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Rapid response wastewater testing to support a polio outbreak investigation

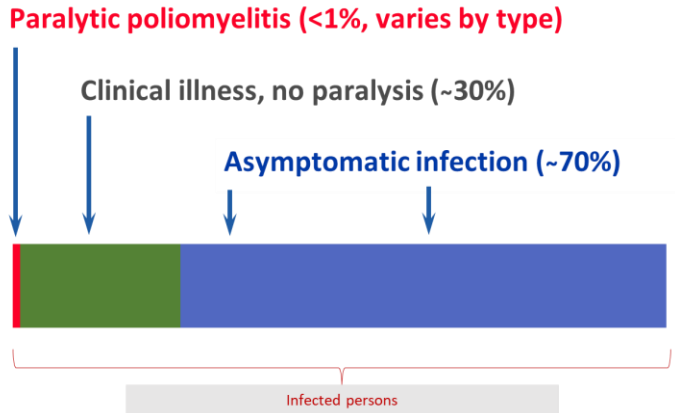
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Poliovirus

- +ssRNA, *Picornaviridae*, *Enterovirus C*
- 3 serotypes of wild type poliovirus
 - Type 1: Endemic in Pakistan and Afghanistan
 - Type 2: Eradicated in 2015
 - Type 3: Eradicated in 2019
- Vaccine-derived
 - Mutated from Sabin strains, types 1, 2, or 3
 - Reversion to neurovirulence

Poliomyelitis

- Transmitted by fecal-oral and oral-oral (respiratory) routes



Poliomyelitis

- Non-paralytic illness
 - Mild, non-specific (fever, malaise, sore throat)
 - Aseptic meningitis
 - Fever, headache, muscle aches, gastrointestinal symptoms, hyperesthesia/paresthesia, stiff neck/back

Poliomyelitis

- Paralytic illness
 - Viral multiplication and damage to neurons in certain areas, e.g., anterior horn of spinal cord
 - Two-phase course
 - Ill-appearing, fever, muscle pain, diminished reflexes
 - Flaccid paralysis
 - May be sudden
 - May be asymmetric, lower extremities more often affected than upper
 - May affect cranial nerves, bladder, bowel, respiratory muscles

Poliomyelitis

- Treatment
 - Symptom relief
 - Physical therapy
 - Investigational antiviral medications
- Prognosis
 - May have some improvement in months after infection
 - Permanent paralysis
 - Post-polio syndrome

Polio Vaccination

- Oral polio vaccine (OPV)
 - Live, attenuated virus (Sabin)
 - Prevents infection, excretion, and paralysis
 - Not used in the US since 2000
 - Risk of reversion to neurovirulence
 - Sabin-like strains, vaccine-derived poliovirus (VDPV)
 - 2016: “The Switch”
 - From trivalent to bivalent (types 1 and 3) OPV
 - Monovalent OPV for outbreaks
 - Novel OPV – serotype 2, further attenuated

Polio Vaccination

- Inactivated polio vaccine (IPV)
 - Protects against all three serotypes
 - Prevents paralysis;
does not prevent infection or excretion
 - Limited mucosal immunity
 - The only polio vaccine licensed in the US

2022 NYS Polio Case

- June 2022: Immunocompetent young adult developed fever, neck stiffness, back and abdominal pain, and constipation
 - Three days later developed lower extremity weakness
 - Two days after weakness onset, presented to emergency department and was admitted to adult neurology service with flaccid weakness
 - Patient tested positive for enterovirus at hospital
- Clinical workup suggested possible enterovirus D68

2022 NYS Polio Case

- Stool x 2, nasopharyngeal swab, oropharyngeal swab and cerebrospinal fluid submitted to Wadsworth Virology Lab for enterovirus confirmation and subtyping
- Stool specimens positive by enterovirus-specific real-time RT-PCR (other specimens negative)
- Sanger sequencing of virus capsid protein 1 (VP1) region identified vaccine-derived poliovirus, type 2 (VDPV2)
- Sample forwarded to CDC – confirmed identification with whole genome sequencing and identified 10 nucleotide changes in VP1 compared to Sabin 2 strain



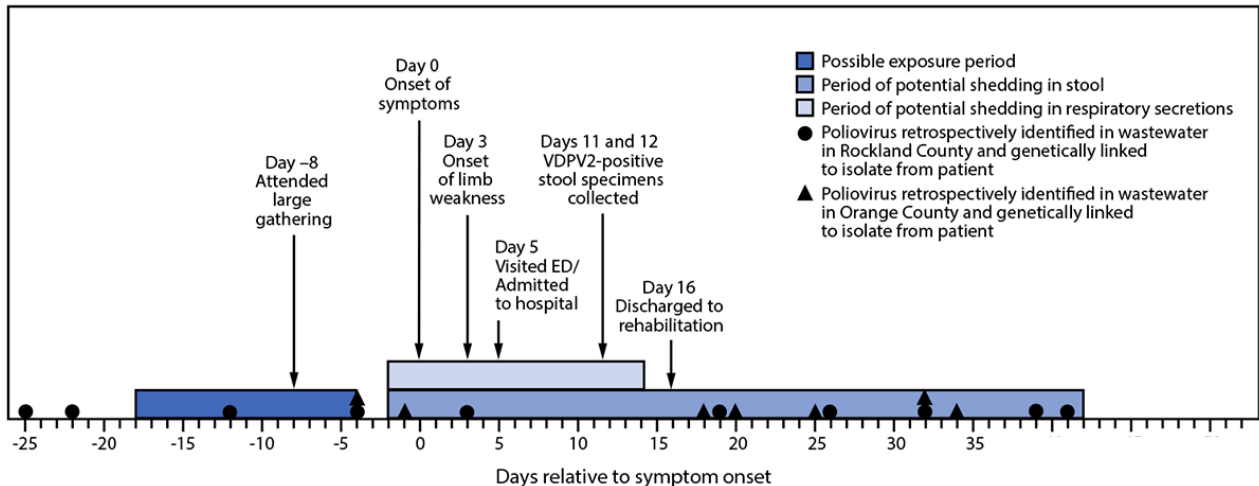
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Case Investigation

- No international travel during the 21 days before onset of paralysis
- Attended a large gathering 8 days before onset of first symptoms

FIGURE. Timeline of patient activities, potential poliovirus exposures, shedding, and poliovirus-positive wastewater* samples† genetically linked to a patient with a case of type 2 vaccine-derived poliovirus — New York, May–August 2022



Abbreviations: ED = emergency department; VDPV2 = type 2 vaccine-derived poliovirus.

https://www.cdc.gov/mmwr/volumes/71/wr/mm7133e2.htm?s_cid=mm7133e2_w

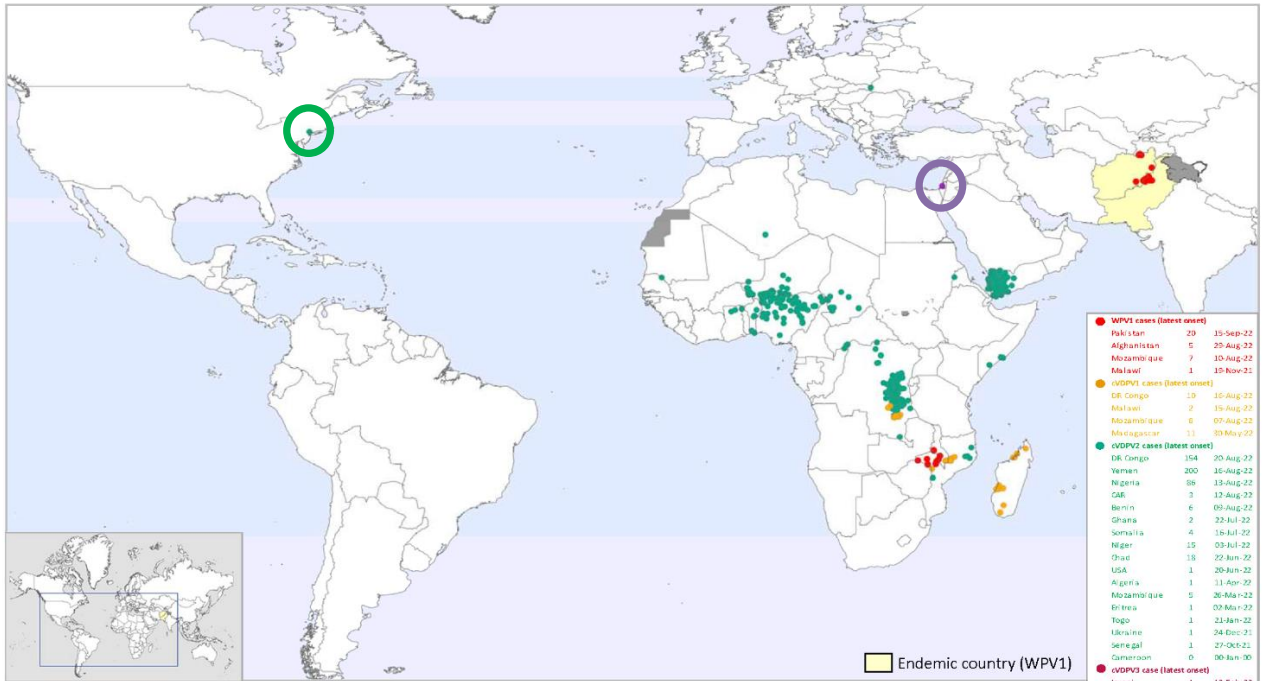
Slide courtesy of Eli Rosenberg and Emily Lutterloh, NYSDOH



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Global WPV1 & cVDPV Cases¹, Previous 12 Months²



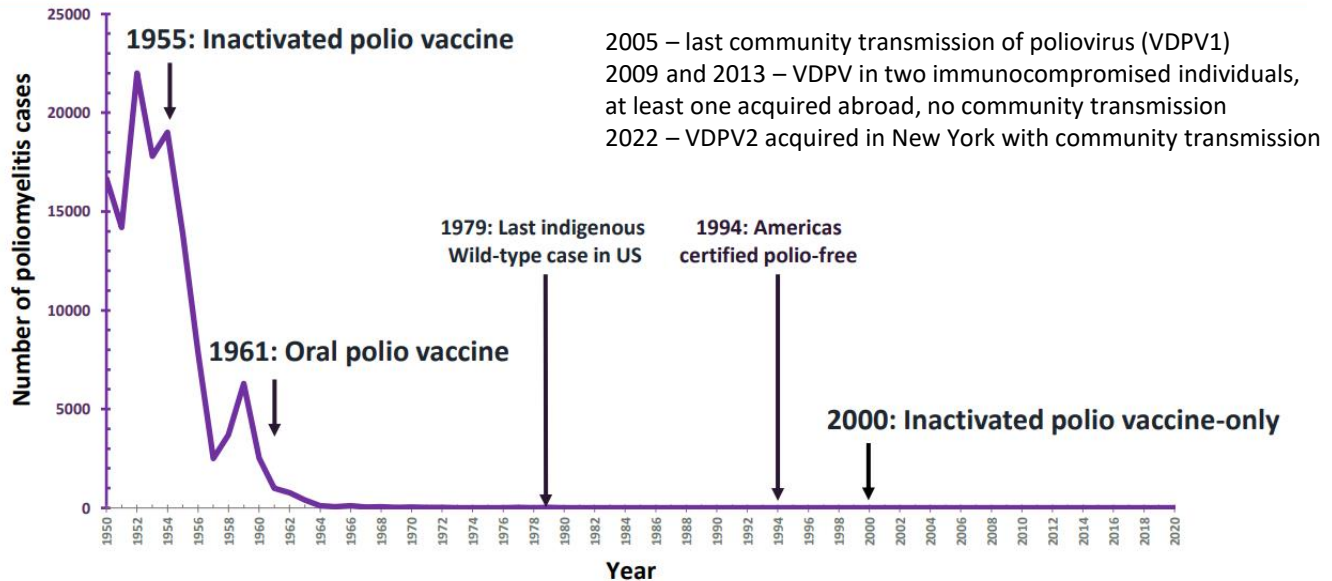
¹Excludes viruses detected from environmental surveillance; ²Onset of paralysis 12 Oct. 2021 to 11 Oct. 2022

Data in WHO HQ as of 11 Oct. 2022

<https://polioeradication.org/polio-today/polio-now/>

Polio in the US

Paralytic polio in the U.S. decreased rapidly after introduction of vaccine



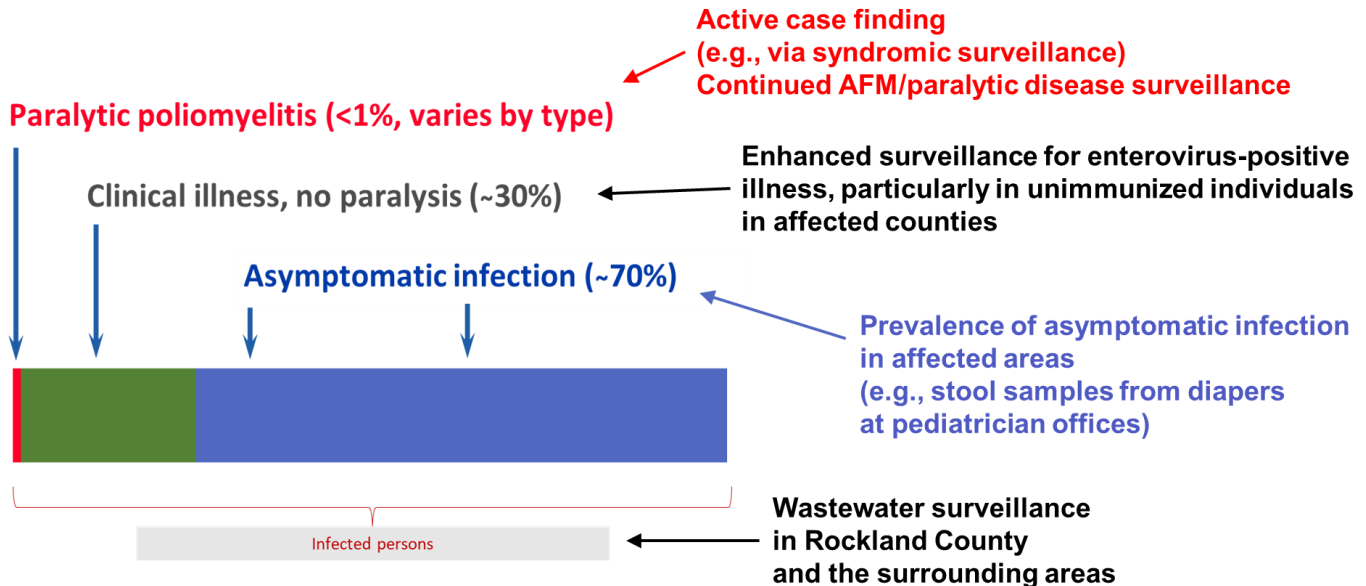
https://emergency.cdc.gov/coca/ppt/2022/090122_slides.pdf



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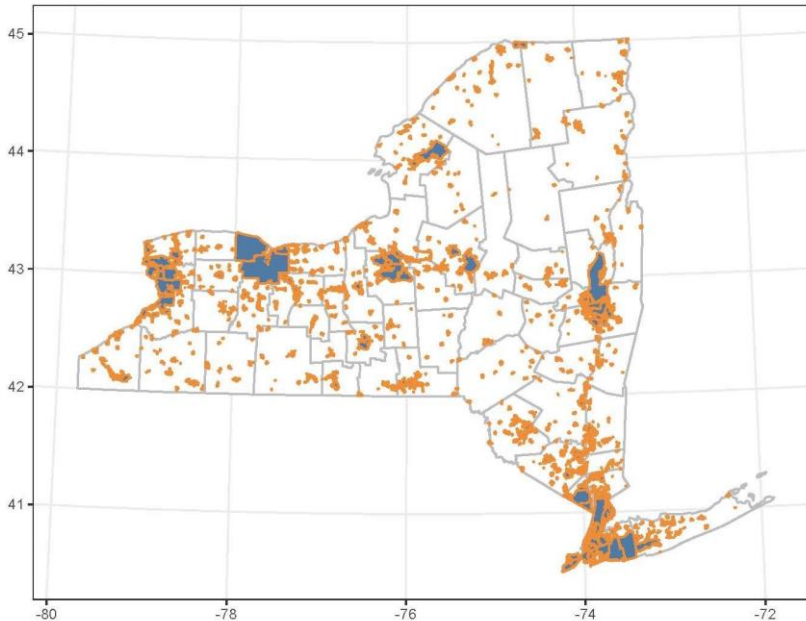
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Polio Surveillance



NYS Wastewater Surveillance System Infrastructure Built with Environmental Public Health Tracking (EPHT) Grant

Municipal sewersheds across New York State



85% of New York State is on sewer

State surveillance network covers 75% of New York State population

State surveillance network covers 70% of the non-New York City population

Slide courtesy Dave Larsen and team, Syracuse University

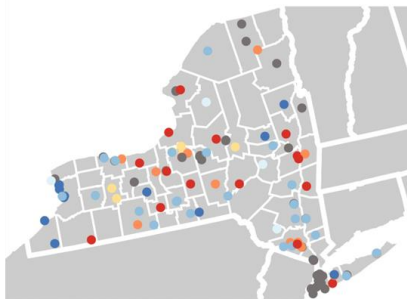


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NYS Wastewater Surveillance System for COVID

Time Period: June 01 – June 15, 2022



Percent change of SARS-CoV-2 in the last 15 days by site, New York

15-day % change category	Num. sites	% sites	Category change in last 7 days
-100%	12	16	-37%
-99% to -10%	24	32	-29%
-9% to 0%	4	5	0%
1% to 9%	0	0	-100%
10% to 99%	6	8	100%
100% to 999%	13	17	225%
1000% or more	16	21	129%

Total sites with current data: 75

Total number of wastewater sampling sites: 112

Time Period: June 01 – June 15, 2022



Percent of wastewater samples with detectable SARS-CoV-2 in the last 15 days by site, New York

15-day detection % category	Num. sites	% sites	Category change in last 7 days
Non-Detect	7	7	-36%
1% to 19%	0	0	N/A*
20% to 39%	4	4	33%
40% to 59%	20	21	-17%
60% to 79%	12	13	20%
80% to 100%	52	55	44%

Total sites with current data: 95

Total number of wastewater sampling sites: 112

Slide courtesy Dave Larsen and team, Syracuse University



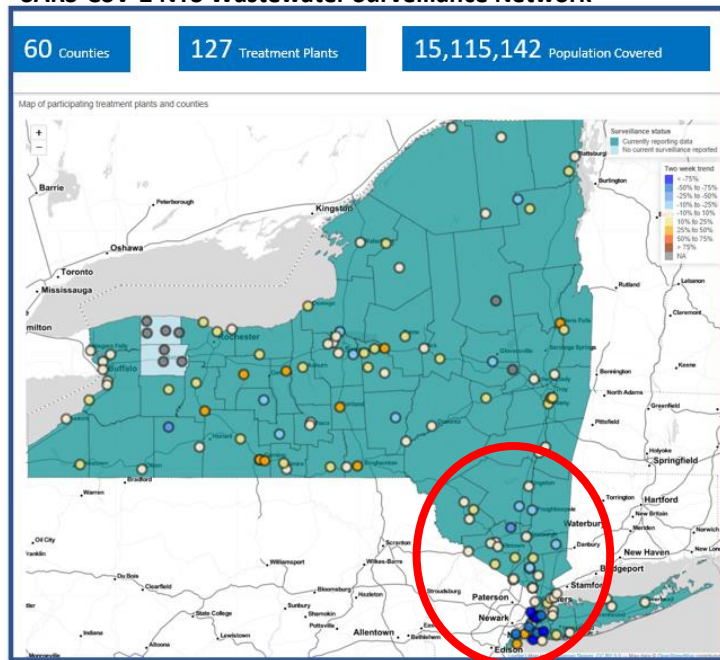
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Wastewater surveillance: Characterizing extent of community spread

- Polio testing was initiated in samples from a subset of NYS Wastewater facilities
 - Beginning with Rockland county, now including 13 NY counties (48 sewer sheds), ~11.4 million persons
 - Mixture of prospective and retrospective samples, collected 1-2x/week
- Sample processing
 - Ultracentrifugation or polyethylene glycol precipitation
 - Nucleic acid extraction
- Testing at CDC
 - pan-polio RT-PCR assay
 - positive samples sequenced to determine:
 - PV2
 - VDPV2
 - VDPV2, linked to case patient

SARS-CoV-2 NYS Wastewater Surveillance Network



<https://mbcolli.shinyapps.io/SARS2EWSP>

Polio testing logistics

- Set up laboratory at Wadsworth for receiving and processing suspected positive wastewater samples
 - Security
 - Separate lab
 - Restricted access
 - Locked freezers
 - Staff vaccination/boosters
- Separate section built in LIMS for wastewater testing
- Shipping protocol and schedule for sending samples to CDC
- Documentation of samples from positive areas to the National Authority for Containment of Polio at CDC



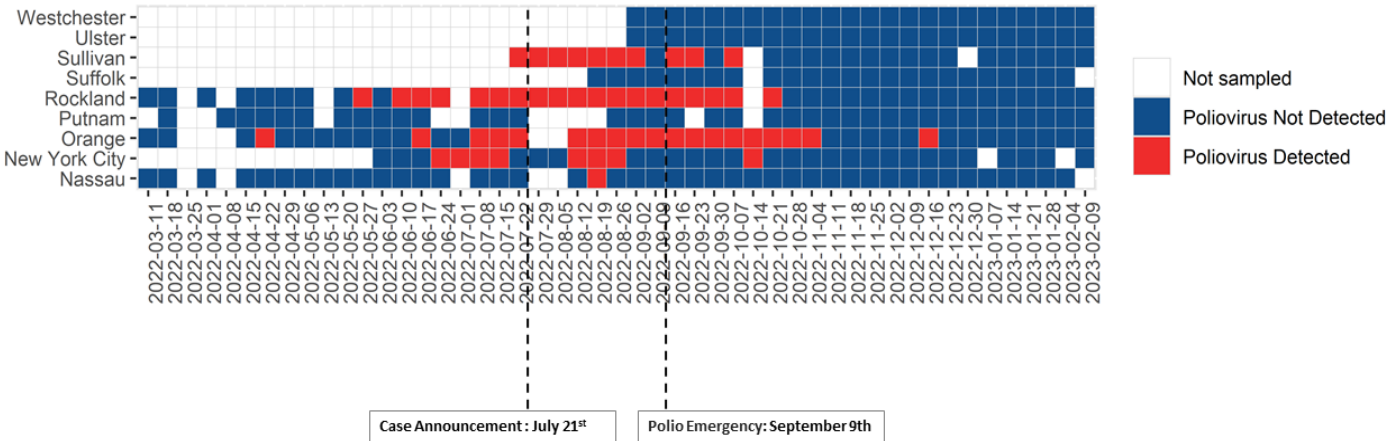
Sample Collection

- CDC Foundation Fellows coordinate delivery of sampling kits and shipping between Quadrant Biosciences and wastewater plants
- Quadrant Biosciences forwards samples to Wadsworth for accessioning and packaging, then forward samples to CDC for analysis

Quadrant Viral Testing		CHAIN OF CUSTODY RECORD FRM-OPS-1013 Version 2											
Client: _____					Project Name: _____					Total Number of Containers Unpreserved Other		Analysis: PCR SARS-CoV-2	Comments
Address: _____					Laboratory Contact(s): _____								
Contact Name: _____													
Contact Phone and Email: _____													
Item #	Sample Identification	pH	Temp.	Volume of Flow (MGD)*	Grab or Composite	If Composite, Circle One** Flow Time	Collection Start Date	Collection Start Time	Collection End Date	Collection End Time			
1													

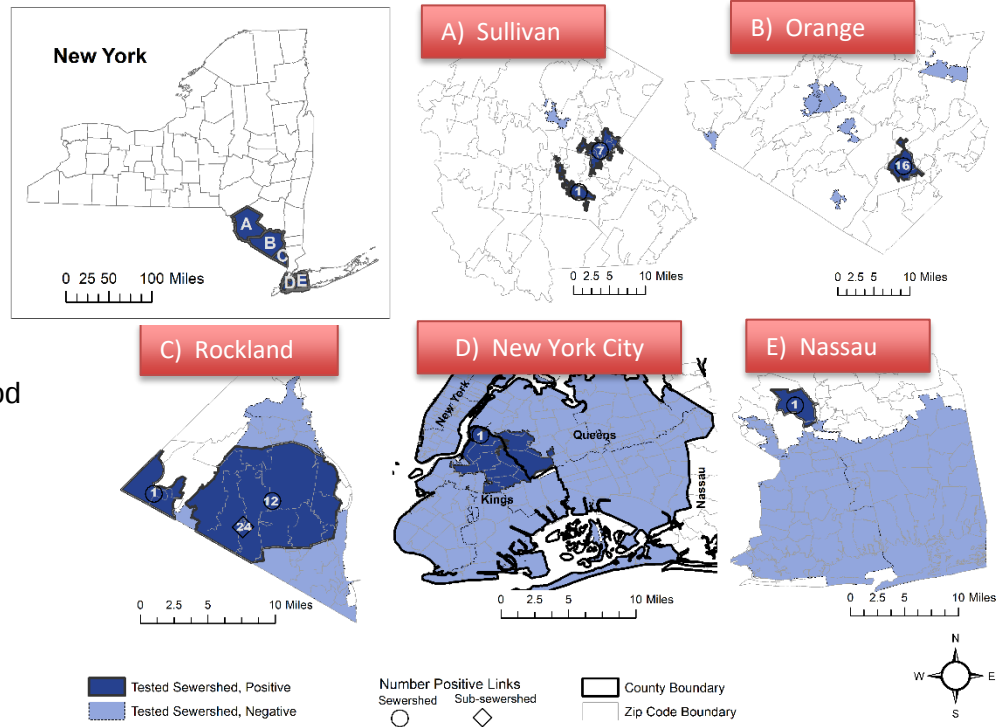


Weekly Pattern of Poliovirus Detection in Wastewater by County



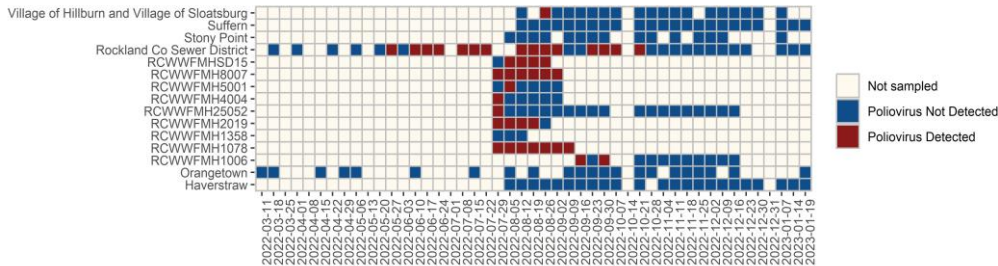
County-level wastewater findings: Areas of detection

- WHO guidelines: ideal wastewater testing in areas with high-risk populations and population <300,000
- Concerns around method sensitivity in higher-population areas...



2022 Upstream wastewater sampling

One-week Pattern Of Poliovirus Detection In Wastewater by Sewershed and Upstream Sampling Point (USP)



Polio Positivity Rate of upstream and influent samples for Counties that conducted upstream Sampling

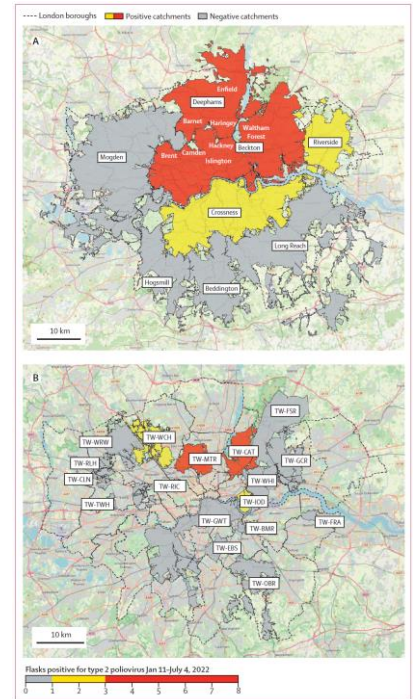
County	Location	Rate
Rockland	Upstream	52%
Rockland	WWTP	20%
Orange	Upstream	0%
Orange	WWTP	8%



NYS case strain linked to wastewater detections in United Kingdom and Israel

- United Kingdom
 - Detection of linked VDPV2 strain in London wastewater February - July 2022 (21 of 52 samples)
 - No clinical cases to-date
- Israel
 - Detection of linked VDPV2 strain in Jerusalem wastewater January – June 2022, with ongoing detection in late 2022 – 2023
 - 4 clinical cases identified Feb 2023, 1 paralyzed
 - VDPV3 outbreak with positive wastewater 2021-22
 - 1 paralytic case

Figure from Klapsa et al. (2022) Lancet, showing location of London sewage sites sampled and positive for type 2 poliovirus: main sewage treatment works (A) or network treatment works sites (B).



Proposed plan for ongoing waster polio surveillance

Routine Surveillance Testing (Baseline):

- Weekly samples from treatment plants located in the initial investigation area
- Biweekly samples from additional treatment plants serving low vaccinated populations
- Monthly samples from additional treatment plants with high population traffic
- Remaining wastewater treatment plants in the network tested monthly for the first 6 months, then once every 3 months thereafter if non-detection is continuous



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Proposed plan for ongoing waster polio surveillance

Scale Up Surveillance Testing (Red Alert):

- Detection of poliovirus in wastewater or a paralytic polio case scale up surveillance in the county to once weekly
- Discussions with state epidemiology will determine whether to expand scale up testing to connected counties

Scale Back Surveillance Testing (Yellow Alert):

- Three consecutive non-detections will indicate to scale back surveillance testing biweekly
- Once elimination confirmed, surveillance will return to baseline.



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Limitations of wastewater testing and remaining questions

- Wastewater surveillance helpful for highlighting areas needing further surveillance, communication and intervention actions, however:
- Challenges to negative predictive value
 - Incomplete coverage of communities and counties
 - Sensitivity and dilution effects of large populations and complex system features not fully characterized
- Challenges to positive predictive value
 - Locations of detection may represent persons away from home → repeat detections add confidence
 - Signal is qualitative only
 - Cannot reliably resolve number of implied infected persons
 - Because of high gut viral loads, can be a few people, but virus mixture hard to resolve
- Other Challenges re: resource needs, broader scaling, timeliness, decision rules for translating findings into public health actions
- Therefore - Important to supplement with other clinical and epidemiological surveillance efforts

Stool surveillance program

- Testing of stool samples from pediatric provider offices in focal communities
 - Diaper-wearing children and older children with diarrhea
 - Free diagnostic testing for enteroviruses
 - Enterovirus PCR and sequencing at Wadsworth Center
 - If positive: Return of results, protocol for monitoring/mgmt. of symptoms, limiting transmission, vaccinating close contacts
- Spring 2023 – planning hospital-based stool surveillance of residual specimens from patients in target areas



Public Health Response: NYSDOH polio response goals

Goal 1: Adequately understand the scope of problem (vaccination and disease), in terms of person, place, time

Goal 2: Protect people from paralytic poliovirus disease with IPV

Goal 3: Interrupt transmission with behavioral/environmental interventions

Goal 4: Enhance vaccination for all vaccine-preventable diseases as part of improved child prevention and wellness

Thank you!

Daniel Lang, Eli Rosenberg, Mohammed Alazawi, Alejandro Godinez, Meghan Fuschino, Kirsten St. George, David Larsen, Milagros Neyra, Dustin Hill, Scott Hughes, Jaume Jorba, Nancy Gerloff, Terry Fei Fan Ng, M. Steven Oberste

Extensive, dedicated 2022 U.S. Poliovirus Response Team:

- New York State Department of Health
- Centers for Disease Control and Prevention
- New York City Department of Health and Mental Hygiene
- Syracuse University
- Rockland County Health Department
- Orange County Health Department
- Sullivan County Health Department
- Nassau County Health Department



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