Wastewater-based variant tracking for SARS-CoV-2

COVID-19 Genomic Epidemiology Toolkit: Module 2.7

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cdc.gov/coronavirus
Part 1: Introduction
1.1 What is genomic epidemiology?
1.2 The SARS-CoV-2 genome
1.3 How to read phylogenetic trees
1.4 Emerging variants of SARS-CoV-2

Part 2: Case Studies
2.1 SARS-CoV-2 sequencing in Arizona
2.2 Healthcare cluster transmission
2.3 Community transmission
2.4 Superspreading event
2.5 Confirming reinfection
2.6 Detecting & prioritizing variants
2.7 Wastewater-based variant tracking

Part 3: Implementation
3.1 Getting started with Nextstrain
3.2 Getting started with MicrobeTrace
3.3 Phylogenetics with UShER
3.4 Walking through NextStrain trees
3.5 Public genome repositories
3.6 Sequencing strategies
**Wastewater surveillance** - Strategic sampling and testing for pathogens or other health targets in wastewater to better understand disease burden within a community.
Advantages of SARS-CoV-2 wastewater surveillance

- Efficient, pooled sample representing hundreds or millions of people
  - Sampling within collection network for added granularity

- Independent of healthcare-seeking behavior or access
  - Captures symptomatic and asymptomatic infections

- Fast, community-level measure of infection burden
  - Results in 5-7 days vs 2 weeks for clinical case counts, hospitalizations
CDC National Wastewater Surveillance System

Website resources:
- Program overview
- Sampling strategies
- Testing methods
- Data reporting, analytics
- Data interpretation for public health action
- Targeted wastewater surveillance
- Low-resource wastewater system
- Limitations

www.cdc.gov/healthywater/surveillance/wastewater-surveillance/wastewater-surveillance.html
Burlington, VT wastewater surveillance

- In summer 2020, city officials had two main concerns:
  - Potential rise in caseloads as school resumed and college students return to campus from across the United States
    - University of Vermont students make up >20% of the local population
  - Lack of equitable access to limited testing resources
    - Potential lag in case identification, particularly among vulnerable groups

- Relative low-cost to implement, minimal staff time
Burlington, VT wastewater surveillance design

- Wastewater collection system separated into sewersheds of three treatment plants:
  - North, East, Main
  - Baseline sampling 2x per week
- Sub-sewershed sampling locations within Main (3), North (2) catchment areas
- All samples collected as 24hr composites due to normal flow variation
- Overnight shipment to commercial laboratory for droplet digital RT-PCR testing of N1 region
- Turnaround time: 2 days
Burlington, VT wastewater surveillance evaluation

- Scenarios in consultation with Vermont Department of Health (VT DOH):
  1. Initial non-detection
  2. Sustained non-detection + low clinical case reporting, similar rate as August 2020
  3. Sustained non-detection + high clinical case reporting, 5-10x higher (termination)
  4. Low detection at wastewater treatment plant(s)
  5. Initial high detection at wastewater treatment plant(s)
  6. Increasing concentration for 2+ weeks

- August 2020 – SARS-CoV-2 RNA detected sporadically
- November 2020 – SARS-CoV-2 RNA detection, clinical cases increased
  - Begin sub-sewershed sampling 1x per week
SARS-CoV-2 RNA detection in Burlington wastewater

Data through June 20, 2021
Public health responses to increasing wastewater detection trends

- Wastewater surveillance as an early indicator of disease risk in the community
- Targeted resource allocation (pop-up testing, contact tracing)
- Communication with disproportionally affected groups (long-term care residents)
- Public awareness and community response (non-pharmaceutical intervention)

Proactive and integrated strategy
Wastewater surveillance informed action

BTVMayor
@BTVMayor
The City's latest Covid-19 wastewater readings are back, and they show a major increase across the city. "I hope all Burlingtonians will look at this graph and see what I see: a call to action." - Miro
burlingtonvt.gov/Press/mayor-mi...
Expanded surveillance – variant mutation tracking

- **December 2020:** First reports of Variant of Concern (VOC) B.1.1.7 (Alpha)
  - Potential increased transmissibility

- **Added RT-PCR targets for two spike mutations:** del69-70, N501Y
  - N501Y also found in other VOCs: B.1.351 (Beta), P.1 (Gamma)

- **January 13, 2021:** Testing 1x per week

*More Toolkit modules on variants:*

- Module 1.4 – Emerging variants of SARS-CoV-2
- Module 2.6 – Detecting and prioritizing variants

Image from *The New York Times* “Inside the B.1.1.7 Coronavirus Variant”

SARS-CoV-2 variant tracking in wastewater

- Wastewater may be useful for variant detection and tracking
  - Targeting mutations by RT-PCR (Burlington, VT)
  - Direct clinical specimen sequencing
- Public health interpretation challenges:
  - Mutation detection by RT-PCR does not indicate presence of a particular variant
  - Target mutations must be known, specific and novel mutations cannot be identified
  - Fragmented SARS-CoV-2 genomes from multiple, circulating variants present in community become mixed in wastewater
- Quantitatively monitoring mutations associated with known variants can provide information on trends in variant infections within a community.
Variant detection and clinical sequence confirmation

**Jan 13**
Burlington wastewater surveillance begins targeting two spike mutations associated with B.1.1.7

**Feb 10**
N501Y and del69-70 mutations detected by RT-PCR in Main sewershed sample collected on February 8

**Feb 11**
Public announcement and actions
- Burlington and Vermont released coordinated press statements to advise the public on the detection and evolving risk, Burlington held press conference
- Distributed high-quality masks to essential workers and delivered HEPA air purifiers to local businesses
- Alerted the local university where new cases were concentrated
Variant detection and clinical sequence confirmation

**Feb 11** Vermont Department of Health (VT DOH) requested specimens from Burlington residents within impacted Main plant sewershed.

**Feb 16 and Feb 23** Clinical specimens from Burlington residents sent to MASPHL for sequencing, no variants of concern identified.

**Feb 21** East plant sample collected for testing

**Feb 25** Variant mutations detected by RT-PCR in the East sewershed which serves most of the University of Vermont (UVM) campus
VT DOH requests clinical specimens from UVM Student Health Clinic. Specimens from suspected symptomatic cases with a positive antigen test diverted to the VT DOH for diagnostic RT-PCR and evaluation for sequencing.

VT DOH Laboratory confirmed S gene target failure (SGTF) commonly associated with B.1.1.7

Specimen sent to MASPHL for sequencing

Confirmation of B.1.1.7 from clinical specimen
B.1.1.7 clinical sequence confirmation
B.1.1.7 clinical sequence confirmation

- B.1.1.7 identified in other Burlington clinical specimens in weeks that followed.
- VT DOH responded by:
  - Informing local guidance for control measures including at the University of Vermont
  - Conducting state-wide educational outreach about variants
  - Focusing on detecting variants in other areas experiencing high rates of disease – critical given limited sequencing capacity

Tree by Andrew Lang, MASPHL
https://nextstrain.org/groups/spheres/ncov/vermont?c=pango_lineage&f_division=Vermont&p=full
### Actions taken at UVM before B.1.1.7 confirmation

- UVM Student Health suspected B.1.1.7 on campus given the presence of variant mutations in wastewater and detection in neighboring states.
- Responded quickly by:
  - Increasing isolation and quarantine housing capacity
  - Separating isolation and quarantine housing into different buildings (rather than separate floors)
  - Increasing contact tracing capacity
    - Added staff
    - Incentivized evening and weekend coverage
  - Increasing student testing from once to twice per week
Monitoring frequency of variant spike mutations, 2021

- **East Plant**
- **Main Plant**
- **North Plant**

Log10 (gene copies per liter)

- Del 69-70 (B.1.1.7)
- N501Y (B.1.1.7)
- E484K
Summary

- Wastewater surveillance provides early detection of increased SARS-CoV-2 infection within the community
  - Fast turnaround time facilitates response
  - Part of integrated approach to disease control

- Improved detection of B.1.1.7 (Alpha) by targeting defining mutations
  - Early warning of potential increased transmissibility
  - Detected mutations 4 weeks before variant confirmation by sequencing
  - Helped prioritize clinical specimens for sequencing, given limited capacity
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  - GT Molecular, www.gtmolecular.com
  - University of Vermont Student Health

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Learn more

- **Other modules**
  - The SARS-CoV-2 genome – Module 1.2
  - Emerging variants of SARS-CoV-2 – Module 1.4
  - Detecting and prioritizing variants – Module 2.6

- **COVID-19 Genomic Epidemiology Toolkit**
  - Find further reading
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  - [go.usa.gov/xAbMw](http://go.usa.gov/xAbMw)
For more information, contact CDC
1-800-CDC-INFO (232-4636)

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