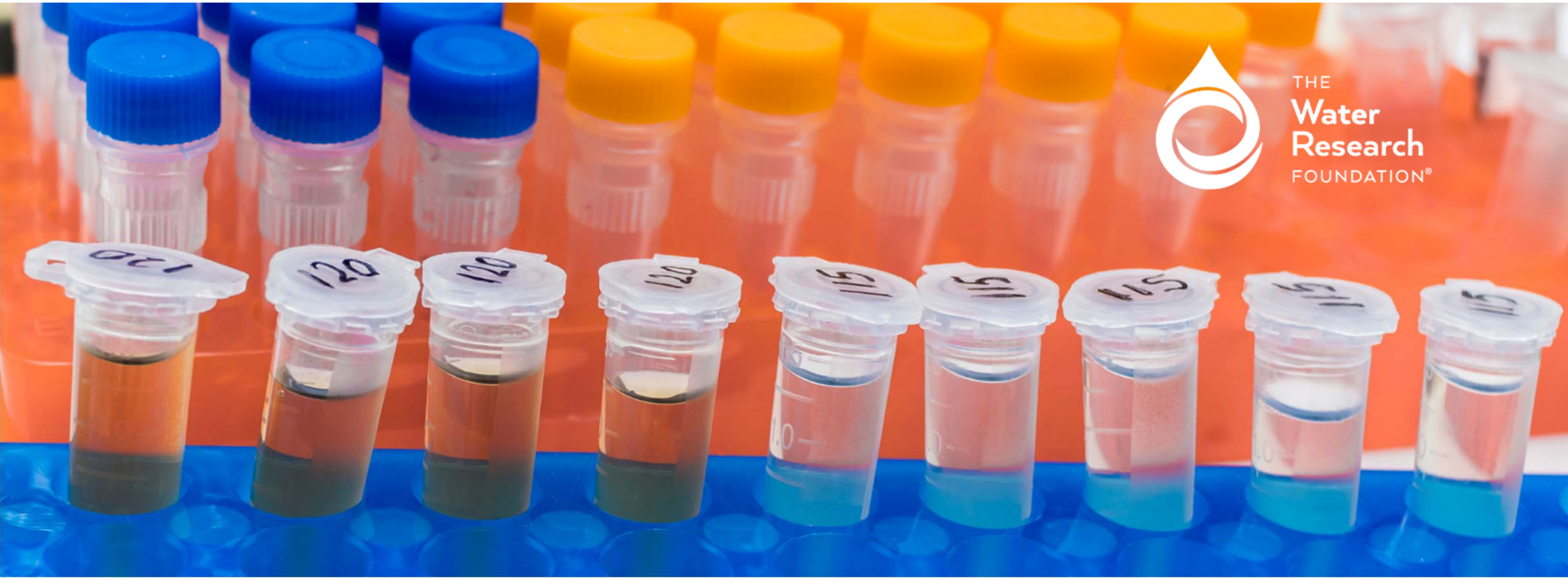


Coordination and Collaboration the fastest path to success

Christobel Ferguson, PhD – CIO, The Water Research Foundation

advancing the science of water®

Overview

Rapid Collaboration

Bringing Existing Knowledge Together

Global Application

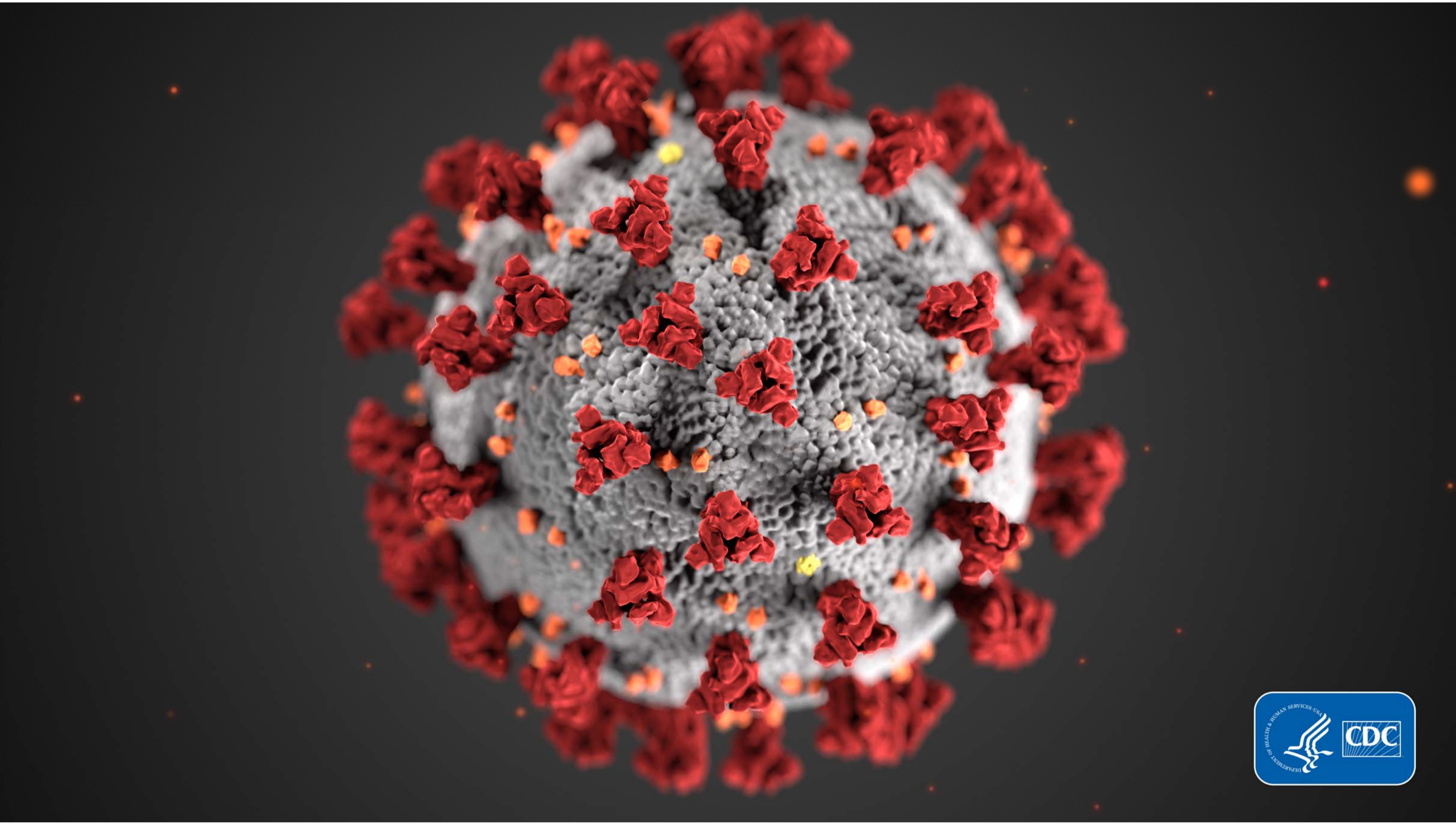
Trends, Variants, and Early Warning

Lessons Learned

Global Update

Knowledge gaps

Future Opportunities


CDC

Rapid Collaboration

Bringing existing knowledge together

AT A GLANCE – 3/31/21

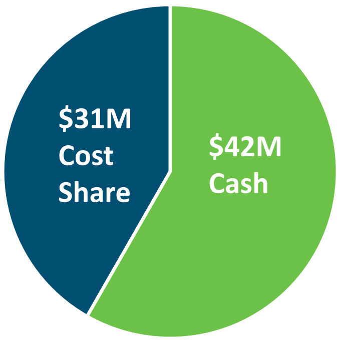
THE Water Research FOUNDATION®

Funded Research

$73M

Contractually Funded Research

Managed by 53 Staff



Research Portfolio

- **1** Federal Contracts
- **2** Private Grants
- **3** Federal/State Grants
- **77** Co-funded Projects

200 Co-funders

210 Active Projects

Subscribers

- **1040** UTILITIES
- **88** CONSULTANTS
- **40** MANUFACTURERS

Research & Innovation Programs

Research Priority	Tailored Collaboration	Emerging Opportunities
Grants/Awards *Paul L. Busch Award*	Facilitated Research	Unsolicited Research

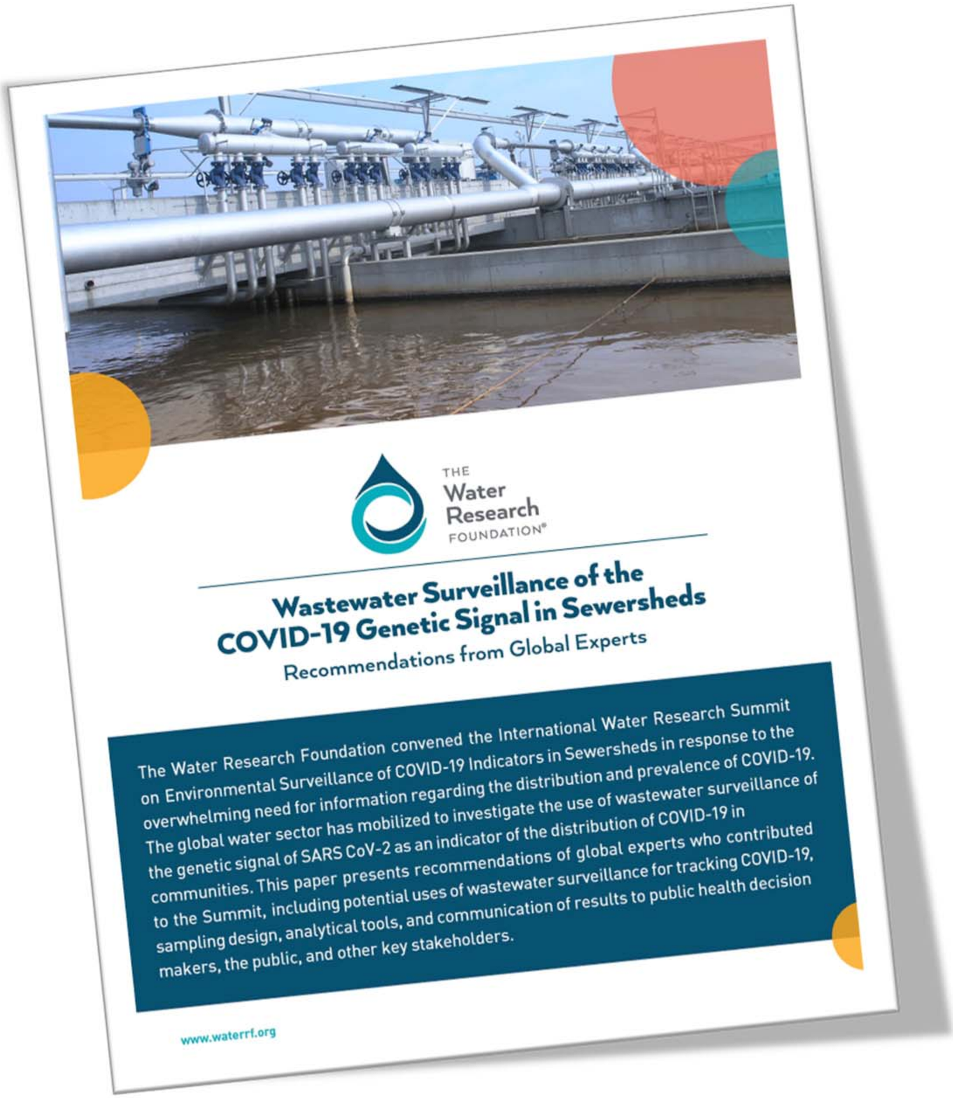
$.84 OF EVERY DOLLAR supports program services.

- **245** Average Contracts/Year
- **20** Ave. Contracts in Process/Month
- **100** Payments/Month
- **15*** Reimbursements Per Month

*not typical

Priority Research Areas to Accelerate the Pace of Progress

1. Recommended procedures for the collection and storage of wastewater samples
2. Use of tools to identify the genetic signal of SARS-CoV-2 in wastewater samples
3. Recommended approaches for the use of data on the genetic signal of SARS-CoV-2 to inform trends and estimates of community prevalence
4. Strategies to communicate the implications of wastewater surveillance results with the public health community, elected officials, wastewater workers, and the public



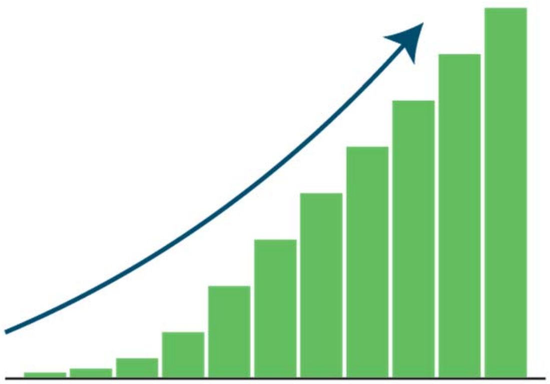
Rapid Water Sector Response & Collaboration

What Can You Use Sewershed Surveillance Data For?

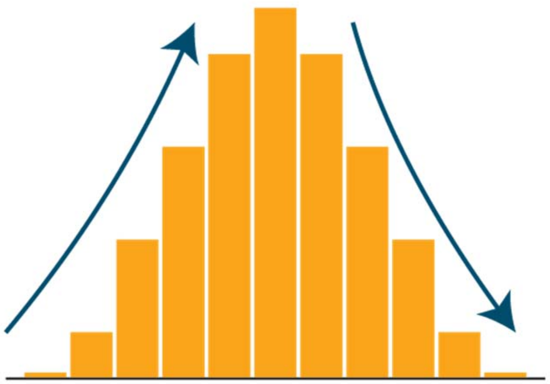
General Use Cases	Can Inform
Assess Level of Community Infection	Tracking disease prevalence in the community. Identification of “hot spots” and areas that are not impacted by the virus
Trends/Changes in Infection	Early detection of disease. Tracking the impact of medical and social interventions
Risk Assessment	Risk to utility workers and those exposed to raw sewage
Viral Evolution	Source tracking of the virus

Use Cases

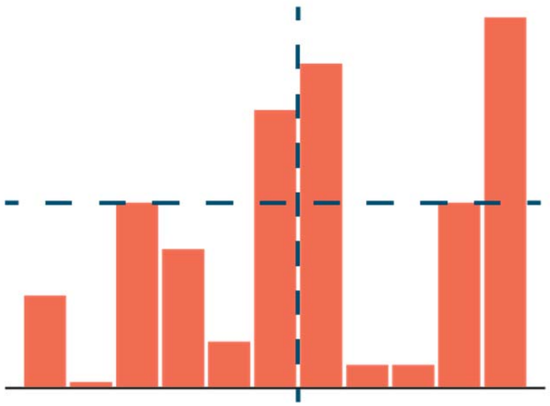
Trend Occurrence



Changes in Trends



Community Prevalence



THE Water Research FOUNDATION

WRF COVID-19 Research

- Interlaboratory and Methods Assessment of the SARS-CoV-2 Genetic Signal in Wastewater (#5089)
- Understanding the Factors that Affect the Detection and Variability of SARS-CoV-2 in Wastewater (#5093)
- Environmental Persistence and Disinfection of Lassa Virus and SARS-CoV-2 to Protect Worker and Public Safety (#5029)
- NSF Research Coordination Network on SARS-CoV-2 wastewater surveillance (awarded)

ADD-ONS TO PROJECTS ALREADY UNDERWAY THROUGH A GRANT FROM CALIFORNIA STATE WATER BOARD

Measuring Pathogens in Wastewater (#4989 & #4952)

SARS-CoV-2 added to list of organisms of concern; research team is investigating the feasibility of analyzing SARS-CoV-2 in samples archived since Nov. 2019 and going forward

Collecting Pathogens in Wastewater During Outbreaks (#4990)

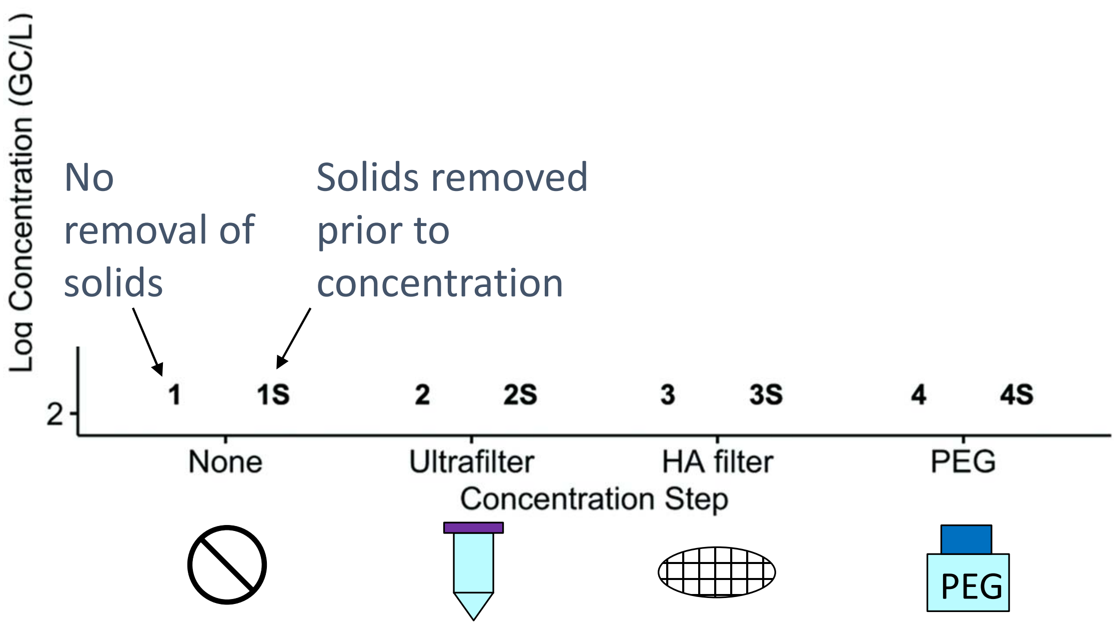
Added coronavirus to the list of organisms of concern

Interlaboratory and Methods Assessment of the SARS-CoV-2 Genetic Signal (5089)

Study included 32 US Labs and evaluated 36 independent methods
Experimental Plan and QAPP – liaised with Canadian Water Network to compare approaches
Wastewater Sampling and Interlaboratory Analysis (Aug 17-28, 2020) Webcast
Environmental Science: Water Research & Technology ***Science of the Total Environment***
Method SOPs and QAP available on the WRF website

Reproducibility within a method group

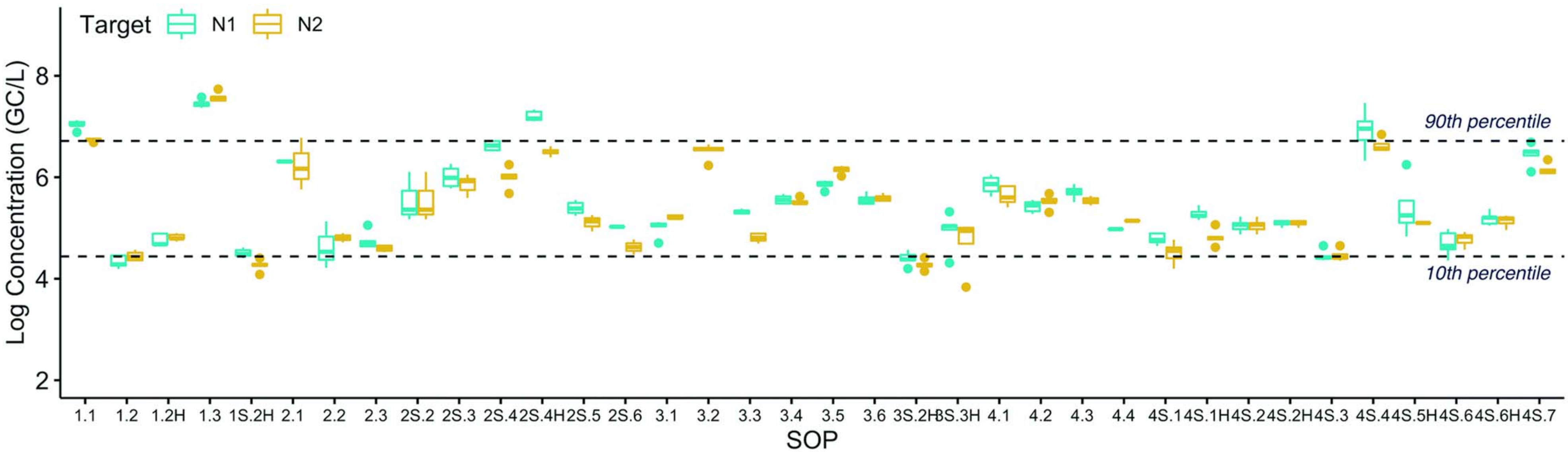
Eight method groups based on solids removal and concentration step



Pecson et al., 2021

Reproducibility across methods after QA/QC filter

With Recovery Correction



Conclusions:

- *Across all groups, 80% of the values fall within +/- 1-log range*

Pecson et al., 2021

Reproducibility within an SOP

- Precision evaluated based on variability in replicates run for each method

	Standard deviation of replicates (in log GC/L)	
SARS-CoV-2 Target	Uncorrected	Recovery-Corrected
N1	**0.15** [0.04 – 0.38]	**0.13** [0.032 – 0.60]
N2	**0.14** [0.01 – 0.53]	**0.13** [0.033 – 0.51]

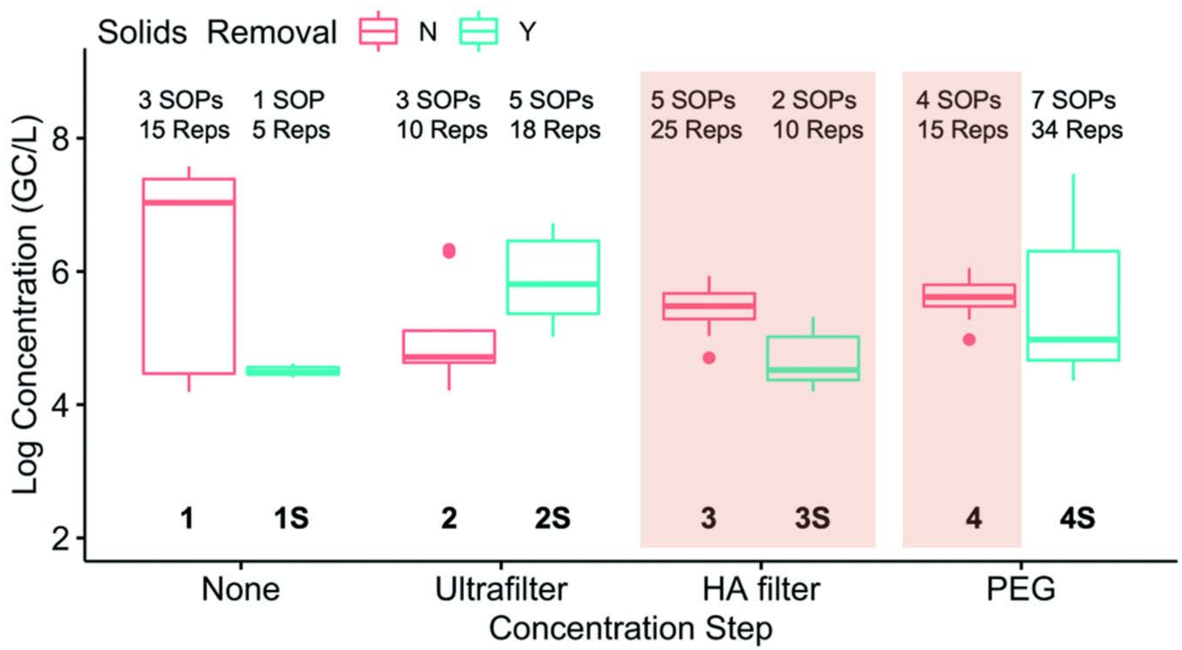
Conclusions:

- Precision within a lab is high based on ~5 replicates
- Higher precision makes it easier to identify differences in raw wastewater concentrations over time

Pecson et al., 2021

Reproducibility within a method group

Eight method groups based on solids removal and concentration step



Conclusions:

- *Correcting for recovery generally brings the concentration methods in line with no-concentration methods*
- *No systematic impact from solids removal step*
- ***Groups 3, 3S, and 4 had the greatest reproducibility***

Pecson et al., 2021

Conclusions from the Interlaboratory Comparison #5089

- Nationwide interlaboratory method comparison showed high reproducibility
  - Multiple methods may be used to obtain reproducible results
  - The same SOP or lab should be used to track trends at a given location
- Quality assurance plans are critical for reproducibility
  - Recovery efficiencies varied by 7 orders of magnitude
  - Matrix spikes critical to quantify recovery and obtain reproducible numbers
- Study showed no systematic impact from key differences between methods
  - Minimal impact of solids removal, concentration, pasteurization, primer selection
- Findings support use of wastewater surveillance for tracking trends
  - Methods with higher sensitivity allow tracking over a wider range of concentrations

Pecson et al., 2021

Next Steps

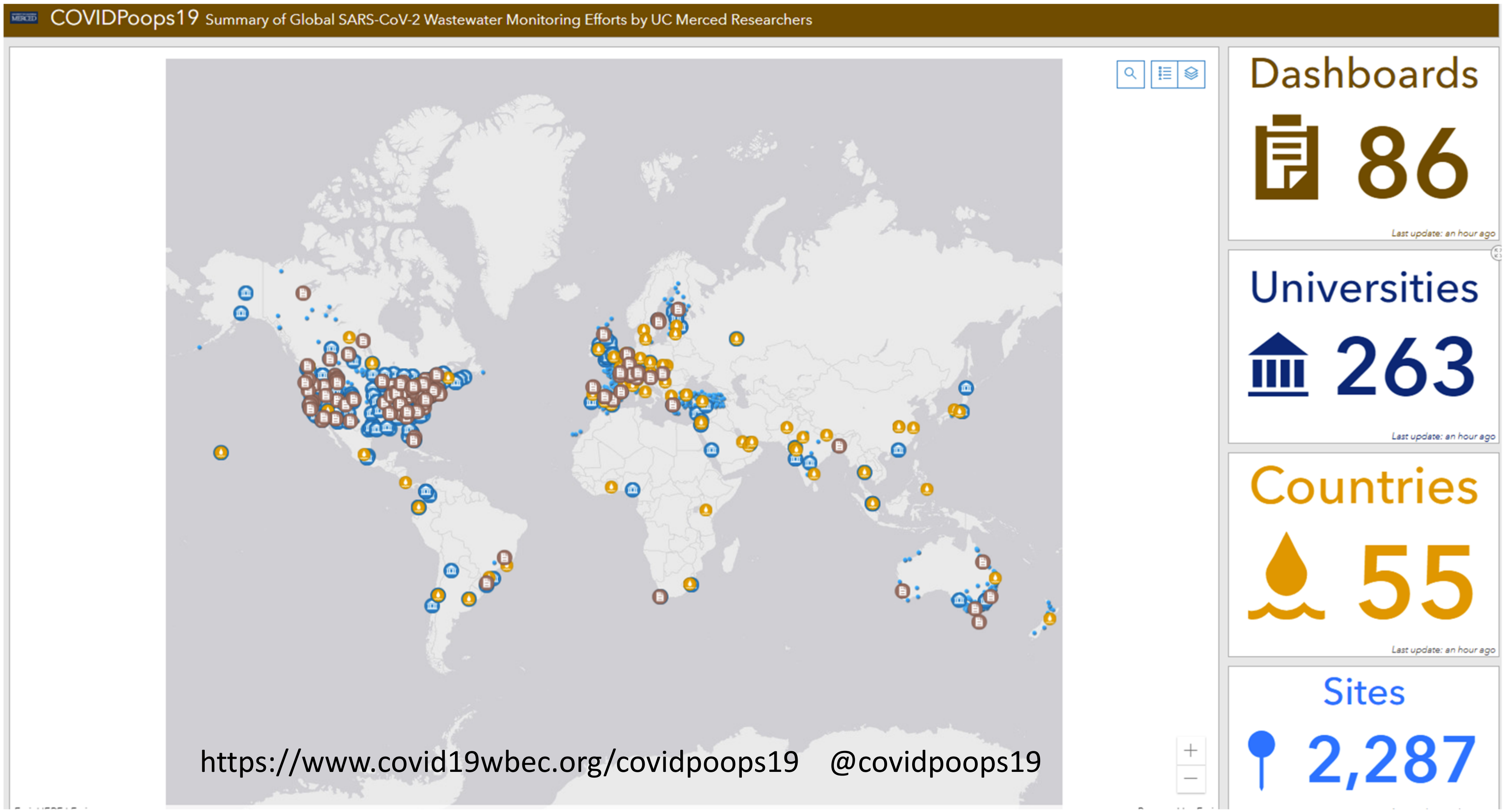
- Additional criteria should be used to select the “best” method for your application
  - Sensitivity
  - Cost
  - Operator experience
  - Material requirements
  - Throughput or processing time
- Address other knowledge gaps for wastewater-based epidemiology
- Continued coordination on methods is encouraged

Pecson et al., 2021

Rapid Global Response & Collaboration

- USA
  - DHS and CDC Project with AquaVitas
  - CDC National Wastewater Surveillance System
  - Biobot
  - US EPA Research with Cincinnati Ohio
- Canada – Canadian Water Network Method Evaluation
- Australia
  - Water Research Australia ColoSSuS project
- South Africa - WRC Pilot Projects on method development
- EU - European Health Emergency Preparedness and Response Authority (HERA)

Implementation across the globe



Global Application

Trends, Variants and Early Warning

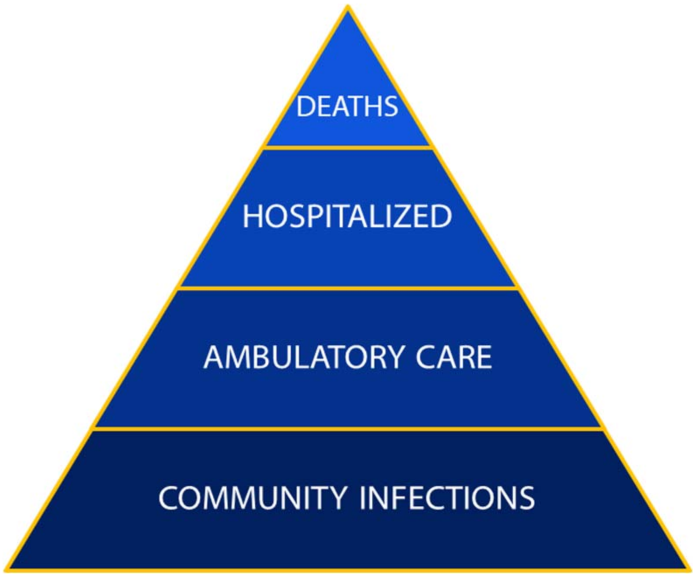
Selecting the approach that meets the community need.

Use of Wastewater Data in Response Decisions

Wastewater data can complement case- and symptom-based surveillance by providing-

- ✓ Independent confirmation of true increases or decreases in cases
- ✓ Infection data for communities where clinical testing data are not available
- ✓ Case or hospital utilization forecasting

✘ Wastewater should not be used to estimate point prevalence or case counts



Amy Kirby, CDC, 2021

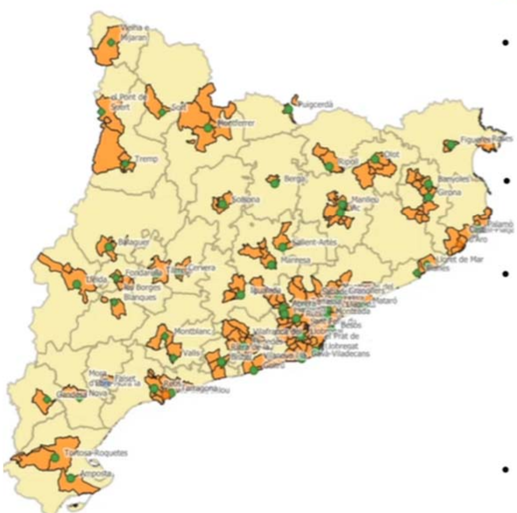
Wastewater Surveillance | Public Health Toolbox

- Captures sub-clinical infections
- Independent of healthcare-seeking behavior and testing access
- Wastewater serves as an efficient pooled sample of community (or sub-community) infection levels
- Data available within days of viral shedding onset versus up to 2-week lag for other surveillance data

Amy Kirby, CDC, 2021

Trends

Activity



On-going since July 2020

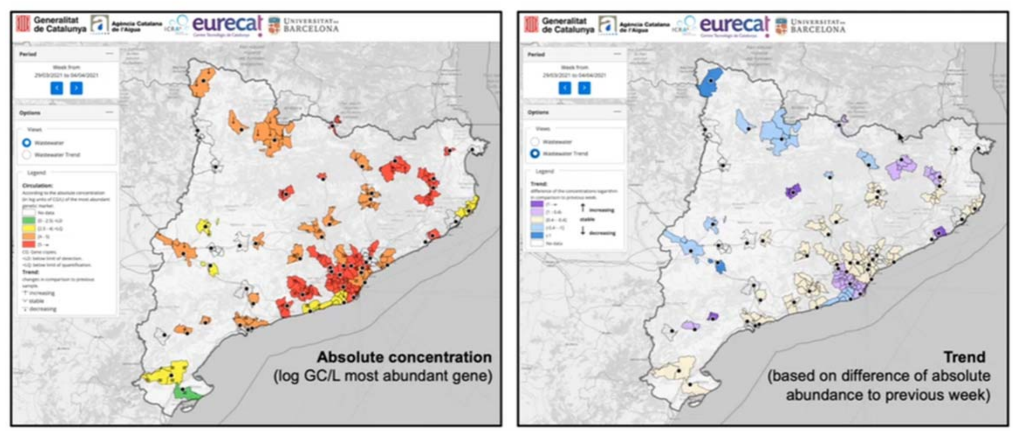
Sampling strategy, frequency and analysis

- A total of **56 WWTPs** selected based on two criteria:
  - *80% coverage of served population*
  - *Territorial evenness* (41 out of 42 regions)
- **Sampling frequency** 36 WWTPs weekly & 18 WWTPs fortnightly
- **Sample collection and analysis**
  - Collecting flow-proportional, 24h-composite (every 20min) INLET samples
  - Shipment and distribution to the labs
  - Results within 48 hours
- **Quantification of three gene targets**
  - N1 (*N* gene)
  - N2 (*N* gene)
  - IP4 (*RdRp* gene)

Borrego, Collado, Corominas, Guerrero & Pueyo
Catalan Surveillance Network, 2021

Visualization dashboard

https://sarsaigua.icra.cat



RT-qPCR analytical method
Overview

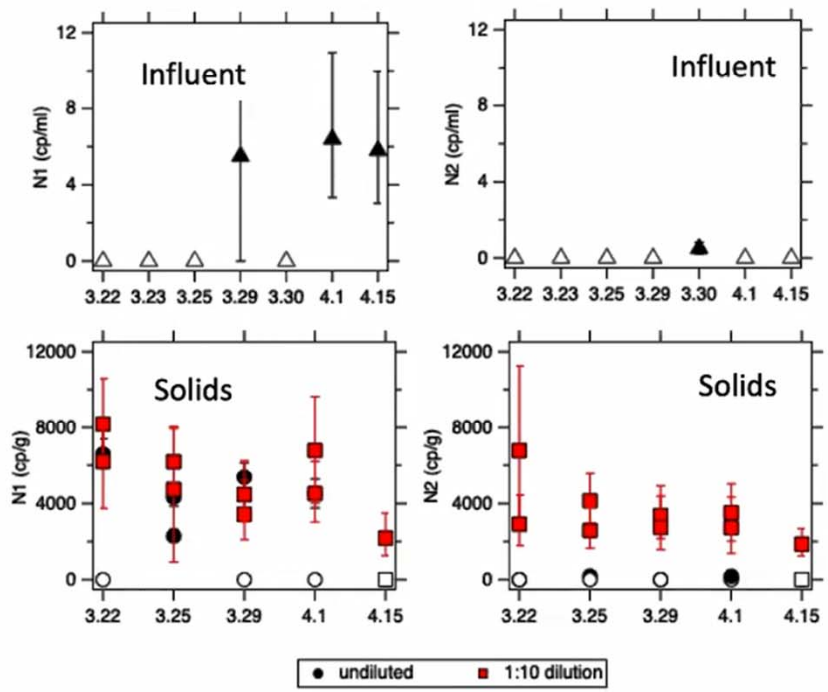
		Concentration	Extraction	Genetic Ta
	Veolia Lazuka *et al.* (submitted)	Ultrafiltration	Silica spin column filter or Magnetic silica beads	N1[1], N2[1], E[2]
	KWR Medema et al. (2020)	Clarification using centrifugation + Ultrafiltration	Silica spin column	N1[1], N2[1], E[2]
French National Network Obépine	Eaux de Paris Wurtzer *et al.* (2020)	Ultracentrifugation	Silica spin column filter	
	CNRS-LCPME Bertrand *et al.* (2020)	Ultrafiltration	Magnetic silica beads	N1[1], N2[1], E[2], RdRp (IP2 & IP4)[3]
	CNRS-LCPME Bertrand *et al.* (2020)	Desorption + Precipitation PEG	Magnetic silica beads	

[1] US CDC; [2] Corman et al. 2020, [3] Centre National de Référence des virus des infections Respiratoires, Institut Pasteur, Paris

- Viral **recovery yield was 5.5 % +/- 0.5%** using heat-inactivated SARS-CoV-2.
- **N1** appeared to be the **most sensitive** biomarker.
- Protocol is **operational, quick and easy to implement**

Lazuka, Soyeux & Lacroix, Veolia, France, 2021

We detected more positive signals by extracting directly from primary solids than with a PEG-based influent method.



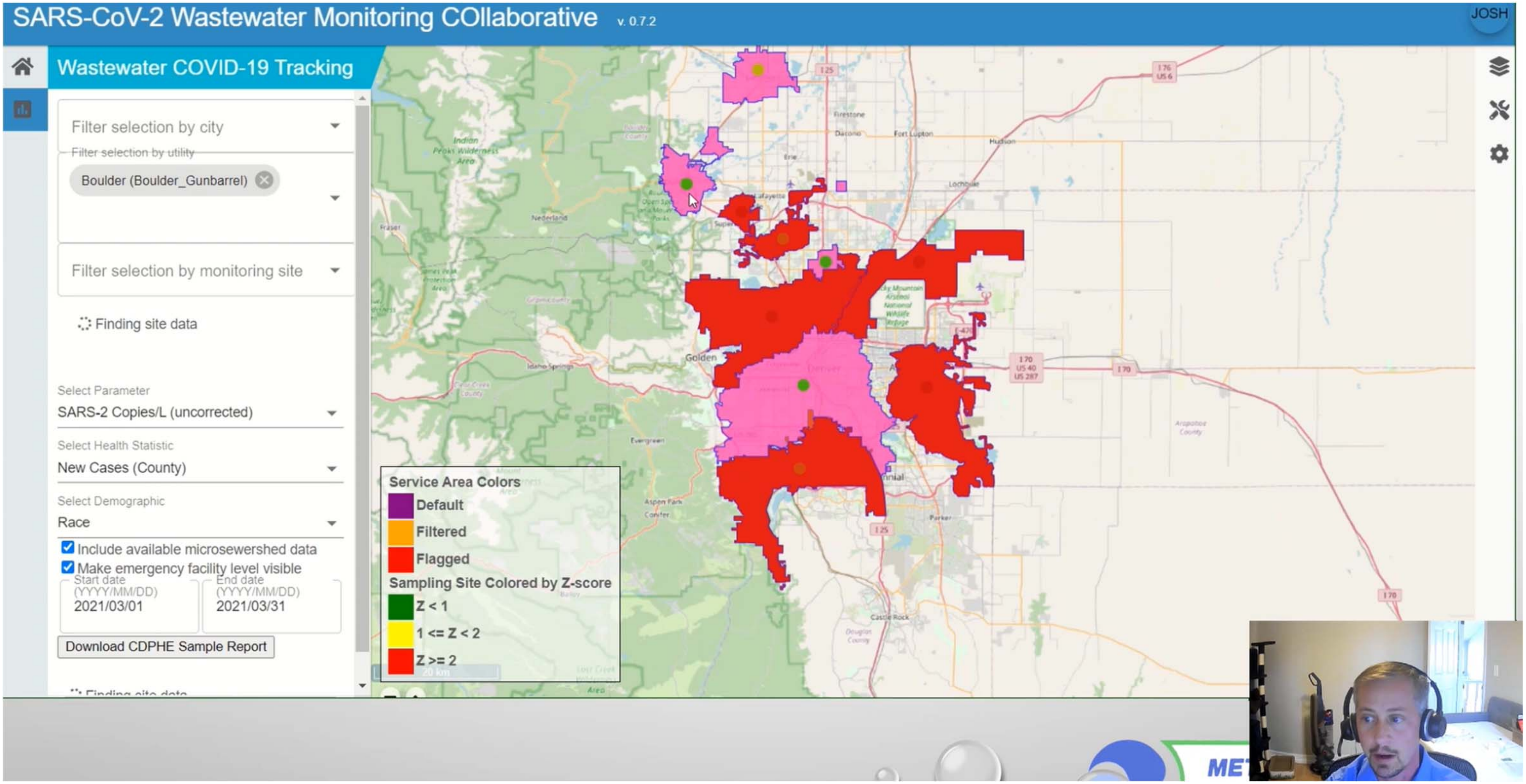
- Limited variation among replicates
- Inhibition an issue for some samples

SARS-CoV-2 RNA in Wastewater Settled Solids Is Associated with COVID-19 Cases in a Large Urban Sewershed

Katherine E. Graham, Stephanie K. Loeb, Marlene K. Wolfe, David Catoe, Nasa Sinnott-Armstrong, Sooyeol Kim, Kevan M. Yamahara, Lauren M. Sassoubre, Lorelay M. Mendoza Grijalva, Laura Roldan-Hernandez, Kathryn Langenfeld, Krista R. Wigginton,* and Alexandria B. Boehm*

Graham, et al. Environmental science & technology (2020) 55, 1, 488–498.

Krista Wigginton, University of Michigan, California, USA 2021



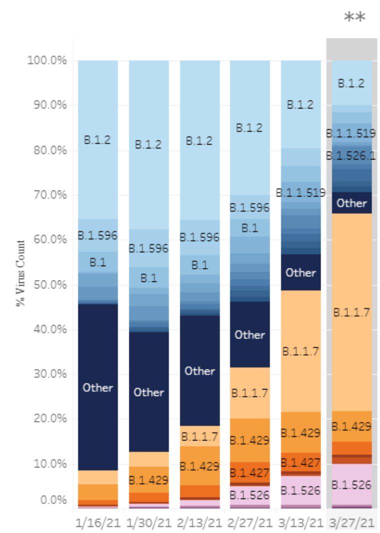
Goldman-Torres, Werth & Fielder, Colorado, USA2021

Variants

- Interpretation is limited by fragmented genomes and unknown method sensitivity
- May be useful for variant **detection** and **tracking** but unlikely to be useful for variant discovery
- Funding evaluation studies to assess public health interpretation and use
- Working with NCBI to establish database and analysis pipeline for wastewater SARS-CoV-2 sequence data

SARS-CoV-2 Variants Circulating in the United States

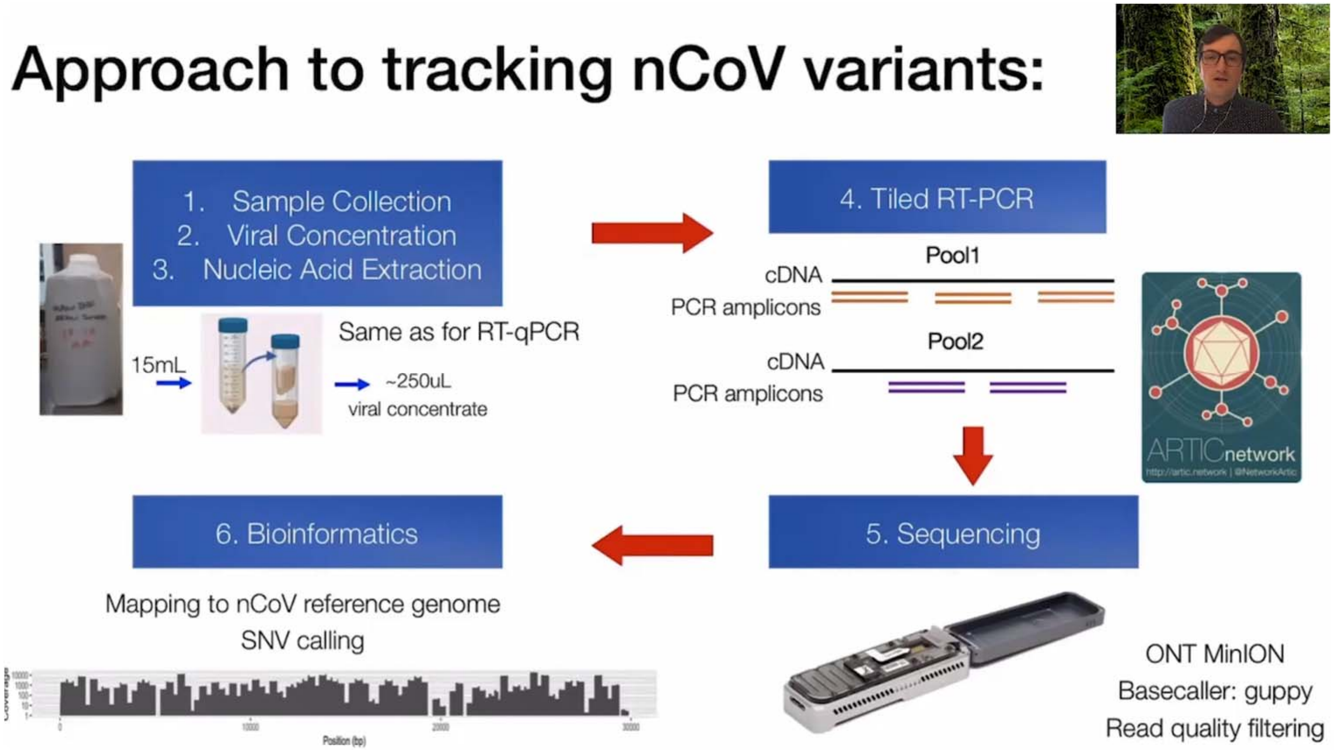
SARS-CoV-2 Variants Circulating in the United States, January 3 – March 27 2021

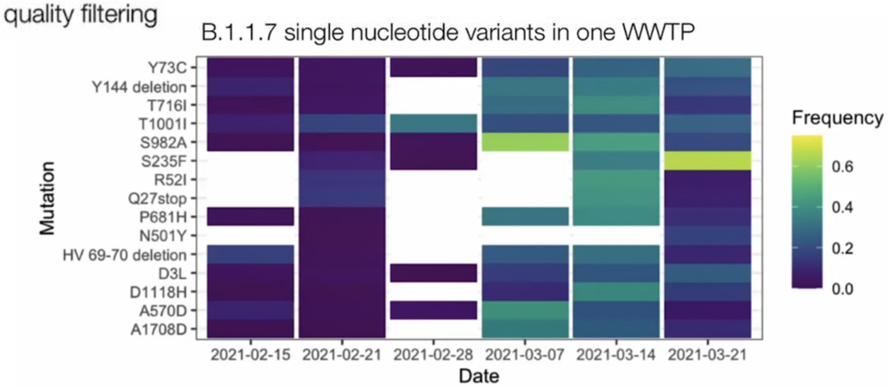


	Lineage	% Total	95%CI	Type
Most common lineages	B.1.1.7	44.1%	41.2-47.1%	VOC
	B.1.2	10.0%	8.9-11.2%	
	B.1.526	9.2%	7.2-11.7%	VOI
	B.1.429	6.9%	5.1-9.4%	VOC
	B.1.1.519	4.1%	3.4-5.0%	
	B.1.526.1	3.9%	3.3-4.7%	
	B.1.526.2	2.9%	2.3-3.8%	
	B.1.427	2.9%	2.2-3.9%	VOC
	B.1	2.4%	2.0-3.0%	
	B.1.596	1.7%	1.3-2.1%	
	P.1	1.4%	1.0-1.8%	VOC
	R.1	1.2%	0.8-1.6%	
	B.1.575	1.1%	0.9-1.5%	
	B.1.1	0.9%	0.6-1.5%	
	B.1.243	0.6%	0.4-1.0%	
	B.1.234	0.5%	0.3-0.7%	
Additional VOI/VOC lineages	B.1.351	0.7%	0.5-1.0%	VOC
	B.1.525	0.5%	0.3-0.7%	VOI
	P.2	0.3%	0.2-0.4%	VOI
Other*	Other	4.7%	4.1-5.4%	

Summary data that appear in the table include specimen collection dates from March 14 through March 27, 2021.
* Other represents >200 additional lineages, which are each circulating at <1% of viruses
** Most recent data (shaded) are subject to change as samples from that period are still being processed.

Amy Kirby, CDC, 2021

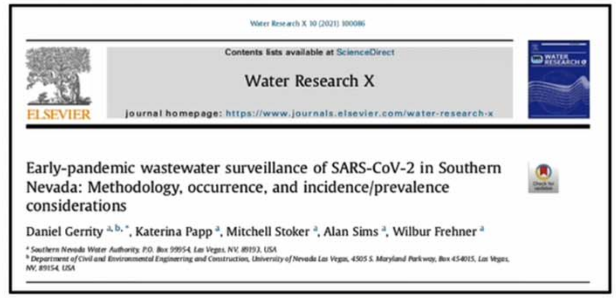




Ryan Ziels, University of British Colombia, British Colombia, Canada 2021

Southern Nevada Wastewater Surveillance

- **No hits in treated wastewater or local drinking water supply**
- **Wastewater influent samples collected weekly**
  - 1 site since March 2020 (100 mgd and 872k people)
  - 1 site since April 2020 (5 mgd and 86k people)
  - 4 sites since August 2020 (6-40 mgd and 115k-757k people)
  - 1 site since December 2020 (0.8 mgd and 16k people)
  - UK variant of concern (B.1.1.7) detected in wastewater prior to clinical confirmation
- **Short-term monitoring of a homeless shelter manhole**
  - 4 weekly samples from Late November – Early December (all positive)
  - Sampling coincidentally occurred during facility-wide outbreak
  - California variant of concern (B.1.427/429) detected in final sample
- **Participated in WRF round robin methods comparison**



Water Research X 10 (2021) 100086

Contents lists available at ScienceDirect

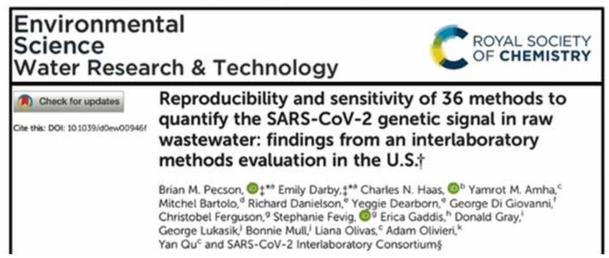
Water Research X

journal homepage: https://www.journals.elsevier.com/water-research-x

Early-pandemic wastewater surveillance of SARS-CoV-2 in Southern Nevada: Methodology, occurrence, and incidence/prevalence considerations

Daniel Gerrity [a,b,*], Katerina Papp [a], Mitchell Stoker [a], Alan Sims [a], Wilbur Frehner [a]

[a] Southern Nevada Water Authority, P.O. Box 99954, Las Vegas, NV, 89193, USA
[b] Department of Civil and Environmental Engineering and Construction, University of Nevada Las Vegas, 4505 S. Maryland Parkway, Box 454015, Las Vegas, NV, 89154, USA



Environmental Science Water Research & Technology

ROYAL SOCIETY OF CHEMISTRY

Check for updates

Cite this: DOI: 10.1039/d0ew00946f

Reproducibility and sensitivity of 36 methods to quantify the SARS-CoV-2 genetic signal in raw wastewater: findings from an interlaboratory methods evaluation in the U.S.†

Brian M. Pecson, ‡*[a] Emily Darby, ‡*[a] Charles N. Haas, [b] Yamrot M. Amha, [c] Mitchel Bartolo, [d] Richard Danielson, [e] Yeggie Dearborn, [e] George Di Giovanni, [f] Christobel Ferguson, [g] Stephanie Fevig, [g] Erica Gaddis, [h] Donald Gray, [i] George Lukasik, [j] Bonnie Mull, [j] Liana Olivas, [c] Adam Olivieri, [k] Yan Qu [c] and SARS-CoV-2 Interlaboratory Consortium§

Daniel Gerrity, Southern Nevada Water Authority, Nevada, USA 2021

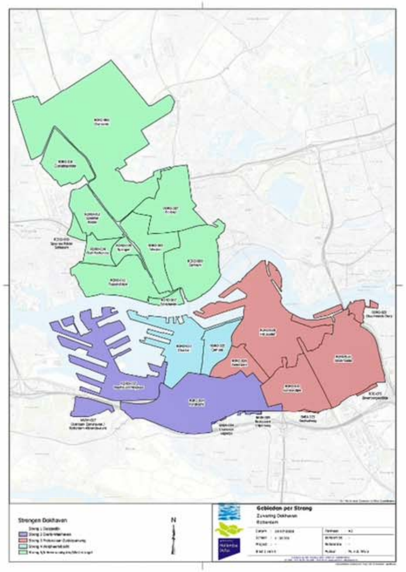
City of Rotterdam

KWR

Below ground

Above ground

- 2 WWTP
  - Including 4 individual influents
- 4 pumping stations (neighbourhoods)
- Sampling since August 2020



- Patient testing in same catchments
- Metadata collection
- Faecal samples for viral shedding and sequencing

TOPSECTOR WATER & MARITIEM 2

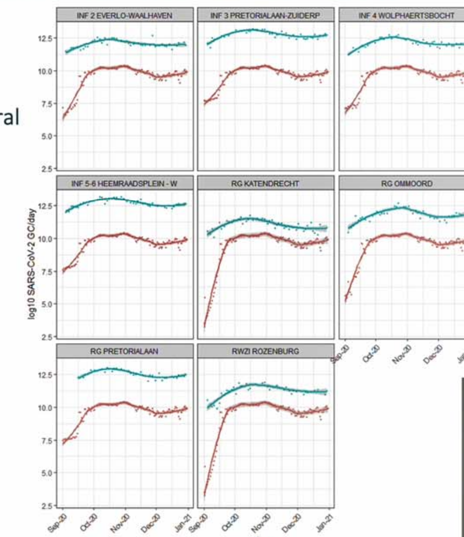
Optimize shedding parameters to ”fit” wastewater observations

KWR

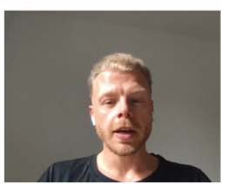
- Use Monte Carlo simulations and kinetic models to derive (estimates) of realistic viral shedding

Goals:

- Observed trends
- Early warning
- Link with what happens above ground
- Incidence estimation



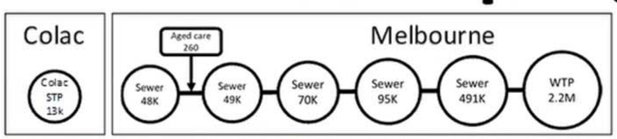
TOPSECTOR WATER & MARITIEM 8



Frederic Beén, KWR Water Research Institute, Netherlands 2021

Early Warning

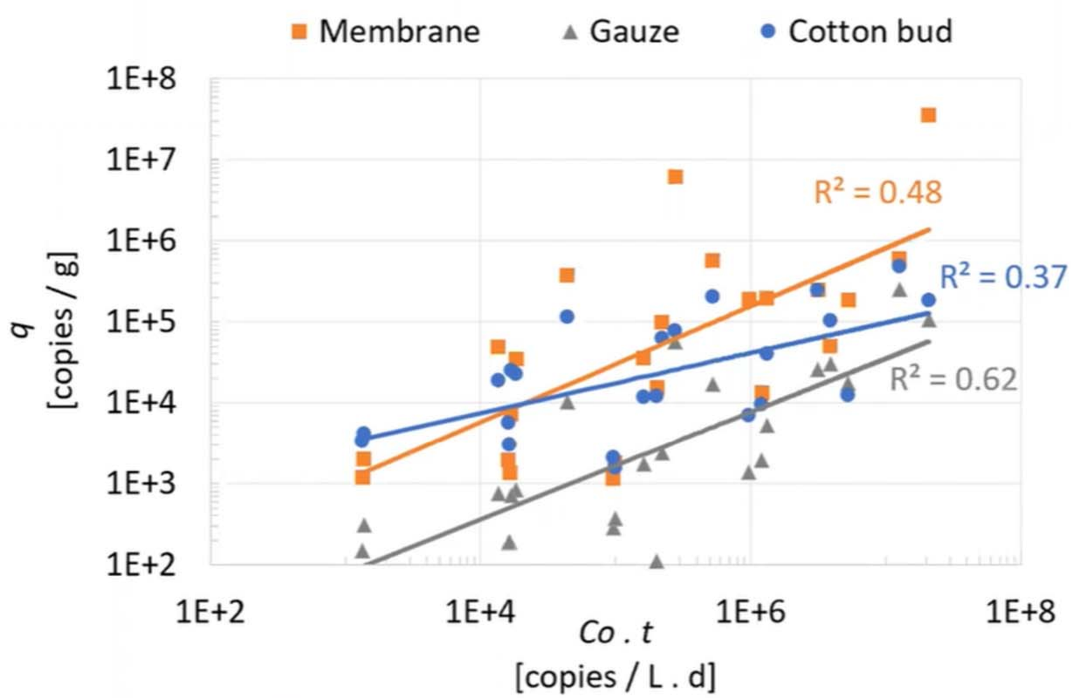
Passive sampling of SARS-CoV-2 in Wastewater: field



- Passive samplers had detection on 100% of days when wastewater concentrations were > DL
- Passive samplers detected SARS-CoV-2 on another 50% of occasions even though WW conc. < DL

McCarthy, Crosbie, Poon & Nolan, Monash Uni, Australia, 2021

Passive sampling of SARS-CoV-2 in Wastewater: lab



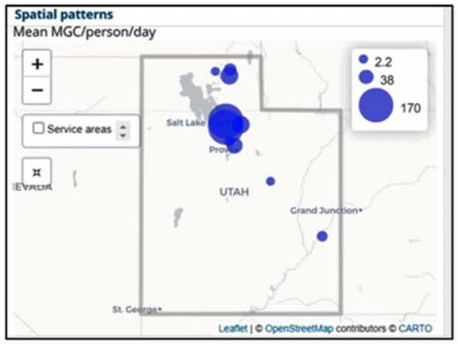
McCarthy, Crosbie, Poon & Nolan, Monash Uni, Australia, 2021

Utah Surveillance Program (wastewatervirus.utah.edu)

Phase I: Proof of concept
March 23 to April 6, 2020

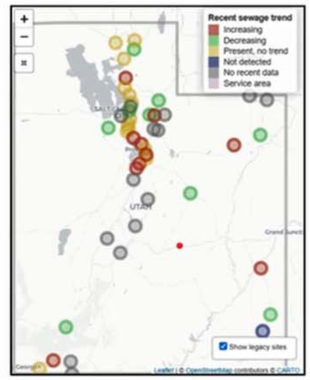
- 2 facilities sampled daily for two weeks (17% population)
- U of U
- Urban center & ski location
- U of U seed funding

Phase II: Pilot
April 13 to May 24, 2020



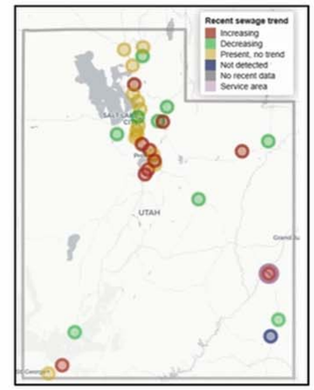
- 10 facilities sampled weekly (39% population)
- U of U, BYU, USU
- Urban centers, tourist locations and rural areas
- Weidhaas, et al. 2021, Sci Total Env, 775: 145790
- DEQ seed funding

Phase III: Monitoring
May 24 to Dec 31, 2020

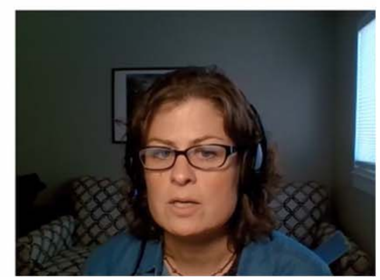


- 43 facilities sampled weekly (87% population)
- U of U, BYU, USU, Soft Cell Bio
- CARES act funding

Phase IV: Optimization
Jan 1, 2021 to current



- 32 facilities sampled bi-weekly (86% population)
- UDOH/CDC funding



~2500 samples processed for Utah environmental surveillance to date

Roper and Weidhaas, Utah State University and University of Utalh, Utah, USA 2021

Results of Utah State University (USU) monitoring wastewater on campus

“Our actions have ‘protected our community from wider spread infections’.”

Utah State Univ. **President Noelle Cockett quoting *Bear River Health Director* Lloyd Berentzen**

Informed USU – BRHD interventions

- ❑ Quarantine + required testing (4 dorms)
- ❑ E-mail advisories (specific housing areas)
- ❑ Targeted directives to test (hot spots)
- ❑ Deployment of mobile testing unit

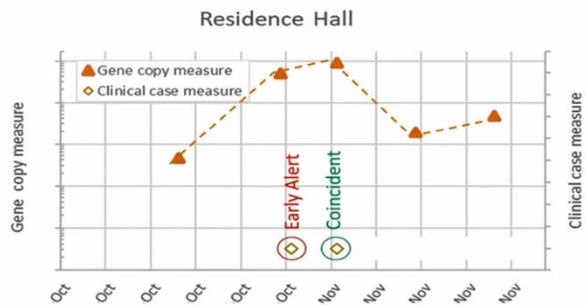
Validated actions

- ❑ Reduced clinical cases in monitored dorms
- ❑ Identified clusters (specific housing areas)
- ❑ Monitored isolated cases & quarantines
- ❑ Feedback & guidance to contact tracing

Improved Fall 2020 to Spring 2021

	Fall 2020 *Oct 21-Nov 20*	Spring 2021 *Jan 14-Feb 12*
Living areas	11	11
Samples/wk	18	30
Early Alert (%)	44	78
Coincident (%)	5	5

https://www.usu.edu/today/story/usu-biological-engineers-monitor-coronavirus-in-sewage



Roper and Weidhaas, Utah State University and University of Utah, Utah, USA 2021

Lessons Learned

Global Update

Innovation through Collaboration

Method Status

- By April 2021 approx 50% of survey respondents were using WBE with recovery controls to track trends and ~60% of those were using Bovine CoV, with human OC43 next most common*
- Most results are not adjusted for recovery efficacy*
- Most groups use at least one of the CDC N gene primers
- Groups needing high throughput and short TAT are using ddPCR
- Many WBE programs are using commercially available kits
- Passive samplers are being used to detect low levels and/or to capture infrequent events to "monitor" for hotspots

*Zhou et al, 2021

Lessons Learned - Methods

- Can reliably detect trends in infection (up and down)
- Provides early warning of increased infections (KWR & CDC ~ 6 days)
- Objective population surveillance, independent of human test behavior
- Feasible for emergence of variants (signature mutations of)
- Fast (ddPCR within days, compared to 3-4 weeks for clinical surveillance)
- Efficient: on population sample, allowing cost-effective, high-resolution surveillance
- Population size affects sewer signal dynamics (smaller populations – more variability)*
- Sites will have different requirements and constraints during selection of methods

* Medema, KWR, Netherlands, 2021

Lessons Learned – Health Decisions

- Decentralized wastewater systems difficult to capture
  - ~25% of US residences are not connected to sewer
  - Onsite treatment increasingly common at correctional facilities, universities
- Negative results do not indicate absence of cases
- Low incidence may be below the limit of detection
- Cannot be used to “clear” a community or facility
- May be impacted by pre-treatment of sewage for odor or worker safety

Amy Kirby, CDC, 2021

Knowledge gaps

Future Opportunities

Continuing Wastewater Based Health Surveillance

Realizing the Potential of Sewershed Surveillance

- Sewershed surveillance can complement clinical data for community assessments or decision making
- Provides a leading indicator of community infection
- The work continues to be rapidly developing
- Different methods and approaches are used to inform health decisions depending on the phase of the epidemic
- Other health indicators can also be easily monitored

Use Cases of Sewershed Surveillance for Other Viruses

Poliovirus

- absence of virus circulation in (unvaccinated) population
- early warning outbreaks

Adenovirus, norovirus, rotavirus, parechovirus, enterovirus, astroviruses, hepatitis A and E viruses

- early warning outbreaks
- virus circulation in population
- virus genotypes circulating in population

REVIEW ARTICLE

Role of environmental poliovirus surveillance in global polio eradication and beyond

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AEM

Detection of Pathogenic Viruses in Sewage Provided Early Warnings of Hepatitis A Virus and Norovirus Outbreaks

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Research article Open Access

Monitoring human enteric viruses in wastewater and relevance to infections encountered in the clinical setting: a one-year experiment in central France, 2014 to 2015

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Maxime Bisseux[1,2], Jonathan Colombet[1], Audrey Mirand[1,2], Anne-Marie Roque-Afonso[3], Florence Abravanel[4], Jacques Izopet[4], Christine Archimbaud[1,2], Hélène Peigue-Lafeuille[1,2], Didier Debroas[1], Jean-Luc Bailly[1], Cécile Henquell[1,2]

Research Needs

- Define ways to account for factors that impact interpretation at different scales and across different methodologies
- Improve TAT for real-time management of early warning use case
- Increased sensitivity to detect decreases in levels as case loads decline and to pick up hot spots for early warning
- Standardization of internal controls and reporting – should signal results be adjusted for recovery or not?
- Assess the applicability and health benefit of using wastewater surveillance to monitor community health for other pathogens and health indices


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