 CAD) being worth more today than in the future.

Integrating wastewater detection of RSV into the CUA

The initiation of monthly government-funded RSV immunization for at-risk infants and young children cannot begin until the RSV season is officially declared, based upon clinical surveillance of RSV (CS-RSV) hospital admissions reaching a designated threshold. Our case study reported the ability to declare the RSV season start in the studied regions from 12 to 36 days in advance of that declared in the surrounding province using CS-RSV.[13] Predicated on the Ontario data, starting the RSV immunization program earlier triggered by WBS-RSV would result in 15.1% more potential episodes of severe RSV being covered (compared to CS-RSV), due to the latter initiating immunization when RSV is already circulating and causing hospitalizations.

To determine the economic significance of this additional protection afforded by earlier initiation of RSV immunization by WBS-RSV, the CUA was updated to include two parallel decision trees: one for WBS-guided RSV immunization vs no immunization; the other for CS-guided RSV immunization vs no immunization (see Figure 3). Each decision tree was identical in terms of uptake of RSV immunization (71% of eligible children immunized) and the impact of RSV disease in immunized and non-immunized infants, except that the 15.1% benefit of WBS-guided immunization was applied. The cost-effectiveness of WBS-RSV compared with CS-RSV was calculated from the differences in incremental costs and QALYs for immunization vs no immunization from the two sides of the decision tree.



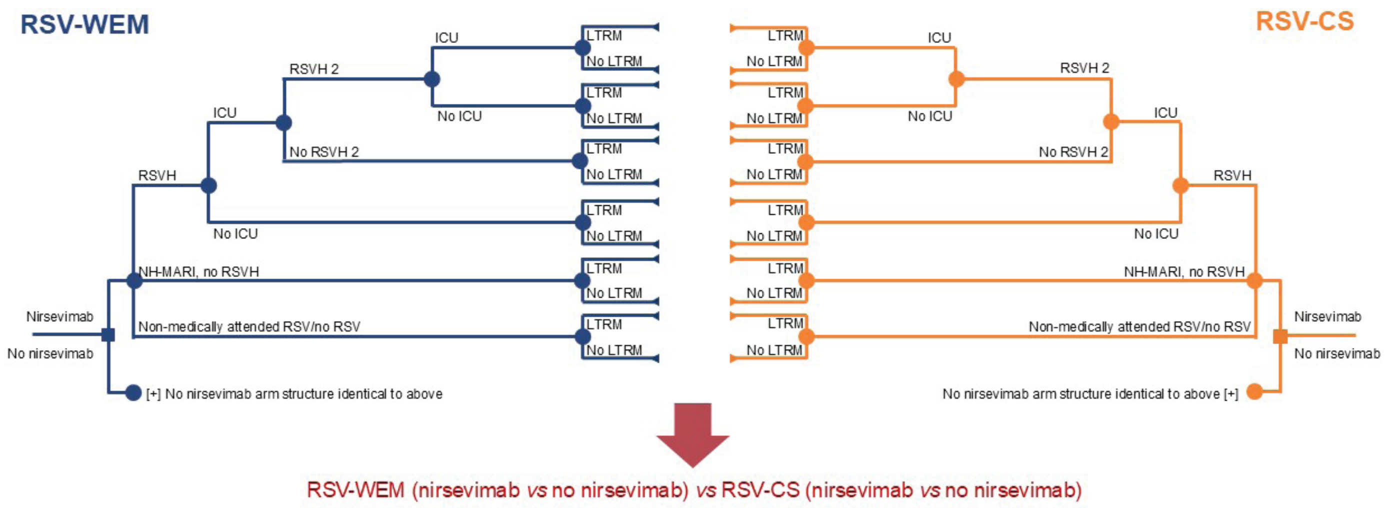


Figure 3: Decision tree describing the clinical pathway used in the model.

Abbreviations: ICU – intensive care unit | LTRM – long-term respiratory morbidity | NH-MARI – non-hospitalized medically attended RSV infection | RSVH – RSV-related hospitalization

- Nodes represent points where more than one event is possible; the square node represents the decision addressed by each side of the model.
- Branches represent the possible events that patients may experience.
- Triangles represent the decision tree endpoints.
- The cost-utility of WBS-RSV vs CS-RSV was calculated from the differences in incremental costs and utilities for immunization vs no immunization from the two sides of the decision tree.

Costing considerations for WBS-RSV

All immunization and RSV-related costs were identical for WBS-RSV and CS-RSV in the CUA. No costs were assumed for CS-RSV, whereas a cost of $12.31 CAD per infant was assumed if a new WBS-RSV system was initiated, with all infrastructure costs included in year one. To be conservative, outcomes were modeled over an 18-year time horizon with 1.5% discounting.

The results of the CUA found WBS-RSV to be a cost-saving approach over CS-RSV to guide a Canadian all-infant immunization program with nirsevimab. This means that the costs of implementing the WBS-RSV program can be offset by the savings from reducing the need for medical care. In other words, implementing WBS-RSV could be considered self-funding and represent a worthwhile investment.

Broader considerations when assessing the cost-effectiveness of WBS-RSV

Importantly, WBS-RSV was cost-saving in a range of scenario analyses, including:

- Amortization of WBS-RSV infrastructure costs over 5 years
- Using existing WBS infrastructure for RSV detection
- 25% reduction in extra cases identified by RSV-WBS
- 50%–90% immunization coverage based on real-world data
- 25% increase in the cost of RSV-WBS

Furthermore, this CUA does not take into consideration the economic and quality of life impact for families related to time off work and the stress associated with having a child hospitalized with RSV, which could be obviated to a greater extent with WBS-guided immunization than CS-guided immunization. Overall, the results of the CUA can be considered robust and reliable and support the implementation of WBS-RSV.

More accurate determination of RSV season onset and community-wide RSV activity with WBS-RSV could also help determine the effectiveness of maternal and older adult (>60 years) RSV immunization programs, and in the future, infant RSV immunization. Earlier detection of RSV activity also allows for more effective planning to mitigate the impact of seasonal RSV outbreaks by allocating appropriate and commensurate resources to alleviate workloads on healthcare systems and staff. Further, monitoring RSV trends by means of WBS can provide early insight into year-on-year seasonal variations, thereby helping healthcare providers to anticipate evolving epidemic timing, distribution and intensity.

CONCLUSION

The CUA evaluated the benefit of WBS for timing of RSV immunization by comparing its implementation costs with the associated health outcomes. The goal was to establish WBS as a sustainable and actionable public health tool, especially for intra-pandemic response and long-term preparedness. Although WBS was rapidly adopted in Canada and globally during the COVID-19 pandemic, integration with public health decision-making has lagged, in part due to the absence of robust economic evaluations that connect operational costs with health outcomes.

Despite the broader lack of WBS integration across Canada, this case study demonstrates how harmonized sampling strategies, timely data reporting and effective partnerships can enable public health action. In this analysis, the health utility gain from WBS-RSV is modeled based on improvements in timing and targeting of clinical interventions, including RSV immunization and resource allocation in pediatric care settings. For WBS to become an integral component of sustained intra-pandemic activities and proactive measures for pandemic preparedness, its cost-effectiveness must be established.[14,15] However, significant gaps remain in the current literature, as most economic evaluations focus narrowly on operational costs without addressing health outcomes or the long-term societal benefits of WBS.[16,17,18]

This CUA supports the integration of WBS-RSV into public health surveillance as a cost-effective strategy to improve respiratory disease outcomes. By linking early, population-level detection with actionable clinical and policy responses, WBS yields measurable gains in health utility while enhancing preparedness for future outbreaks.

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Canadian Water Network thanks contributing authors Robert Delatolla, Elisabeth Mercier, Barry Rodgers-Gray and John Fullarton.

For more information:
Talia Glickman, Senior Program Advisor, Canadian Water Network

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Advanced Environmental Molecular Analytics Ltd.

Contact Us

Canadian Water Network
Talia Glickman
Senior Program Advisor
Email: tglickman@cwn-rce.ca
cwn-rce.ca

National Collaborating Centre for Infectious Diseases
Rady Faculty of Health Sciences,
University of Manitoba
Tel: (204) 318-2591
Email: nccid@umanitoba.ca
www.nccid.ca

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