Metropolitan Water Reclamation District of Greater Chicago

Welcome to the September Edition of the 2023 M&R Seminar Series

NOTES FOR SEMINAR ATTENDEES

- Remote attendees' audio lines have been muted to minimize background noise. For attendees in the auditorium, please silence your phones.
- A question and answer session will follow the presentation.
- For remote attendees, Please use the "**Chat**" feature to ask a question via text to "**Host.**" For attendees in the auditorium, please raise your hand and wait for the microphone to ask a verbal question.
- The presentation slides will be posted on the MWRD website after the seminar.
- This seminar has been approved the ISPE for one PDH and approved by the IEPA for one TCH. Certificates will only be issued to participants who attend the entire presentation.

Niall M. Mangan, Ph.D.

Assistant Professor of Engineering Sciences
and Applied Mathematics
Northwestern University, Evanston, Illinois

Niall M. Mangan received dual Bachelor of Science degrees in mathematics and physics, with a minor in chemistry, from Clarkson University, Potsdam, New York, and Ph.D. in systems biology from Harvard University, Cambridge, Massachusetts. Dr. Mangan worked as a postdoctoral associate in the Photovoltaics Lab at MIT from 2013-2015 and as an Acting Assistant Professor at the University of Washington, Seattle, from 2016-2017. She is currently an Assistant Professor of engineering sciences and applied mathematics at Northwestern University, where she works at the interface of mechanistic modeling and data-driven statistical inference. Her group applies these methods to biological, chemical, and material problems.

Relating SARS-CoV-2 RNA measured in Chicago-area Wastewater Treatment Plants and Cook County COVID-19 Public Health Data

Niall M. Mangan
Assistant Prof.
Eng. Sci. & Applied Math
Northwestern University

Application areas & My Team:

Biological Networks

Andre Archer

Dr. Sasha Shirman

Model Identification and genetic circuit design

Katie Dreyer

Julie Nguyen

Dr. Cody FitzGerald

Image analysis for *C. elegans*

Isabel Zhong

Covid-19 Dynamics in Wastewater

Dr. Katelyn Leisman

Maria Warns

Catalysis & Numerics

Jithin George

Big Picture Wastewater Surveillance Project

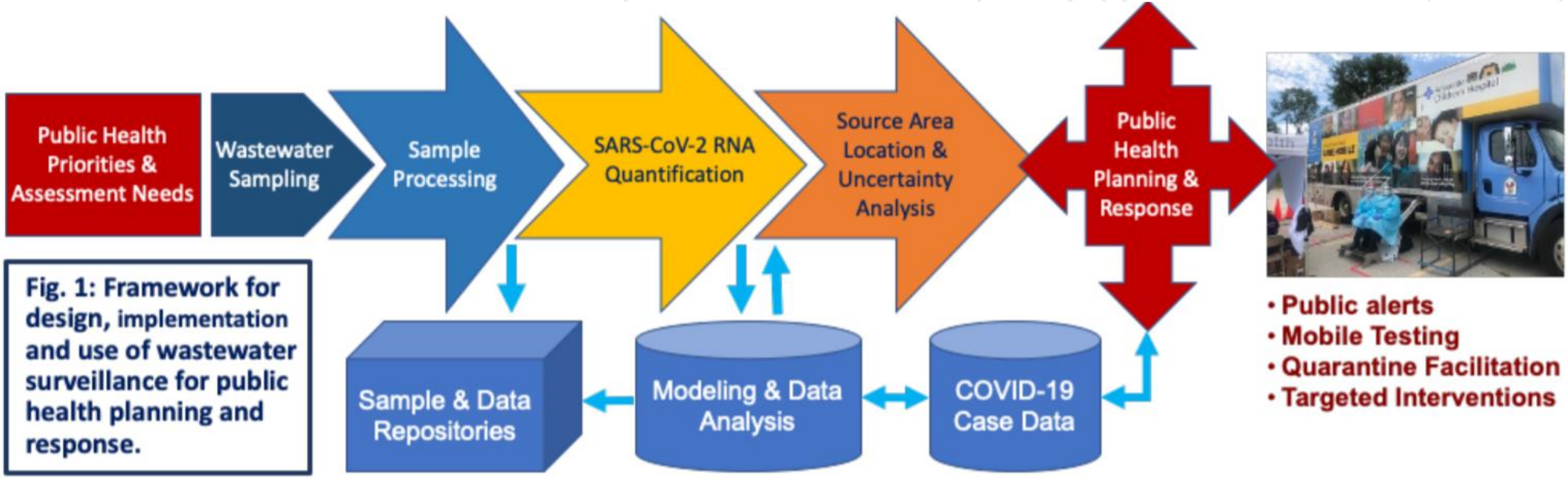

Fig. 1: Framework for design, implementation and use of wastewater surveillance for public health planning and response.

- WW Surveillance in Illinois is being conducted at WWTPs & sewers in Chicago & Illinois and facilities like Cook County Jail and O'Hare Airport
- Non-intrusive monitoring, viral RNA shedding occurs regardless of symptomology

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DPI DISCOVERY PARTNERS INSTITUTE PART OF THE UNIVERSITY OF ILLINOIS SYSTEM
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Argonne NATIONAL LABORATORY
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Big Picture Wastewater Surveillance Project

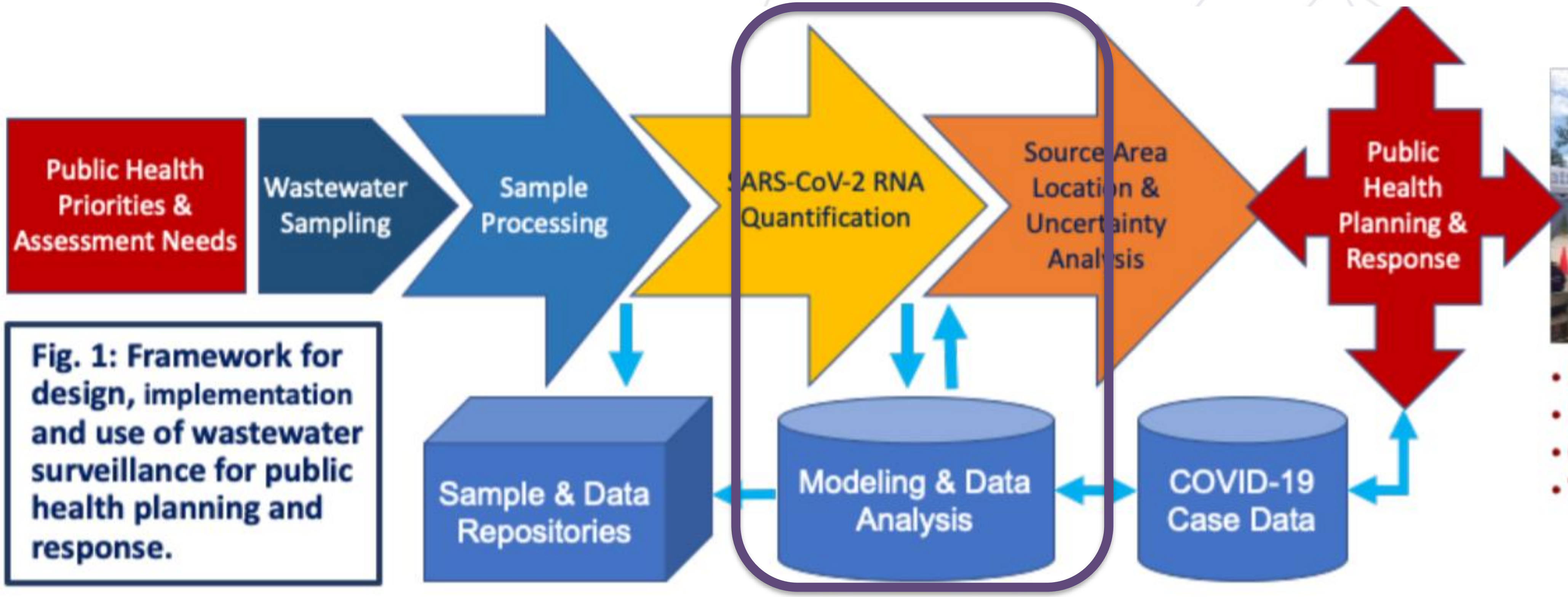

Fig. 1: Framework for design, implementation and use of wastewater surveillance for public health planning and response.

- **Public alerts**
- **Mobile Testing**
- **Quarantine Facilitation**
- **Targeted Interventions**

- WW Surveillance in Illinois is being conducted at WWTPs & sewers in Chicago & Illinois, Cook County Jail, O’Hare Airport
- Non-intrusive monitoring, viral RNA shedding occurs regardless of symptomology

Current Team

DISCOVERY PARTNERS INSTITUTE

PART OF THE UNIVERSITY OF ILLINOIS SYSTEM

Dr. Sandra Gesing
Supervisor, DPI lead

Dr. Melissa Pierce
Senior Data Scientist

Laura Clements
Senior Project Mgr

Krystal White
Project Mgr

Dr. Anuj Tiwari
Senior Research Scientist

Dr. Rachel Poretsky
Professor, Science Lead/Project Director

- Dr. Abhilasha Shrestha, Professor
- Dolores Sanchez & Adam Horton, Lab Managers
- Chi-Yu & Jarju Mordu, Lab technicians

Northwestern University

Charlie Catlett
"The Godfather" of the IWSS program

Argonne NATIONAL LABORATORY

Dr. Aaron Packman
Professor, Analysis & Modeling

Dr. Katelyn Leisman
Research Asst. Professor

Sarah Owens
Sequencing Lab Manager

Dr. Niall Mangan
Asst. Professor

- Dr. David Morton, Professor
- Dr. Sonny Diao, Postdoc
- Guyi Chen & Maria Warns, Graduate Students

- Stephanie Greenwald, Sequencing Specialist
- Andreas Wilke, Principal Software Development Specialist

Experimental quantification team

Prof. Abhilasha Shrestha

OXFORD FEMS

FEMS Microbes, 2022, 3, 1–11
DOI: 10.1093/femsmc/xtac015
Advance access publication date: 7 May 2022
Research Article – Microbes & Environment

Reduction and discharge of SARS-CoV-2 RNA in Chicago-area water reclamation plants

Christopher Owen[1], Dorothy Wright-Foulkes[1], Prisila Alvarez[1], Haidy Delgado[1], Eva C. Durance[1], George F. Wells[2], Rachel Poretsky[1,*], Abhilasha Shrestha[1]

Christopher Owen

Prof. Rachel Poretsky

Prof. George Wells

Leah Kelly

IDPH · Healthy Chicago · DPI Discovery Partners Institute · UIC · Northwestern · Argonne National Laboratory · Illinois · Current · Stemloop

Modeling Team


Dr. Katelyn Leisman


Maria Warns


Prof. Aaron Packman


Prof. Dave Morton


Dr. Charlie Catlett


Guyi Chen


Sonny Diao


Melissa Pierce


Dr. Anuj Tiwari

George Bian
Kaye Zhou Kim
Nguyen Carol Liu
Adam Gokcan
Kevin Li

Dr. Mark Grippo
Edwin Saavedra
Prof. Ahmed Abokifa
Ali Salem
Prof. Marcelo Garcia
Ari Feldman
Manuel Reyna

Illinois Department of Public Health IDPH Protecting Health, Improving Lives
HEALTHY CHICAGO Chicago Department of Public Health
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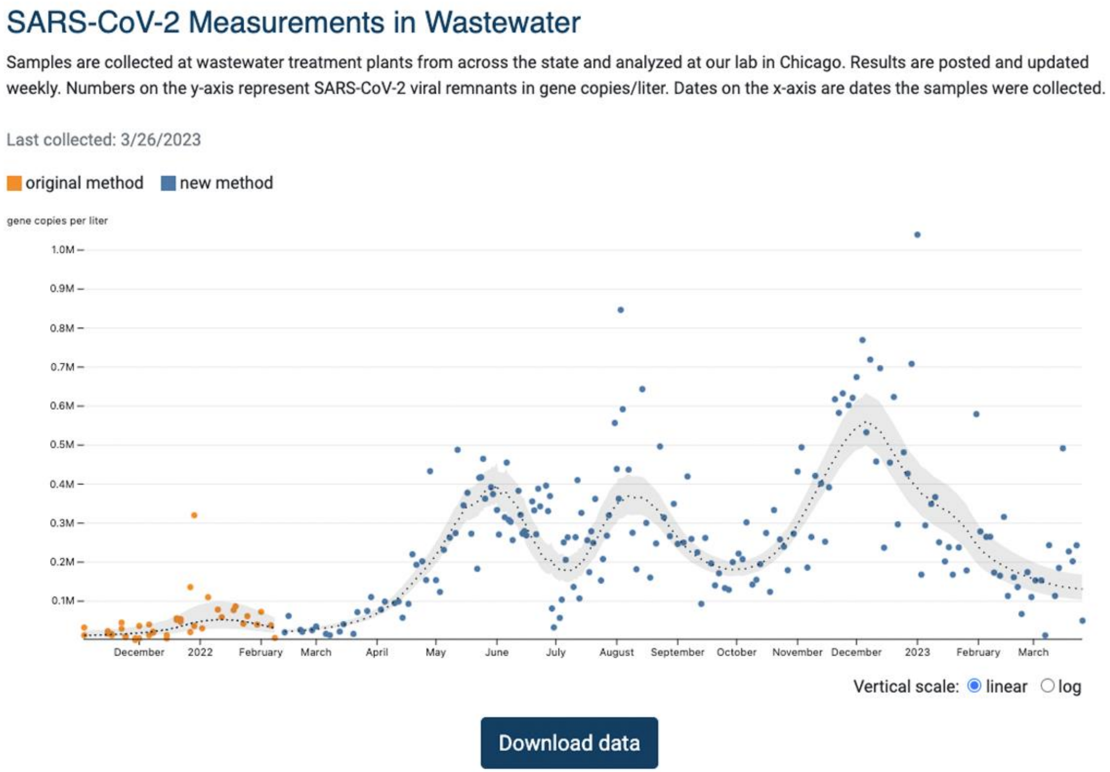
Flushed with Insights: The Promising Potential of Poop-Based Testing for Public Health



Photos by Alex Garcia

Melissa Pierce, PhD
Discovery Partners Institute

Katelyn Leisman, PhD
Northwestern University

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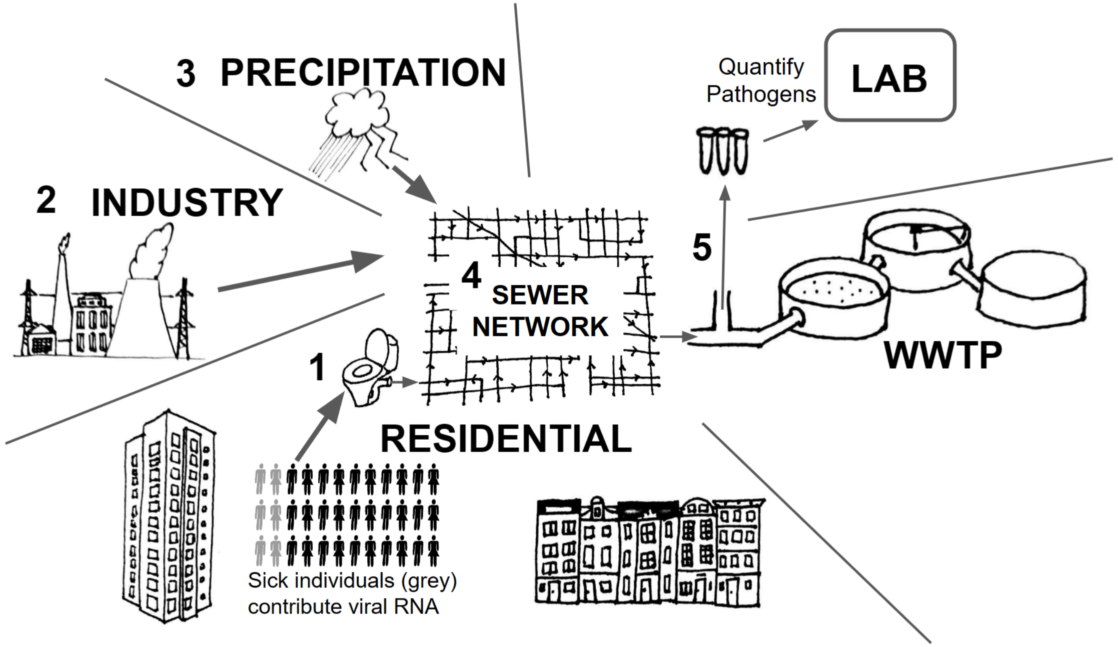
Wastewater is complex!

- Toilet, shower, sink, washing machine, etc. water from residential & commercial properties.
- Includes industrial waste
- Can be impacted by weather events



Metropolitan Reclamation Water District of Greater Chicago

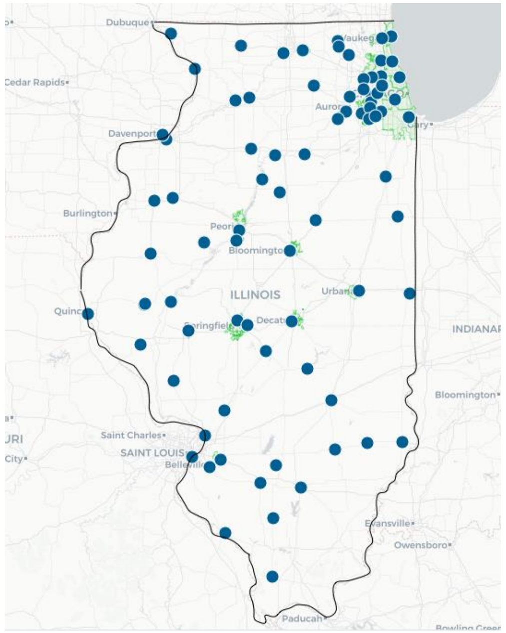
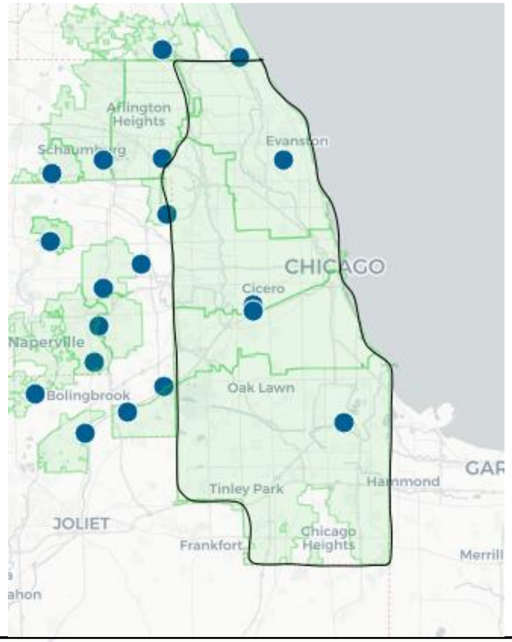
Why monitor disease using wastewater?

- Anonymous, inexpensive, & represents an entire community
- Data can be used by public health departments to make decisions on where to send resources
- Testing is less accurate for COVID-19 with at-home testing
- Helps fill in the gaps when clinical data is lacking or missing (e.g., influenza)
- Helps detect pathogens early before cases show up in hospitals (e.g., Polio in NY summer 2022)

Illinois Wastewater Surveillance System

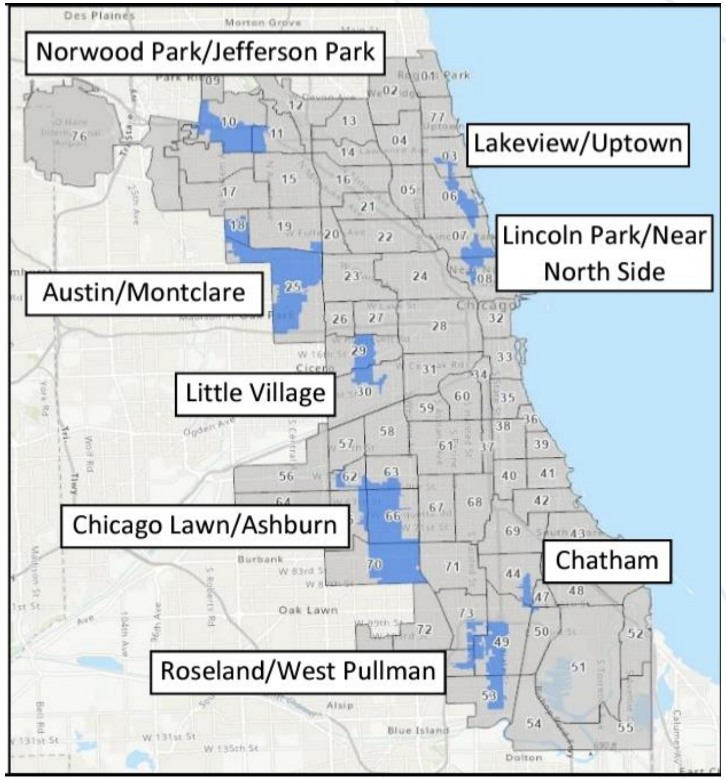
Illinois Dept Public Health (IDPH)

State-wide, ~77 WWTPs, 2x weekly sampling

Illinois – Largest Population Center in Each County	Chicagoland – Major WWTPs
	

Chicago Dept Public Health (CDPH)

8 neighborhoods, Cook County Jail, O'Hare, long term care facility, 1-2x weekly sampling



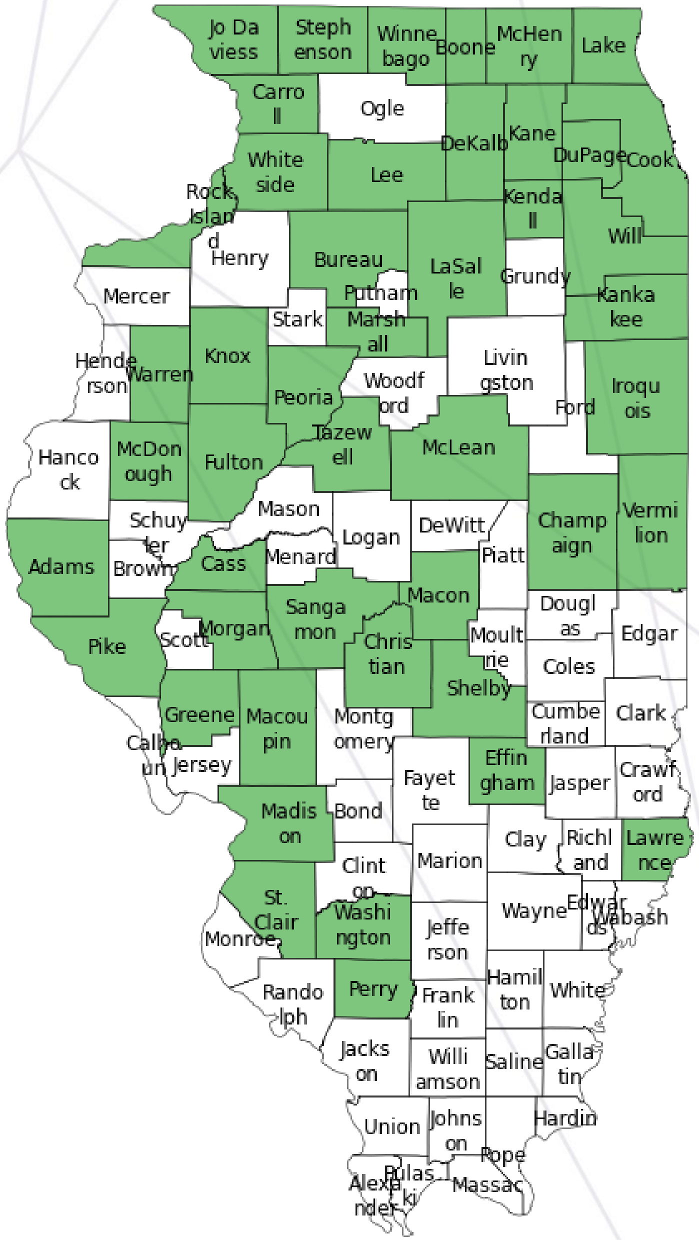
Surveillance Program stats

- Currently 79 active WWTPs (in 46 counties)

- 8.5+ million people across Illinois
  - ~70% of total Illinois residents

- Processed >18,000 samples since 2021

- Goal: Work towards health equity by reaching as many people as possible.



Pathogens Tested in Wastewater

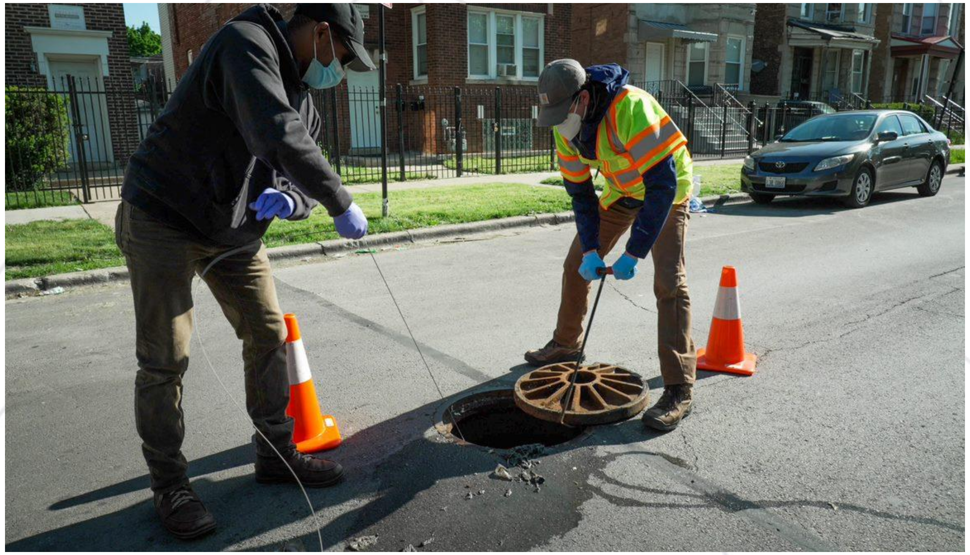


Photo by Alex Garcia

- Currently testing for:
  - SARS-CoV-2
  - Influenza A/B
  - RSV

- Broad range of options to scale the program (e.g., antimicrobial resistance genes, emerging pathogens)

- All testing in our program is at the request of the DPHs/CDC guidance

WBE Workflow

Sample Collection → Viral RNA Quantification → Variant Sequencing → Modeling, Analytics, & Reporting

Photos by Alex Garcia

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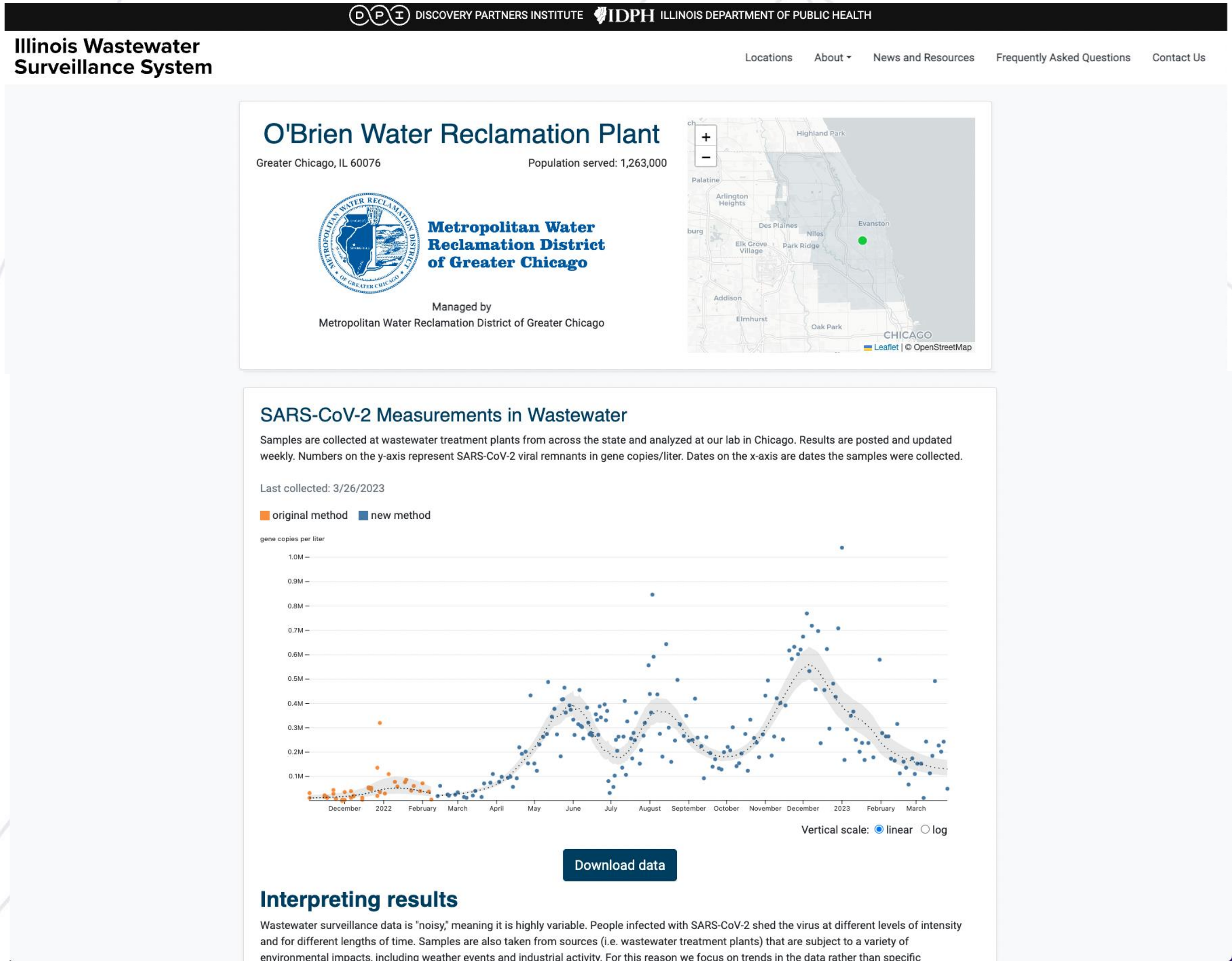
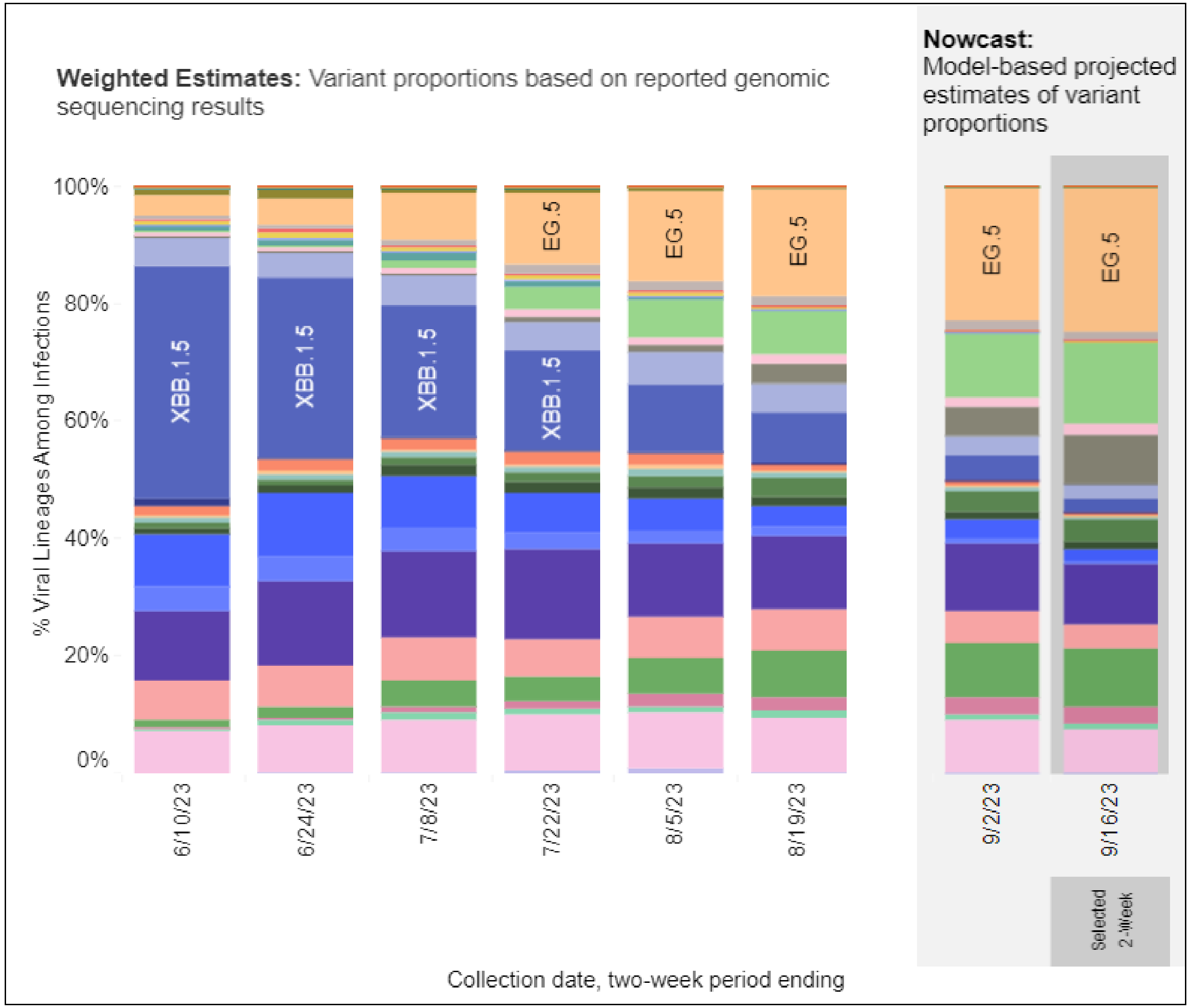
Dashboard - https://iwss.uillinois.edu/



https://covid.cdc.gov/covid-data-tracker/#variant-proportions

Variant Sequencing

CDC COVID Data Tracker, Midwest Region



USA

WHO label	Lineage #	%Total	95%PI
Omicron	EG.5	24.5%	22.5-26.6%
	FL.1.5.1	13.7%	9.8-18.7%
	XBB.1.16	10.2%	8.6-11.9%
	XBB.1.16.6	9.9%	8.4-11.7%
	HV.1	8.4%	6.6-10.5%
	XBB.2.3	7.2%	6.2-8.5%
	XBB.1.16.1	4.1%	3.4-4.9%
	XBB.1.5.70	3.8%	2.9-4.9%
	XBB.1.16.11	3.0%	2.3-3.8%
	XBB	2.5%	2.1-2.9%
	XBB.1.5	2.2%	1.9-2.6%
	XBB.1.9.1	1.9%	1.6-2.2%
	GE.1	1.7%	1.3-2.3%
	EG.6.1	1.5%	1.0-2.1%
	XBB.1.5.72	1.2%	0.9-1.6%
	XBB.1.42.2	0.9%	0.5-1.7%
	XBB.1.9.2	0.7%	0.6-0.9%
	XBB.1.5.68	0.6%	0.4-0.9%
	XBB.1.5.10	0.6%	0.4-0.7%
	XBB.2.3.8	0.4%	0.2-0.6%
	CH.1.1	0.3%	0.2-0.4%
	FD.1.1	0.3%	0.2-0.4%
	XBB.1.5.59	0.2%	0.1-0.4%
	FE.1.1	0.2%	0.1-0.3%
	EU.1.1	0.0%	0.0-0.1%
	XBB.1.5.1	0.0%	0.0-0.0%
	BQ.1	0.0%	0.0-0.1%
	BA.2.12.1	0.0%	0.0-0.0%
	B.1.1.529	0.0%	0.0-0.0%
	BA.5	0.0%	0.0-0.0%
	FD.2	0.0%	0.0-0.0%
Other	Other*	0.1%	0.0-0.1%

Dashboard – Data Analysis

What the data DOES tell us:

- The concentration of viral RNA in a sample
- How trends change over time (increasing/decreasing/no change)

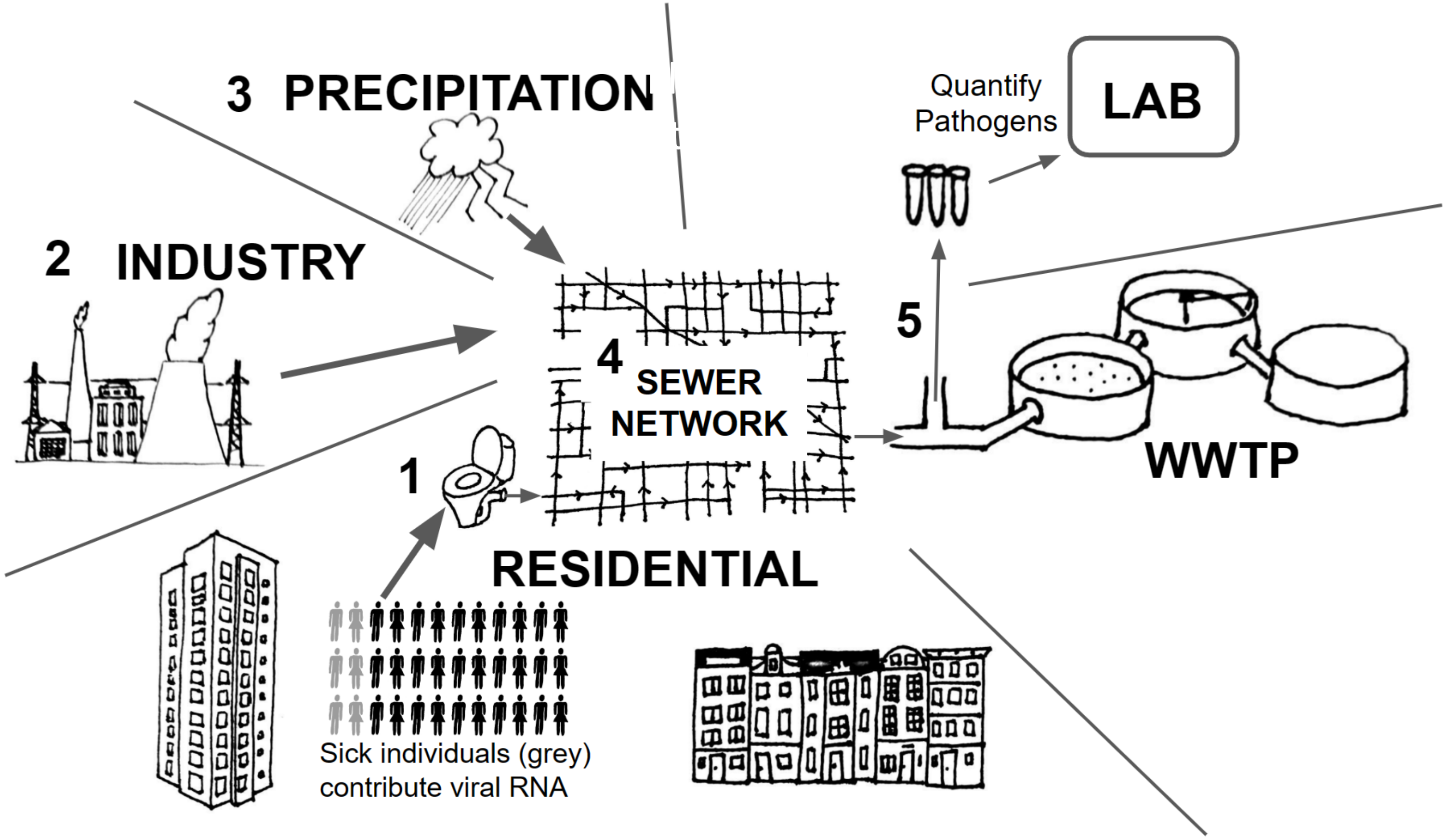
Photos by Alex Garcia

What the data DOES NOT tell us:

- How many people are sick
- Differences between sites (can't directly compare concentrations)
- Differences between pathogens at a site (can't directly compare concentrations)

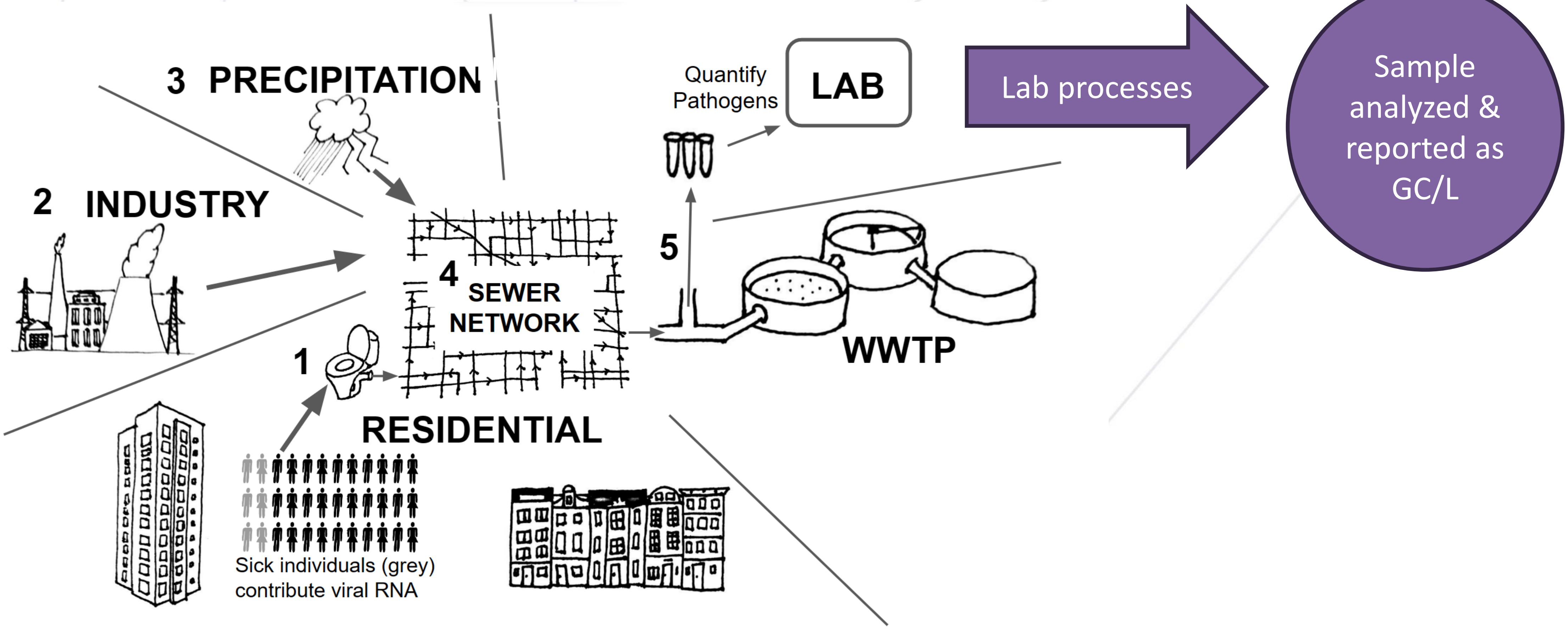
Wastewater data should always be interpreted alongside other reliable public health metrics, like hospitalization rates.

Relating RNA in Wastewater to public health



WWTP: Waste Water Treatment Plant

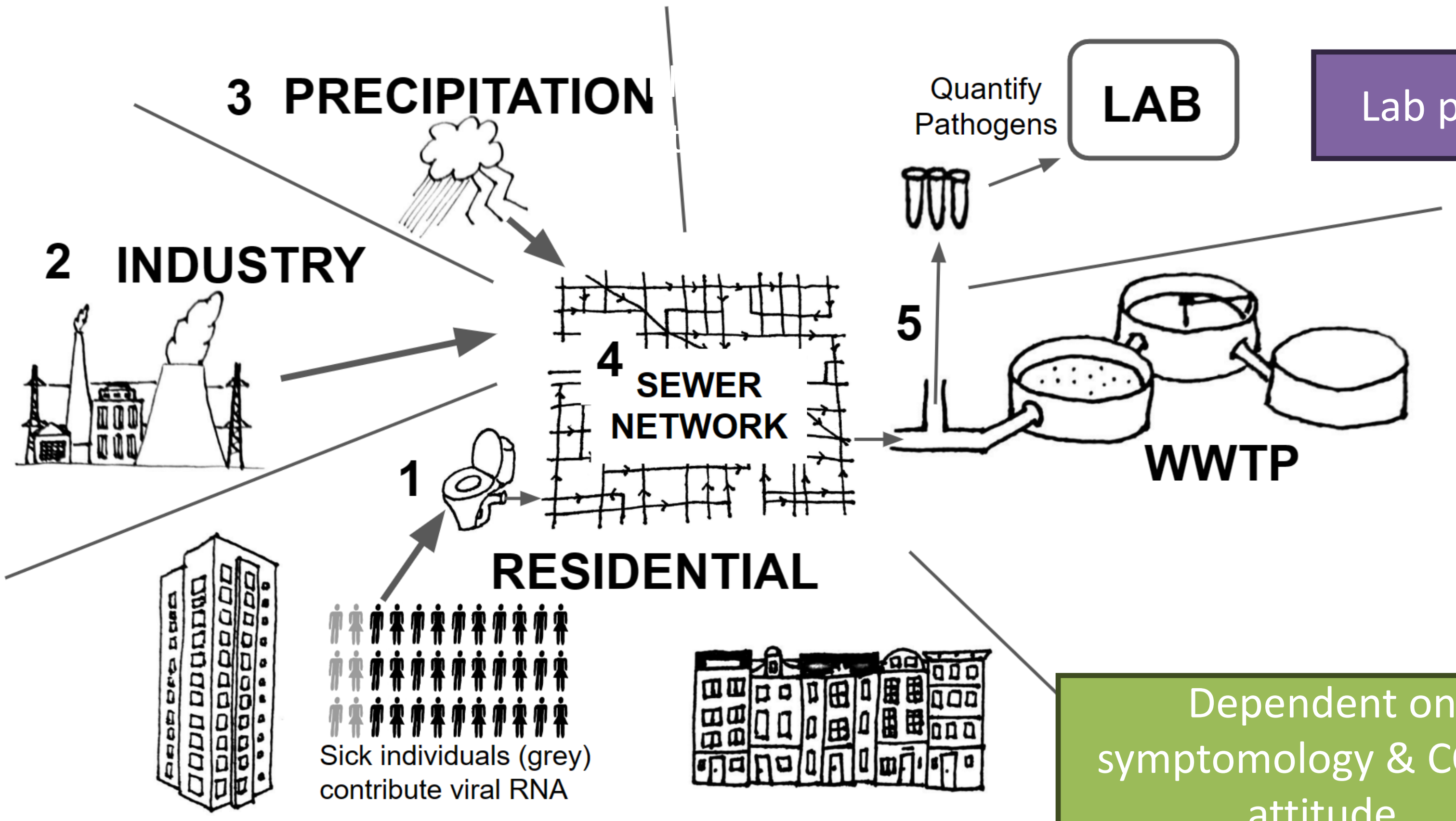
Relating RNA in Wastewater to public health



Northwestern

WWTP: Waste Water Treatment Plant

Relating RNA in Wastewater to public health

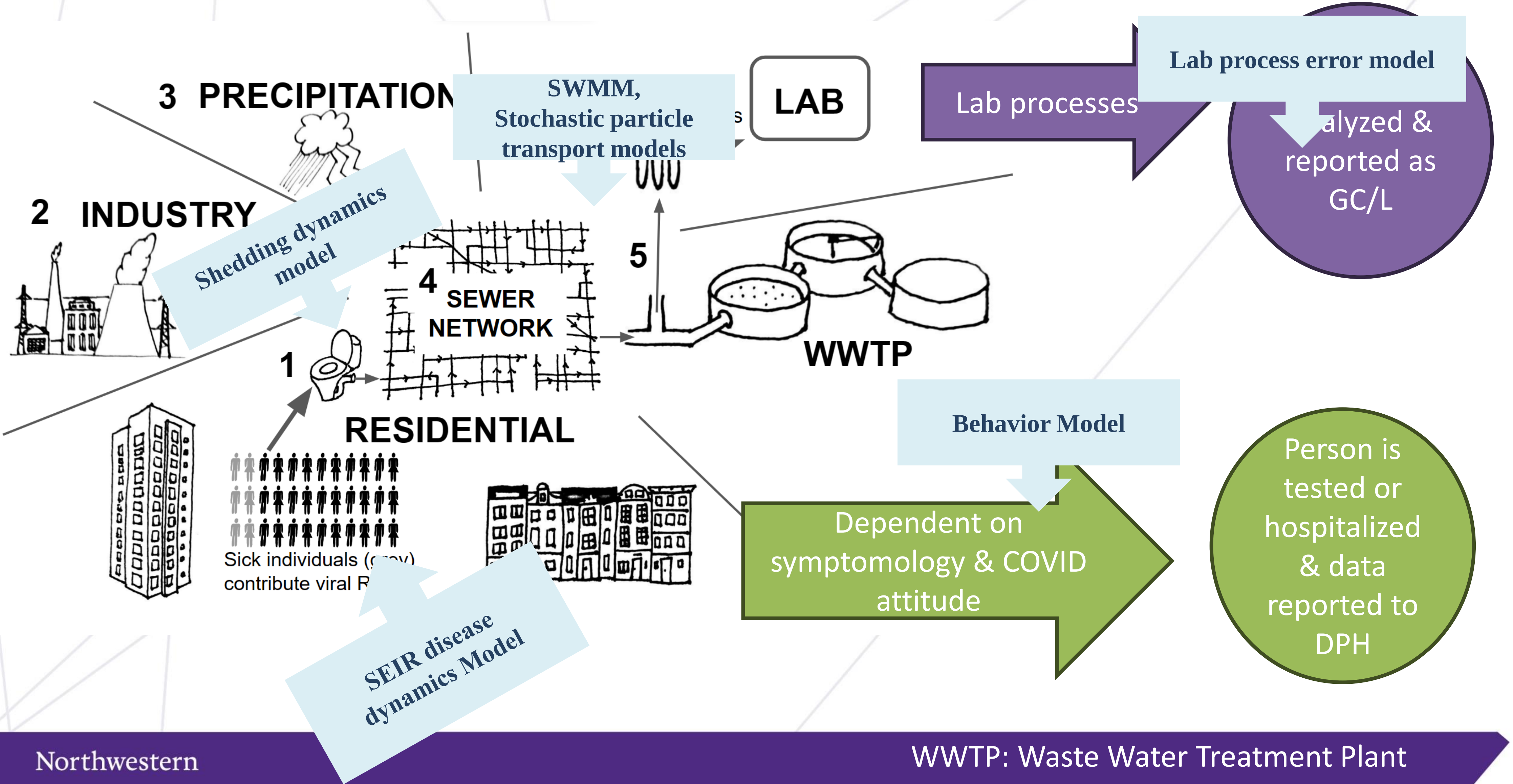


Lab processes → Sample analyzed & reported as GC/L

Dependent on symptomology & COVID attitude → Person is tested or hospitalized & data reported to DPH

WWTP: Waste Water Treatment Plant

Relating RNA in Wastewater to public health



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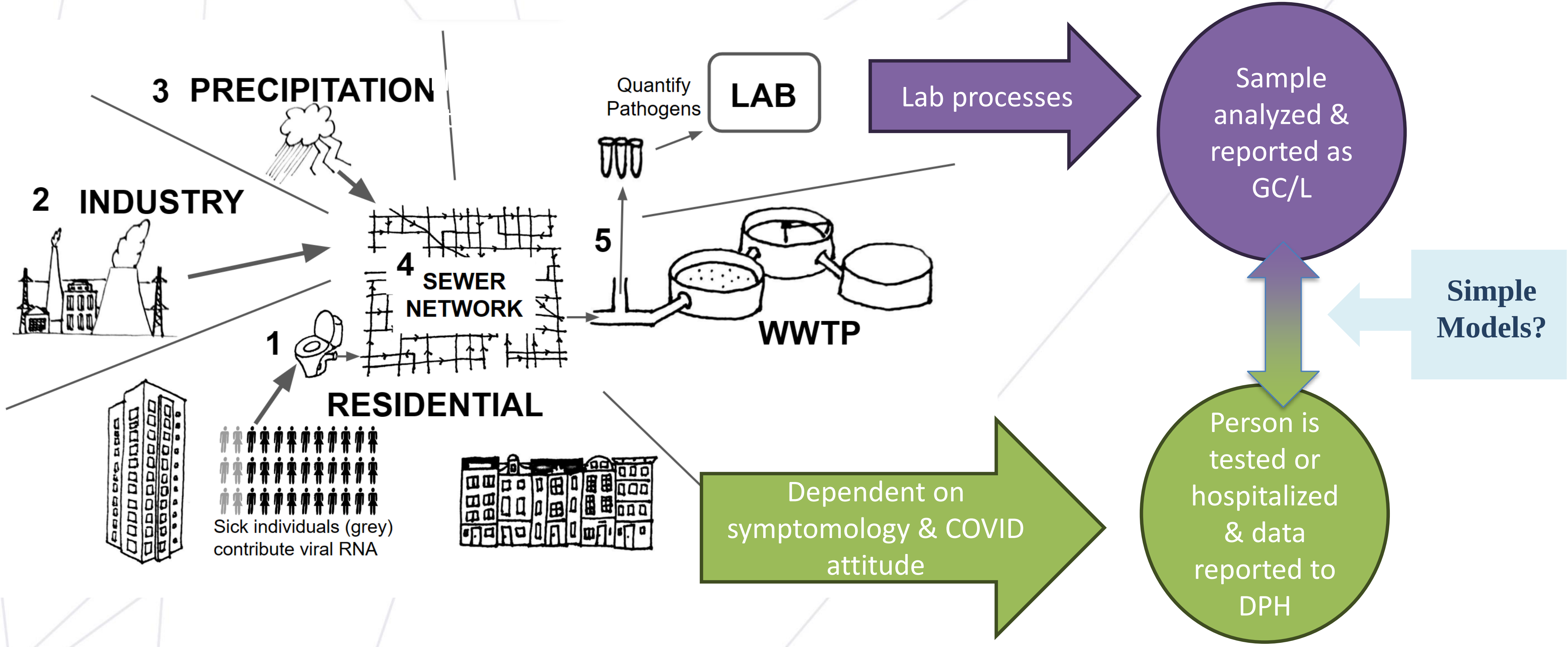

WWTP: Waste Water Treatment Plant

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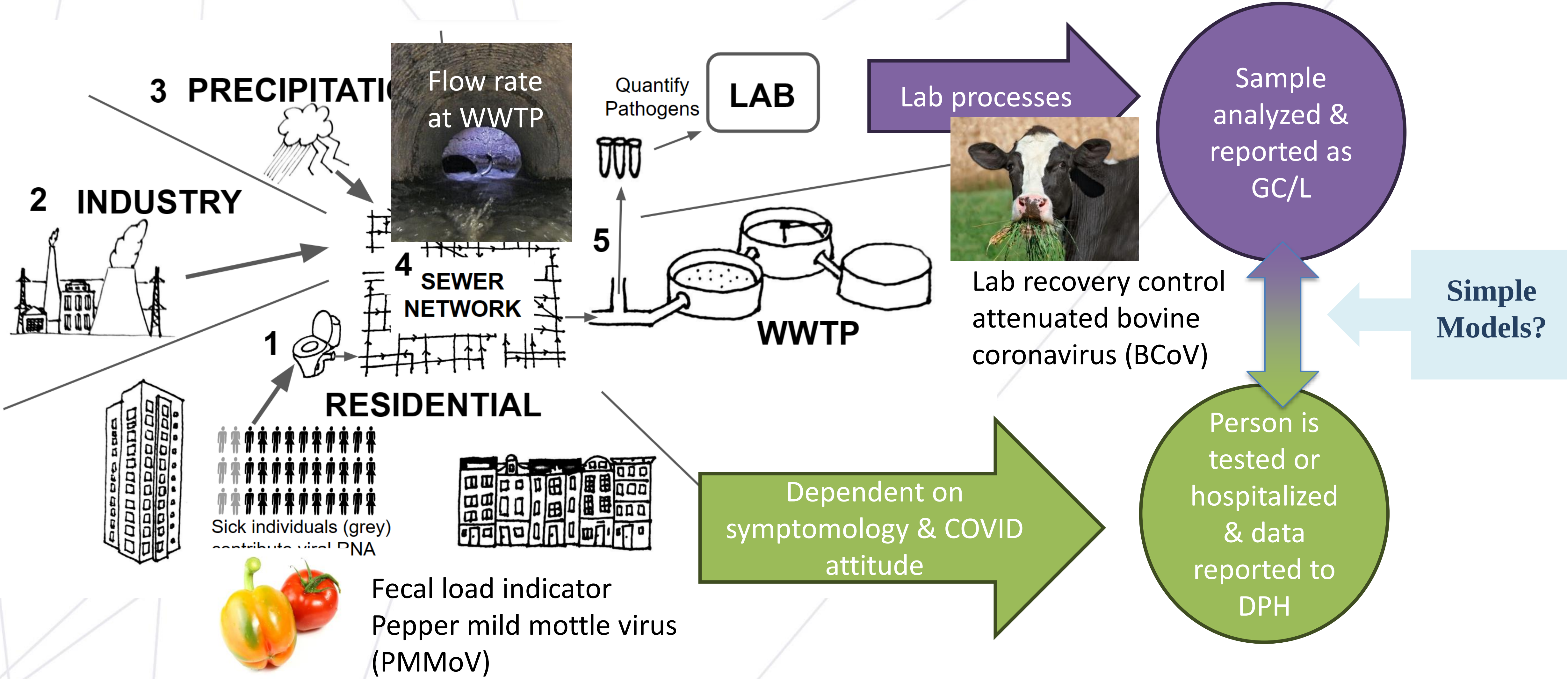
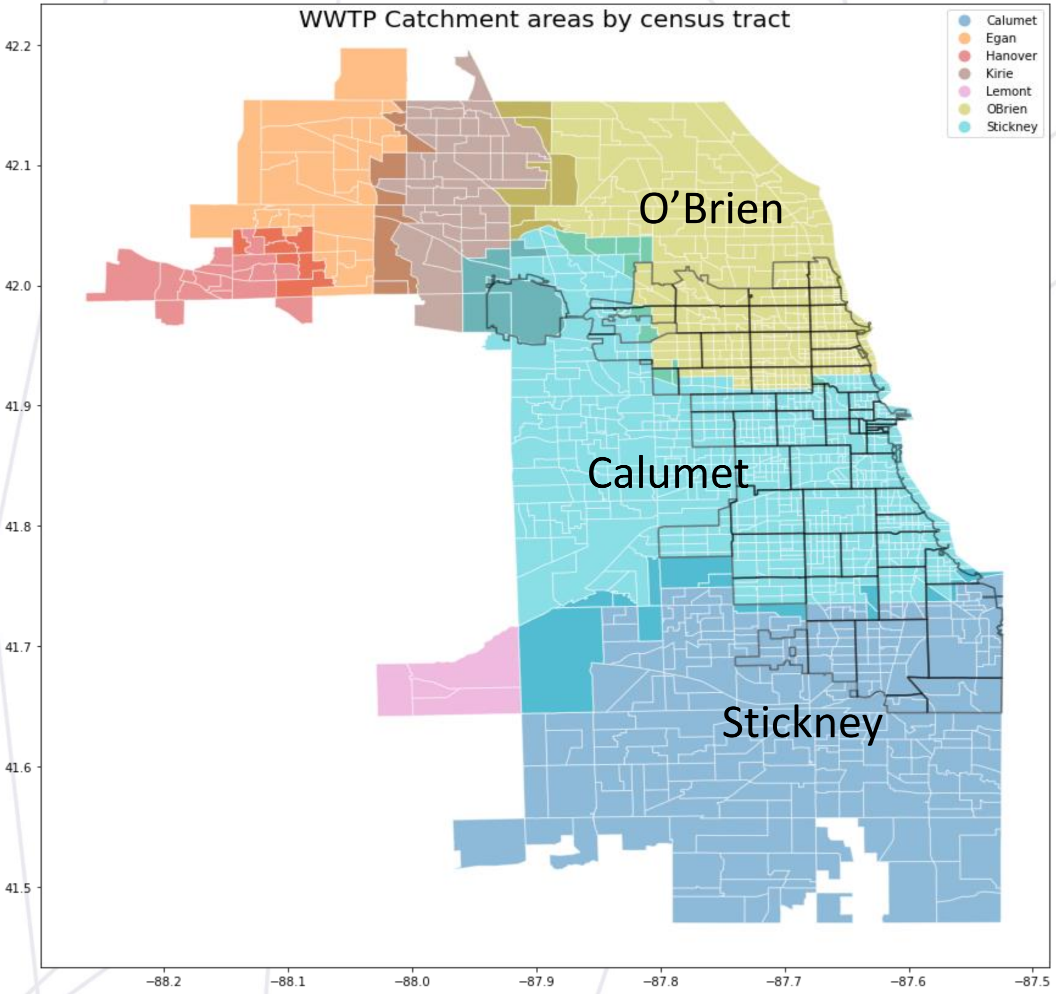
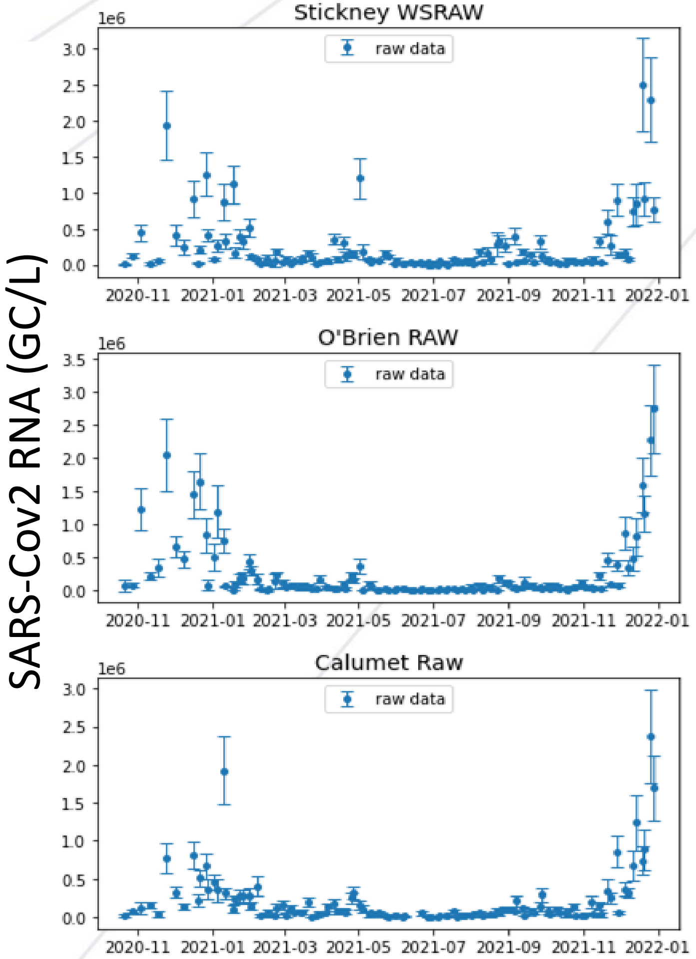


WWTP: Waste Water Treatment Plant

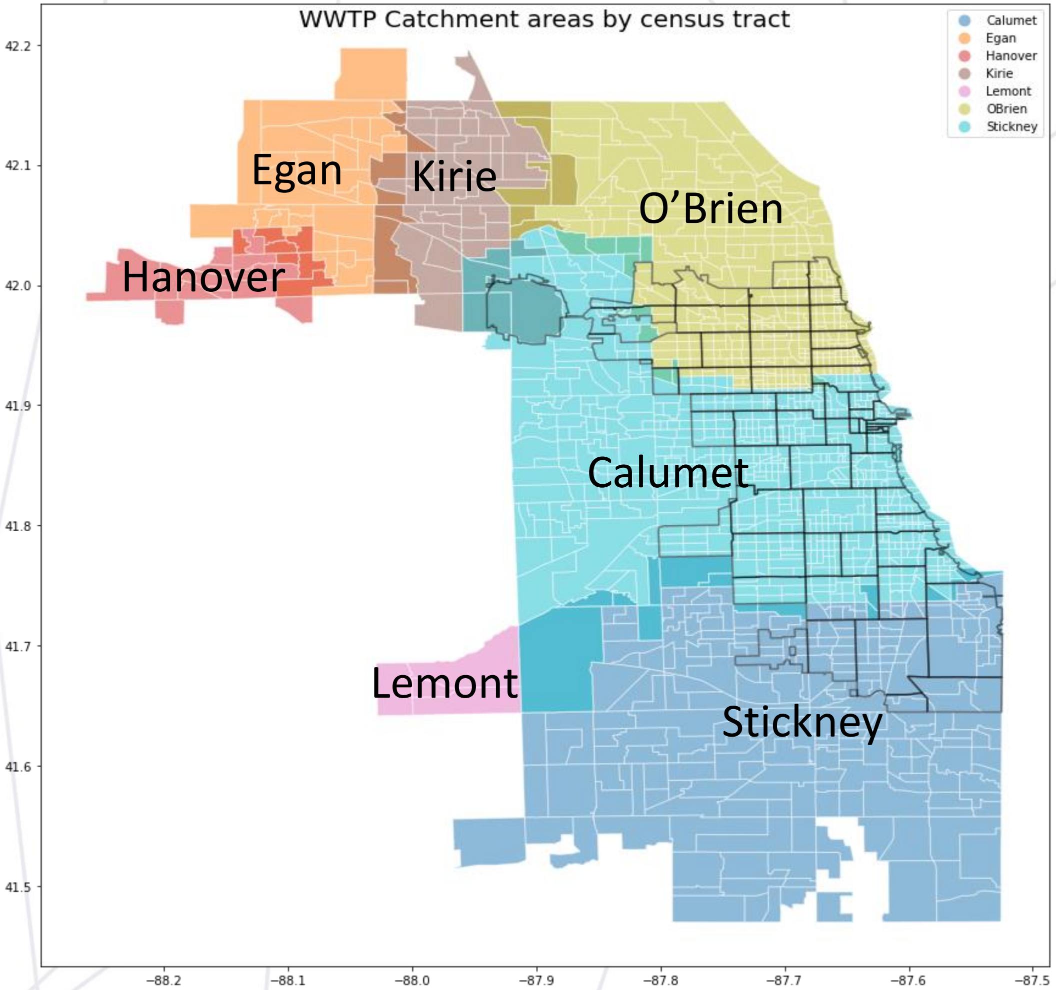
SARS-Cov2 RNA Data from Wastewater Catchment Areas

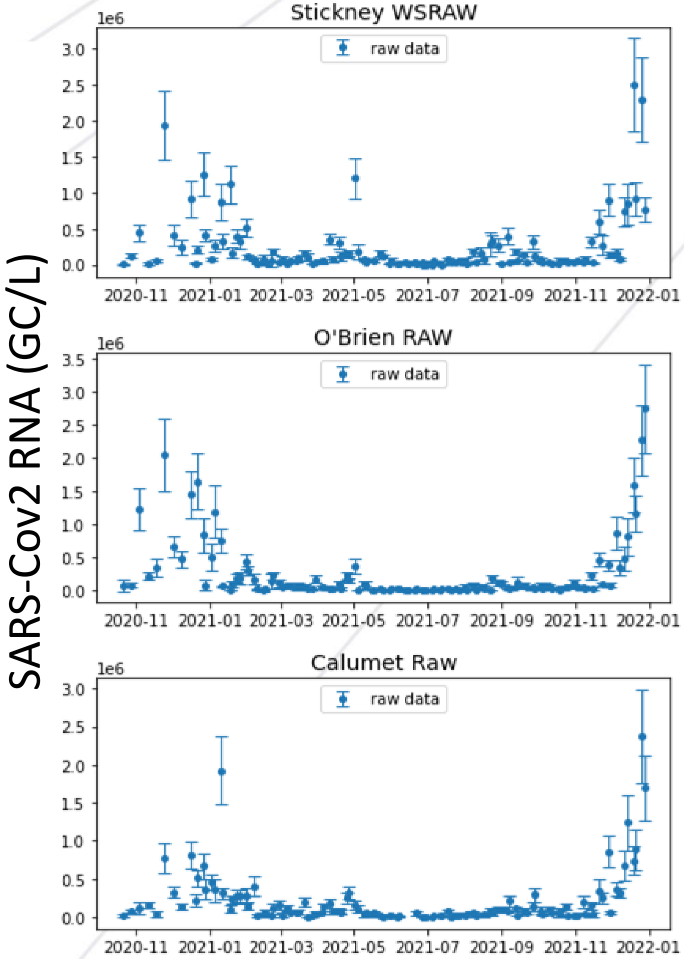




October 2020 to December 2021

SARS-Cov2 RNA Data from Wastewater Catchment Areas

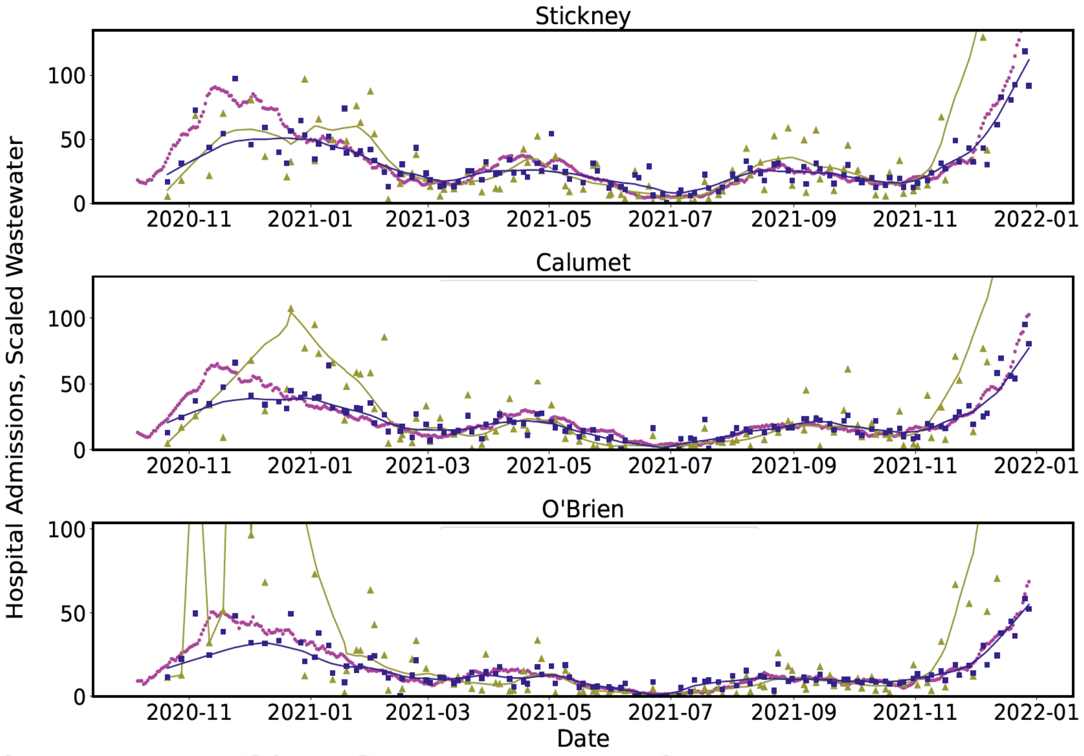


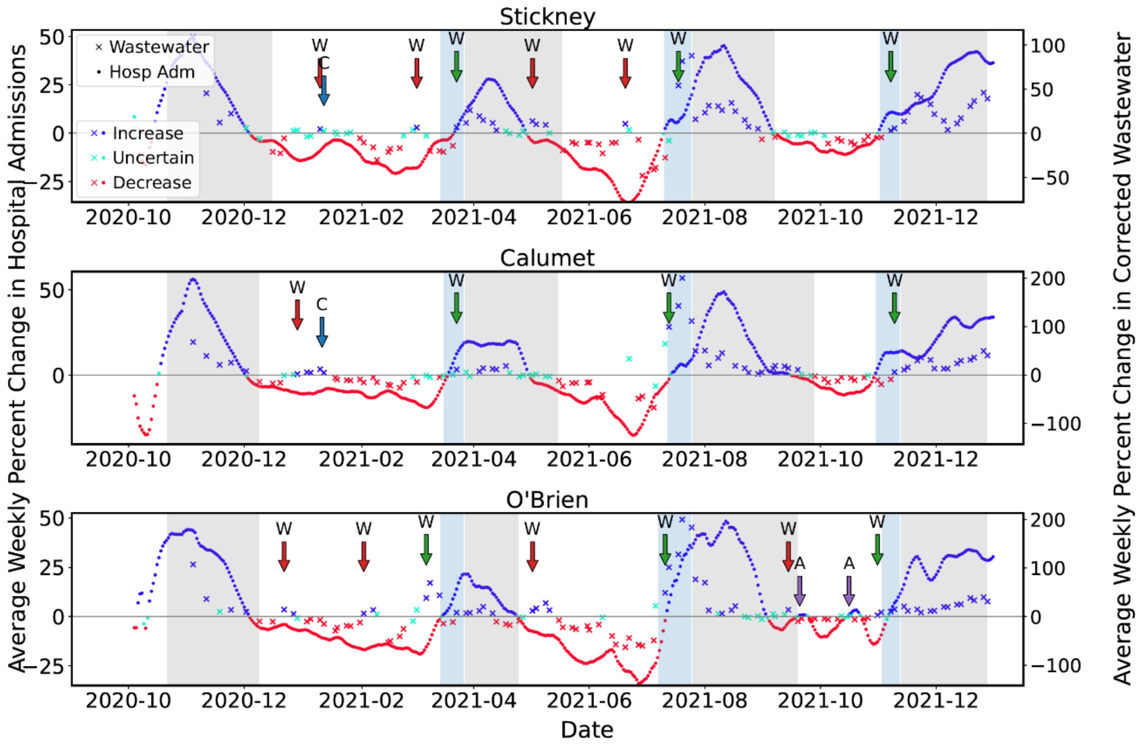


October 2020 to December 2021

Smaller Catchments:
December 2020
to February 2021

Punchline: RNA measurements in wastewater correlate with other public health indicators





Over the course of outbreak dynamics!

Specifically in capturing new surges!

Modeling improves these correlations.

Model development and selection pipeline

CHOOSE

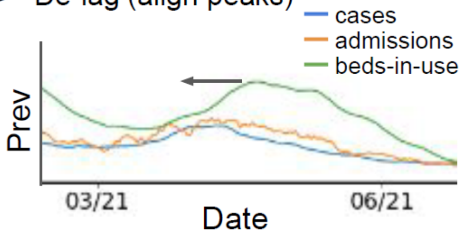
1. Most General Wastewater Model

$$(\text{prev}) = \frac{(\text{SARS-CoV-2})^a(\text{flow})^d(\text{const})}{(\text{PMMoV})^b(\text{BCoV recovery})^c}$$

- ➢ Include terms based on available data
- ➢ Include additional parameter for time lag

2. Prevalence Estimates

- ➢ Multiple indicators: cases, test positivity, hosp adm, beds-in-use
- ➢ Apply smoothing (7-day rolling ave)
- ➢ De-lag (align peaks)



Thank you CDPH & IDPH for working with us on epi-data

Model development and selection pipeline

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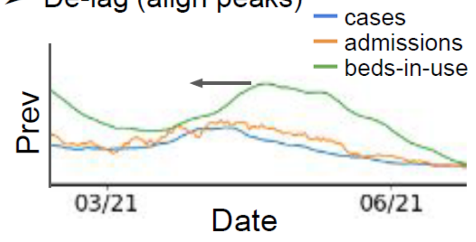

Dimensional/Physical analysis

$$(\text{prevalence [infected people/total people]})$$

$$= \frac{(\text{measured viral concentration [GC/L]})\ (\text{daily sewage volume [L]})}{(\text{viral shedding [GC/infected person]})\ (\text{viral recovery rate [\%]})\ (\text{contributing population [total people]})}$$

Model development and selection pipeline

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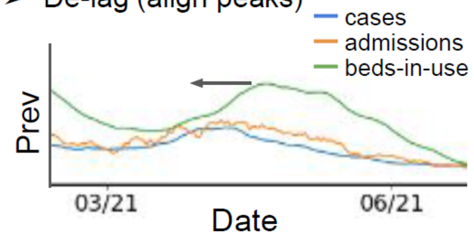

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Want to estimate terms based on measured:

N1 SARS-CoV2 RNA extracted from WW sample

Lab recovery control attenuated bovine coronavirus (BCoV)

Fecal load indicator Pepper mild mottle virus (PMMoV)

Flow rate at WWTP

Model development and selection pipeline

$$(\text{prevalence [infected people/total people]})$$

≈ Flow rate

$$= \frac{(\text{measured viral concentration [GC/L]})\ (\text{daily sewage volume [L]})}{(\text{viral shedding [GC/infected person]})\ (\text{viral recovery rate [\%]})\ (\text{contributing population [total people]})}$$

≈ Flow rate

$$(\text{N1 recovery}) \approx (\text{BCoV recovery})^{\alpha}$$

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Model development and selection pipeline

$\approx$ Flow rate

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$$= \frac{(\text{measured viral concentration [GC/L]})\ (\text{daily sewage volume [L]})}{(\text{viral shedding [GC/infected person]})\ (\text{viral recovery rate [\%]})\ (\text{contributing population [total people]})}$$

$$(\text{N1 recovery}) \approx (\text{BCoV recovery})^{\alpha}$$

$$(\text{N1 recovery}) \approx (\text{BCoV recovery})^{\alpha}$$

$$(\text{population from PMMoV [people]}) = \frac{(\text{measured PMMoV [GC/L]})\ (\text{daily sewage volume [L]})}{(\text{PMMoV shedding rate [GC/person]})\ (\text{PMMoV recovery rate [\%]})}$$

Model development and selection pipeline

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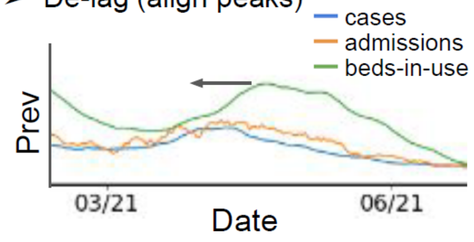

≈ Flow rate

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$(\text{N1 recovery}) \approx (\text{BCoV recovery})^{\alpha}$

≈ Flow rate 

≈ constant

≈ constant

$(\text{PMMoV recovery}) \approx (\text{BCoV recovery})^{\gamma}$

Model development and selection pipeline

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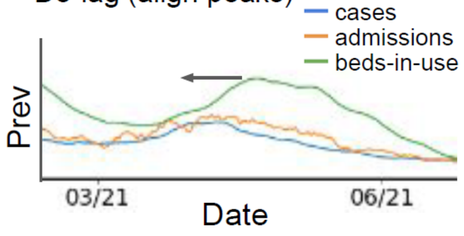

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$$(\text{N1 recovery}) \approx (\text{BCoV recovery})^{\alpha}$$

$\approx$ Flow rate

$\approx$ constant

$\approx$ constant

$$(\text{PMMoV recovery}) \approx (\text{BCoV recovery})^{\gamma}$$

$$\text{prev} \approx \frac{(\text{SARS-CoV-2})^a(\text{flow})^d}{(\text{PMMoV})^b(\text{BCoV recovery})^c}(\text{constant})$$

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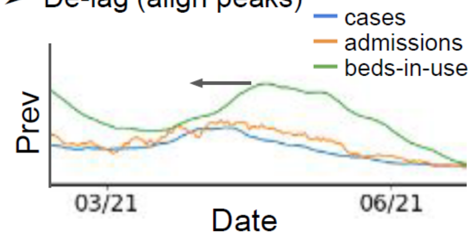

FIT

3. Select Submodels

- Choose specific sub-models, e.g.

$$(\text{prev}) = \frac{(\text{SARS-CoV-2})(\text{const})}{(\text{PMMoV})}$$

$$(\text{prev}) = \frac{(\text{SARS-CoV-2})^a(\text{const})}{(\text{BCoV recovery})^c}$$

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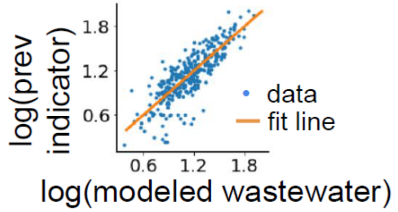
4. Fit Model Parameters

- Fit each combination of model, lag, prevalence estimate separately



Model development and selection pipeline

CHOOSE

1. Most General Wastewater Model

$$(\text{prev}) = \frac{(\text{SARS-CoV-2})^a (\text{flow})^d (\text{const})}{(\text{PMMoV})^b (\text{BCoV recovery})^c}$$

- Include terms based on available data
- Include additional parameter for time lag

2. Prevalence Estimates

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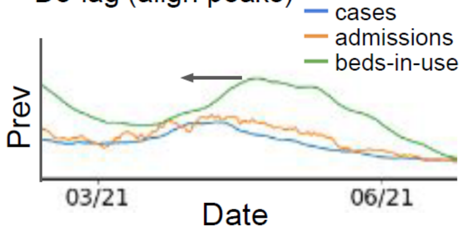

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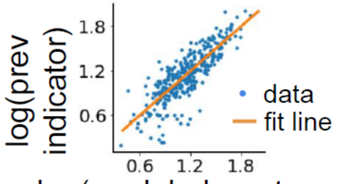

Power-law Models:

No additional terms	$\text{prev} = (\text{const})\,(N_1)^a$
Correct with flow rate only	$\text{prev} = (\text{const})\,(N_1)^a\,(\text{Flow})^d$
Correct with PMMoV only	$\text{prev} = (\text{const})\dfrac{(N_1)^a}{(\text{PMMoV})^b}$
Correct with BCoV only	$\text{prev} = (\text{const})\dfrac{(N_1)^a}{(\text{BCoV recovery})^c}$
Correct with BCoV and flow rate	$\text{prev} = (\text{const})\dfrac{(N_1)^a\,(\text{Flow})^d}{(\text{BCoV recovery})^c}$
Correct with BCoV and PMMoV	$\text{prev} = (\text{const})\dfrac{(N_1)^a}{(\text{PMMoV})^b\,(\text{BCoV recovery})^c}$
Correct with PMMoV, BCoV, and flow rate	$\text{prev} = (\text{const})\dfrac{(N_1)^a\,(\text{Flow})^d}{(\text{PMMoV})^b\,(\text{BCoV recovery})^c}$

Model development and selection pipeline

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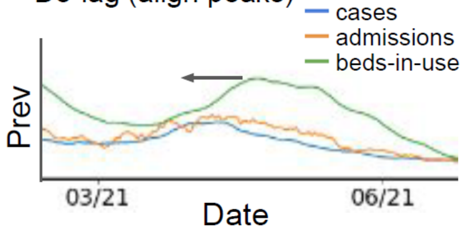

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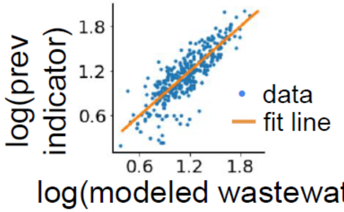

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Non-Power-law Models:

Set powers a,b,c,d = {0, 1}

Similar to commonly used normalization

Model development and selection pipeline

CHOOSE

1. Most General Wastewater Model

$$(\mathrm{prev}) = \frac{(\mathrm{SARS\text{-}CoV\text{-}2})^a(\mathrm{flow})^d(\mathrm{const})}{(\mathrm{PMMoV})^b(\mathrm{BCoV\ recovery})^c}$$

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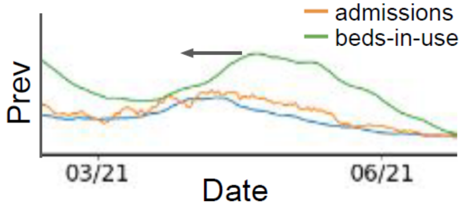

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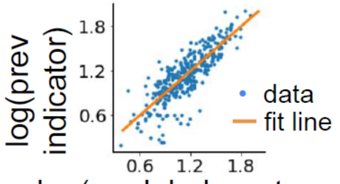
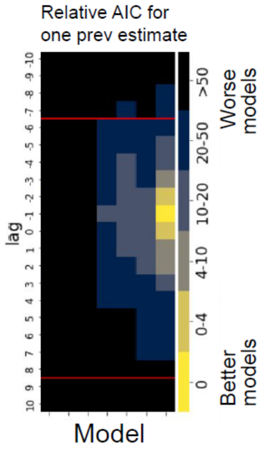


EVALUATE

5. Downselect

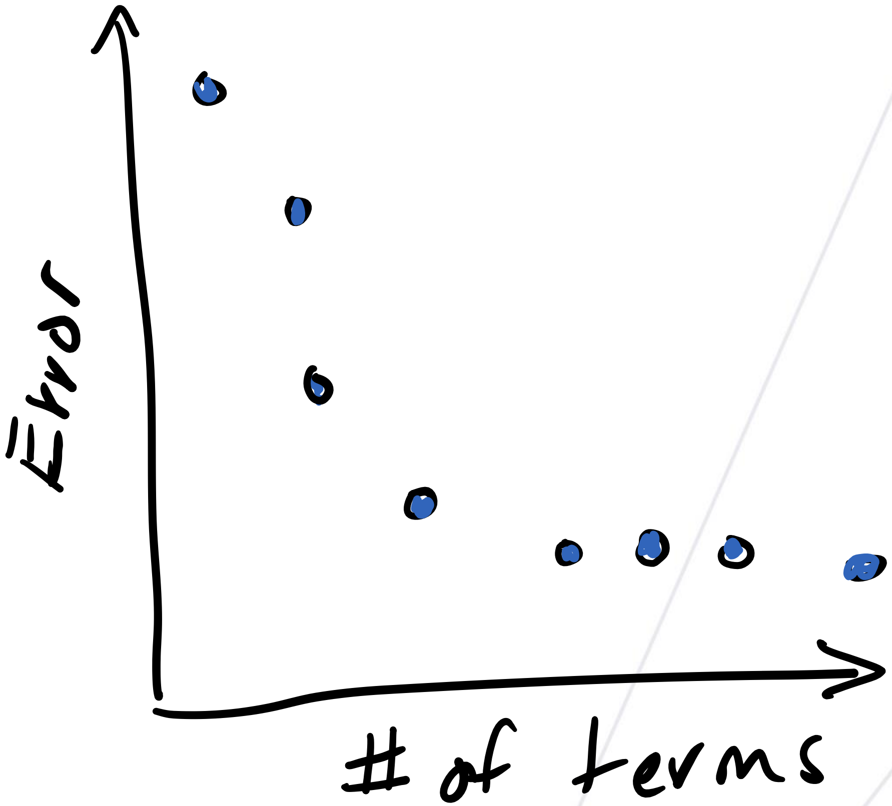
- Calculate relative AIC for all model - lag combinations within each prev estimate
- Eliminate models that consistently have relative AIC > 20
- Keep range of lags for each prevalence estimate with relative AIC<10 for any model
- Be careful of less trustworthy prevalence estimates (i.e. cases)



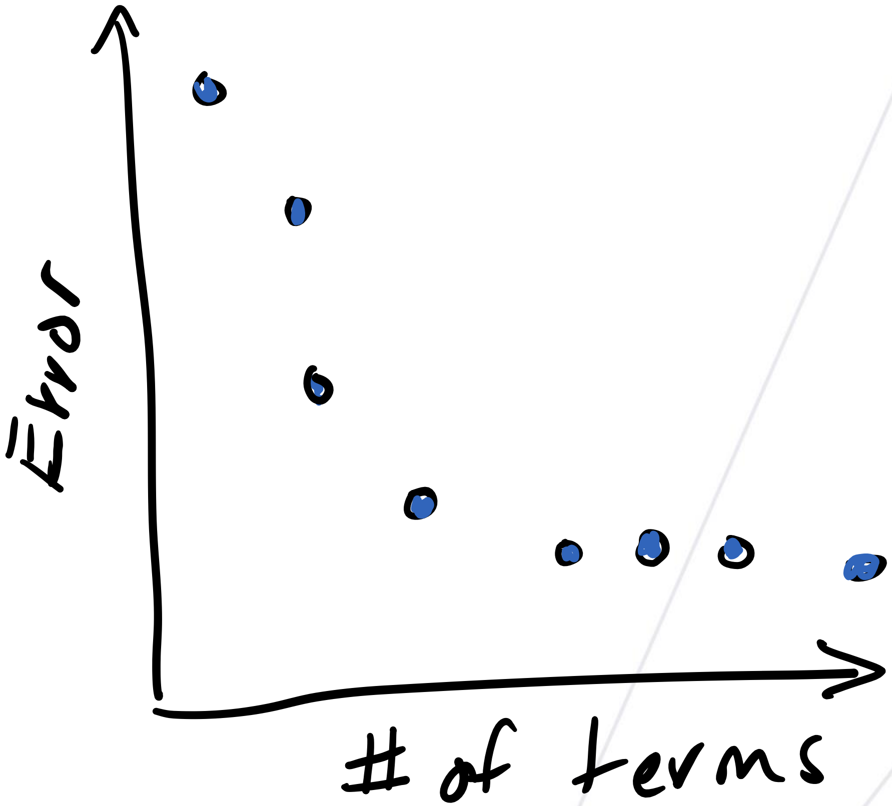
6. Check

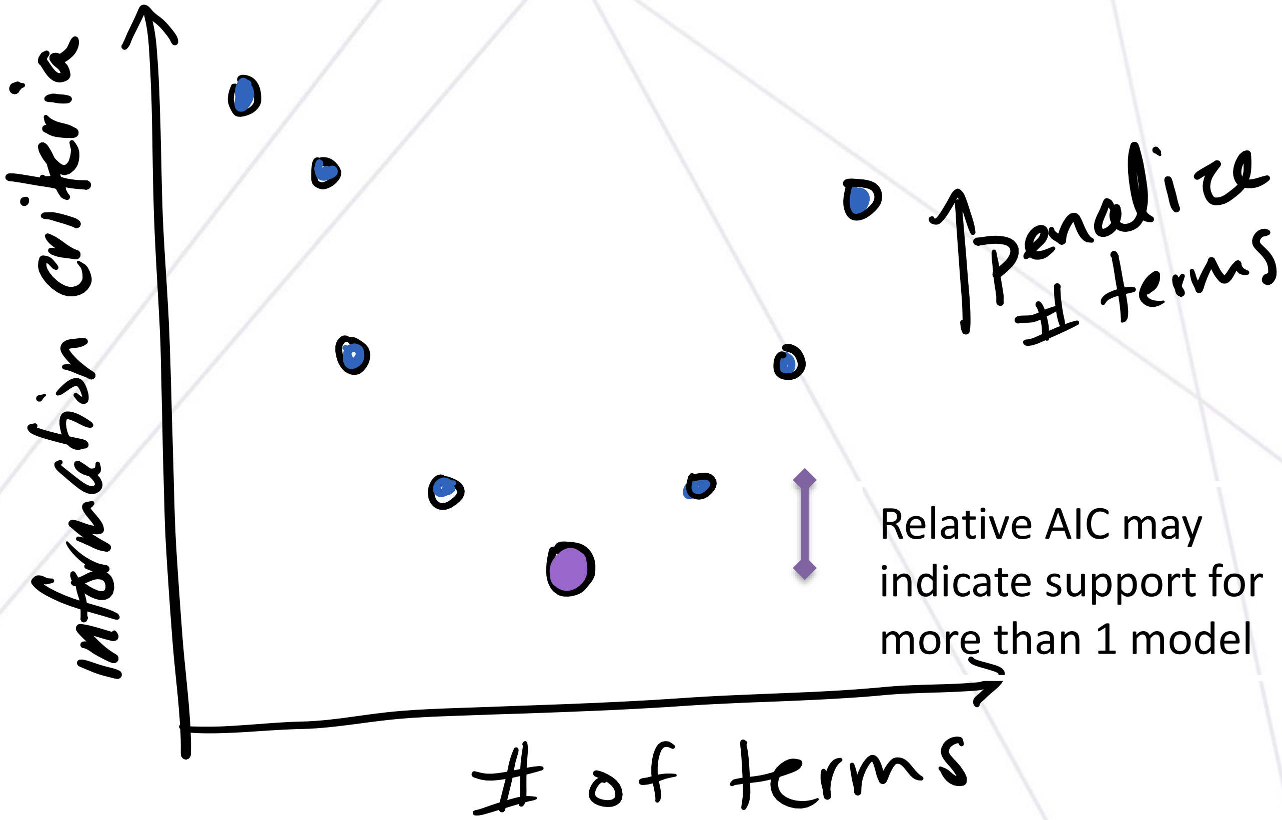
- Are optimal lags within a reasonable range?
- How different are the parameter values for different lags and models?
- Evaluate parameter signs with possible interpretation
- Evaluate performance of best models for desired outputs (e.g. correlation, trend analysis)

Finding parsimonious models: Akaike information criteria

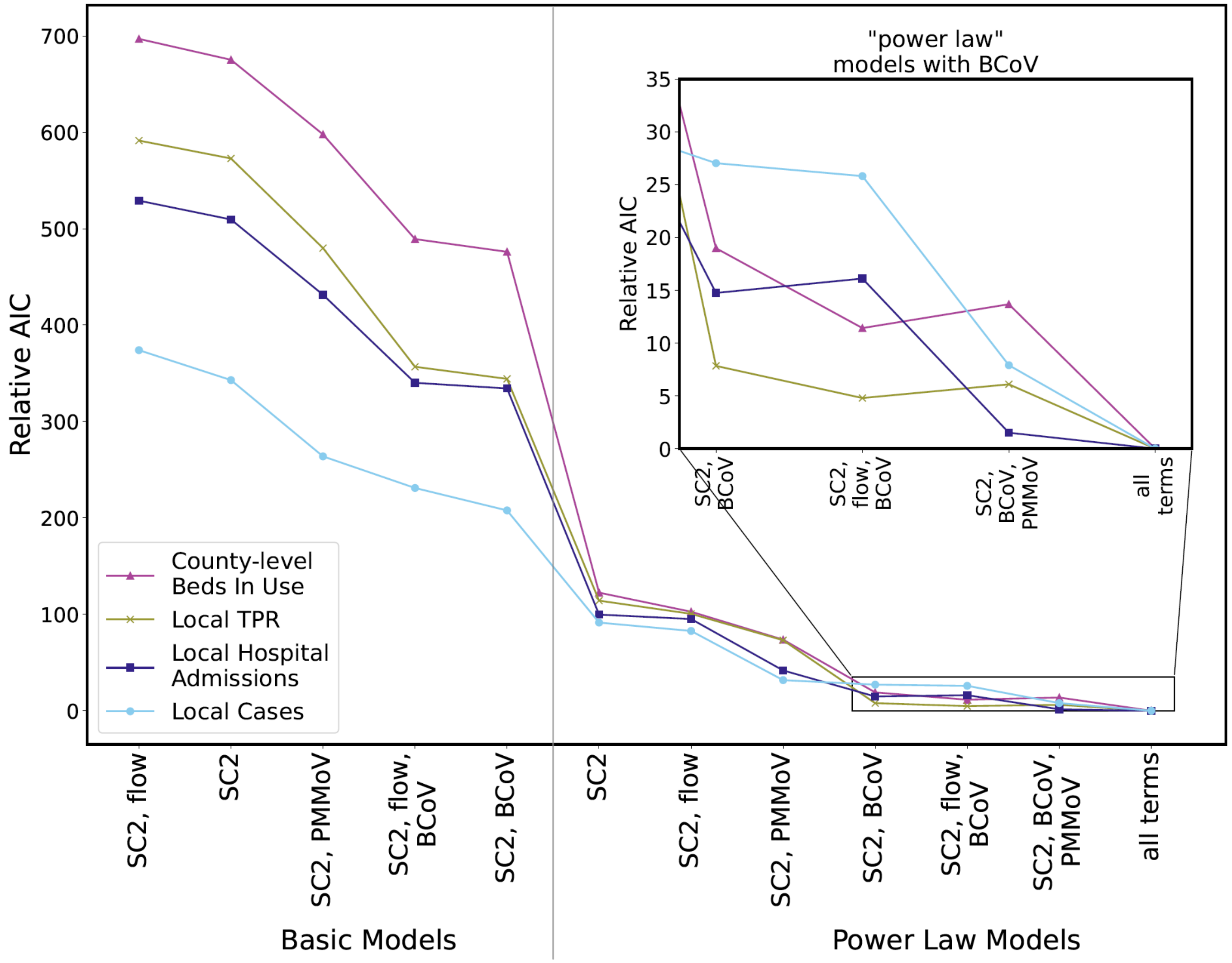


Finding parsimonious models: Akaike information criteria

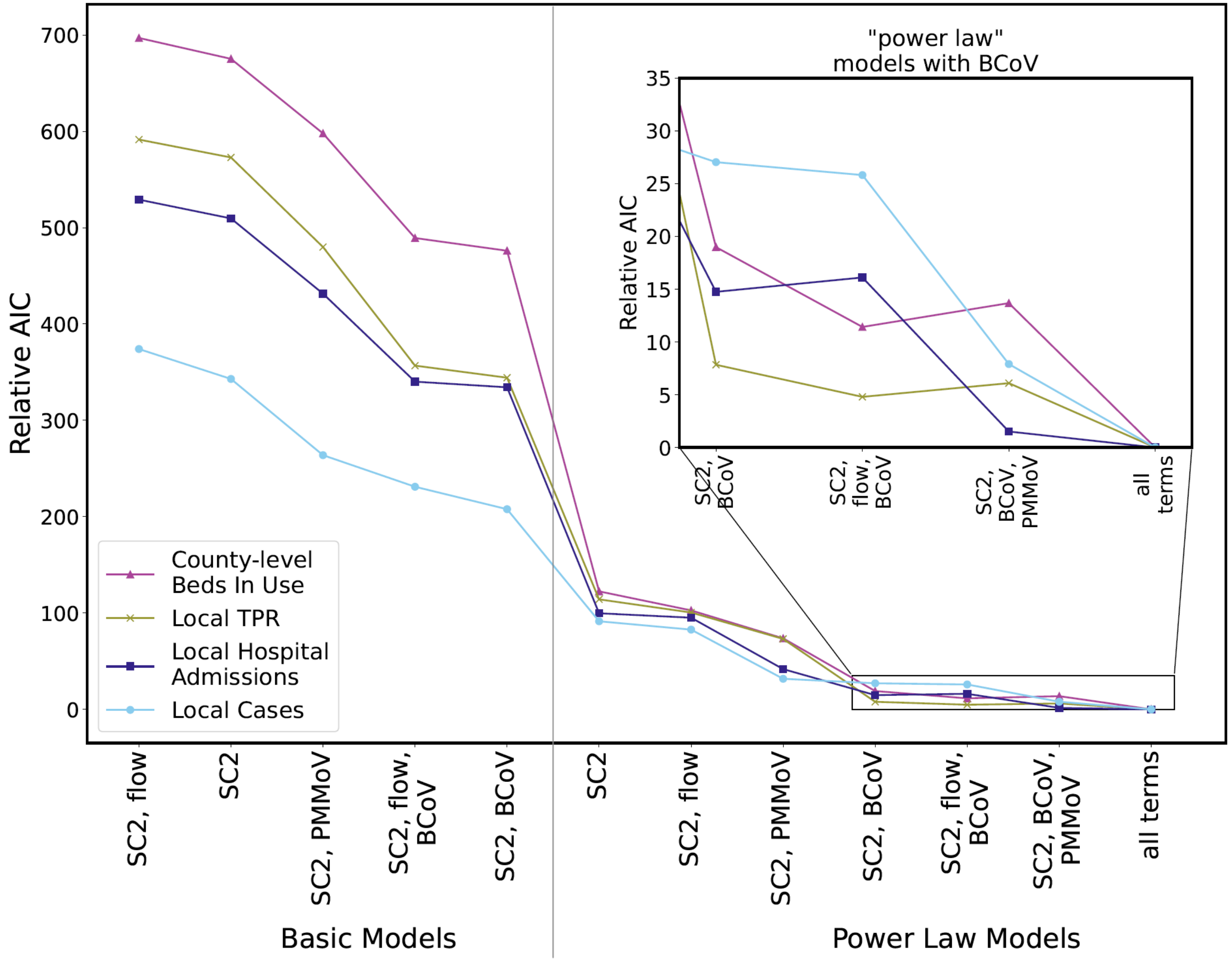




Model ranking and recommendations



Model ranking and recommendations



Always ranked best!


Correct with PMMoV, BCoV, and flow rate

$$\text{prev} = (\text{const})\frac{(N_1)^a\,(\text{Flow})^d}{(\text{PMMoV})^b\,(\text{BCoV recovery})^c}$$


Also better than nothing:


Correct with BCoV and PMMoV

$$\text{prev} = (\text{const})\frac{(N_1)^a}{(\text{PMMoV})^b\,(\text{BCoV recovery})^c}$$

Correct with BCoV only

$$\text{prev} = (\text{const})\frac{(N_1)^a}{(\text{BCoV recovery})^c}$$

Correct with BCoV and flow rate

$$\text{prev} = (\text{const})\frac{(N_1)^a\,(\text{Flow})^d}{(\text{BCoV recovery})^c}$$

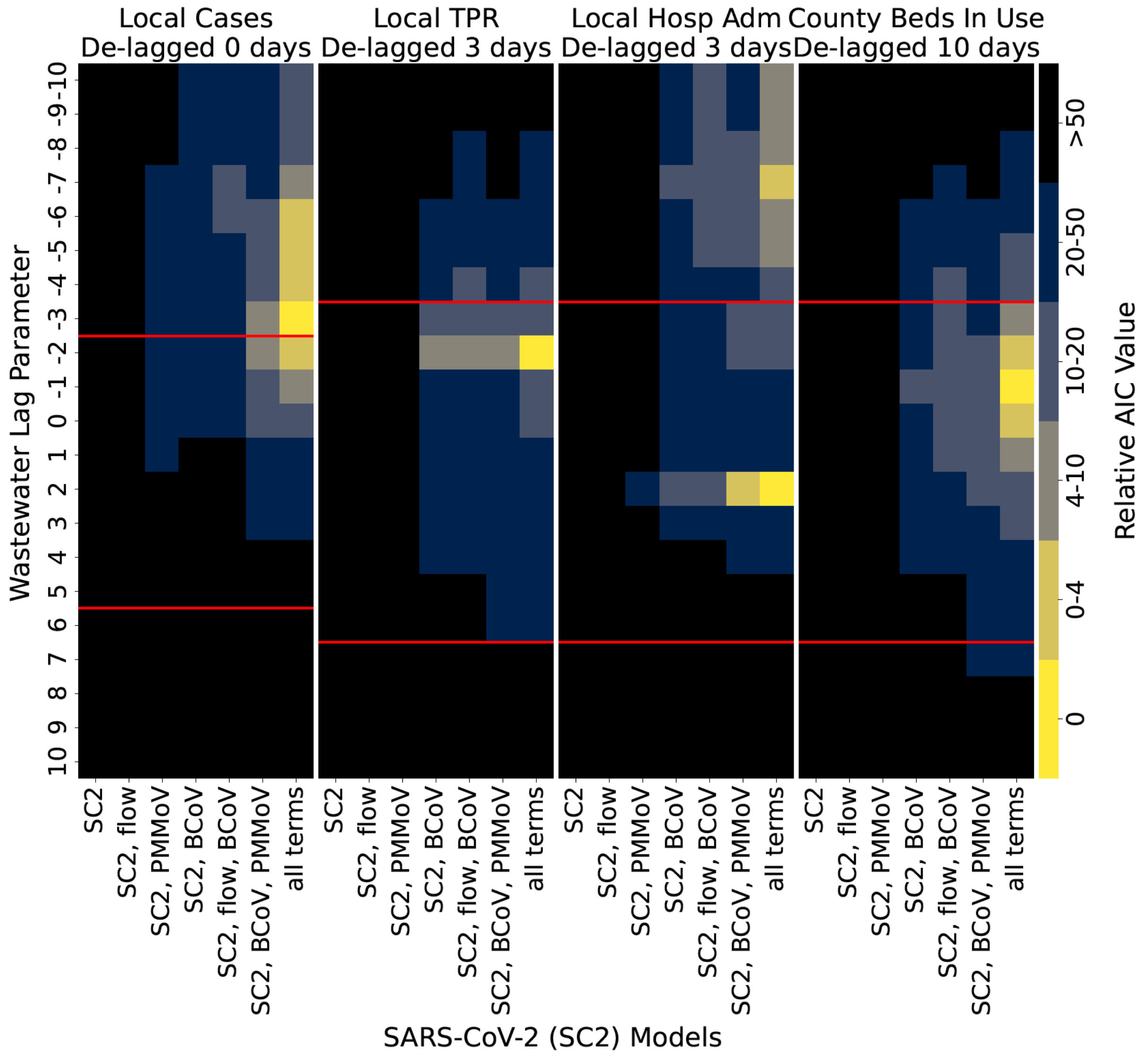

Limited improvement:


Flow rate only

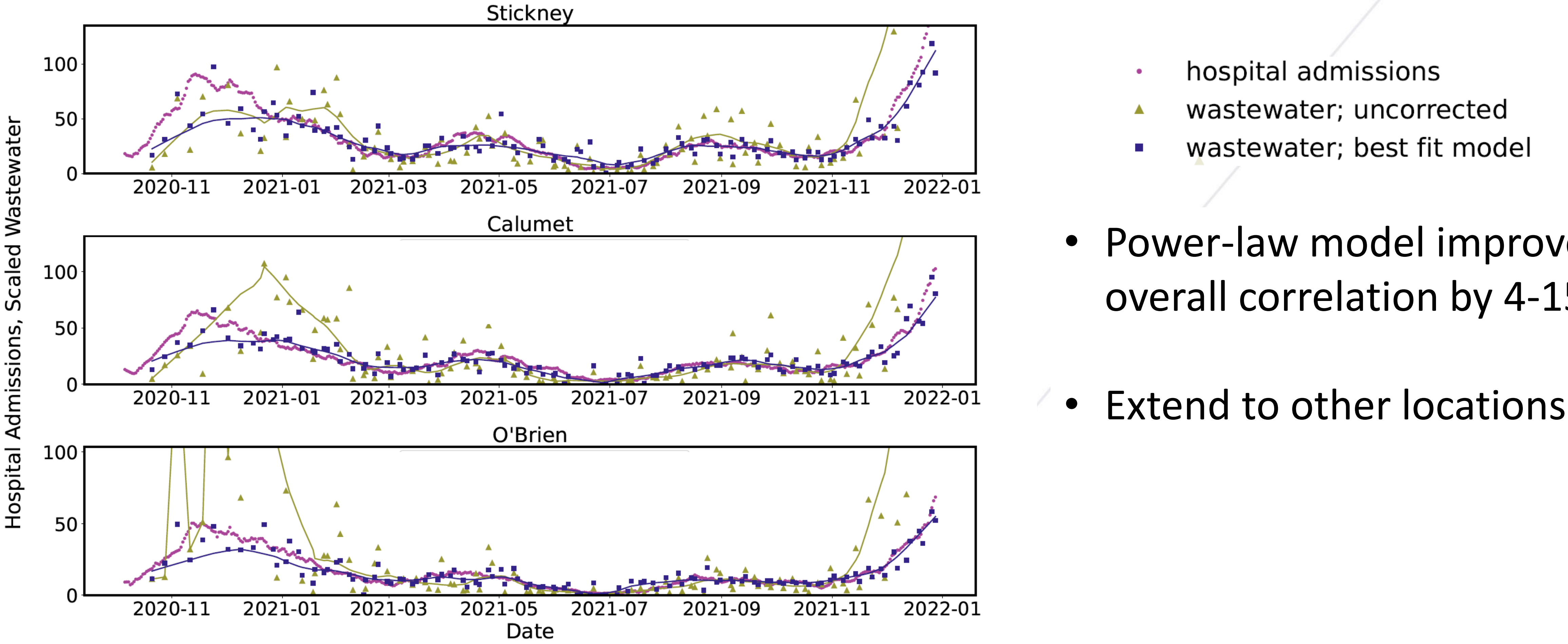

PMMoV only

Power-law model ranking and lag analysis

- Best models are within physical lags
- Robust across prevalence indicators
- Cases is less reliable

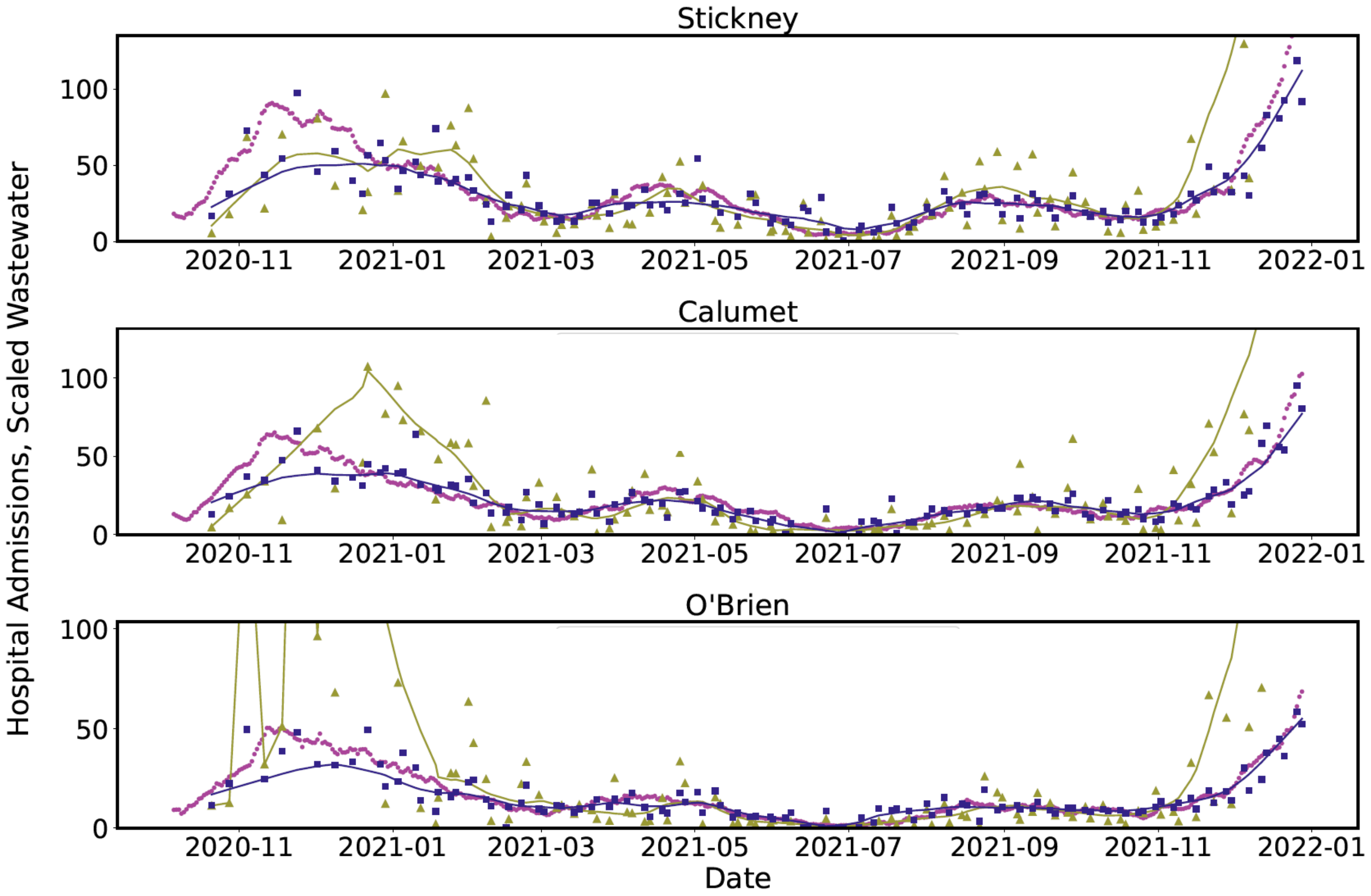


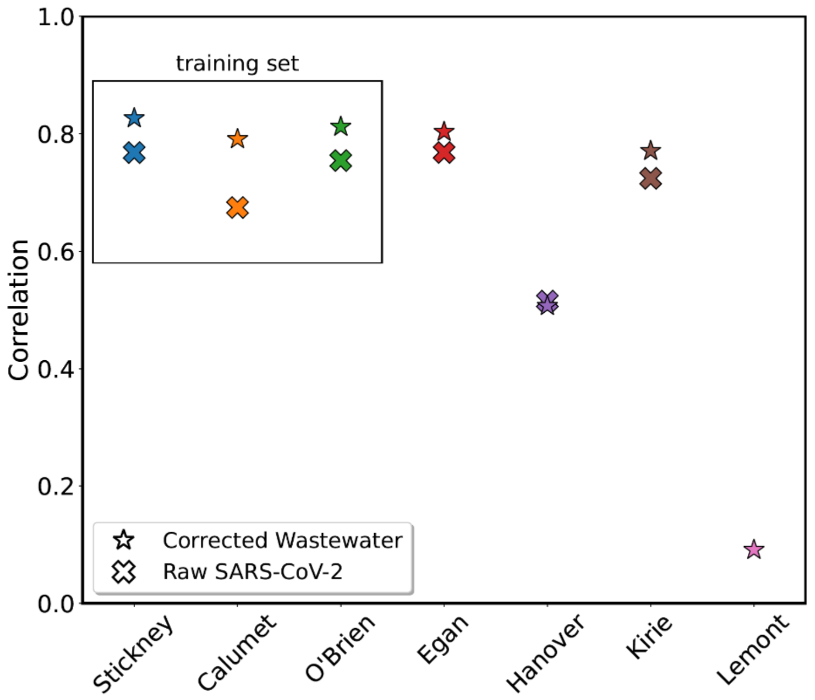
RNA in wastewater correlates with hospitalization data



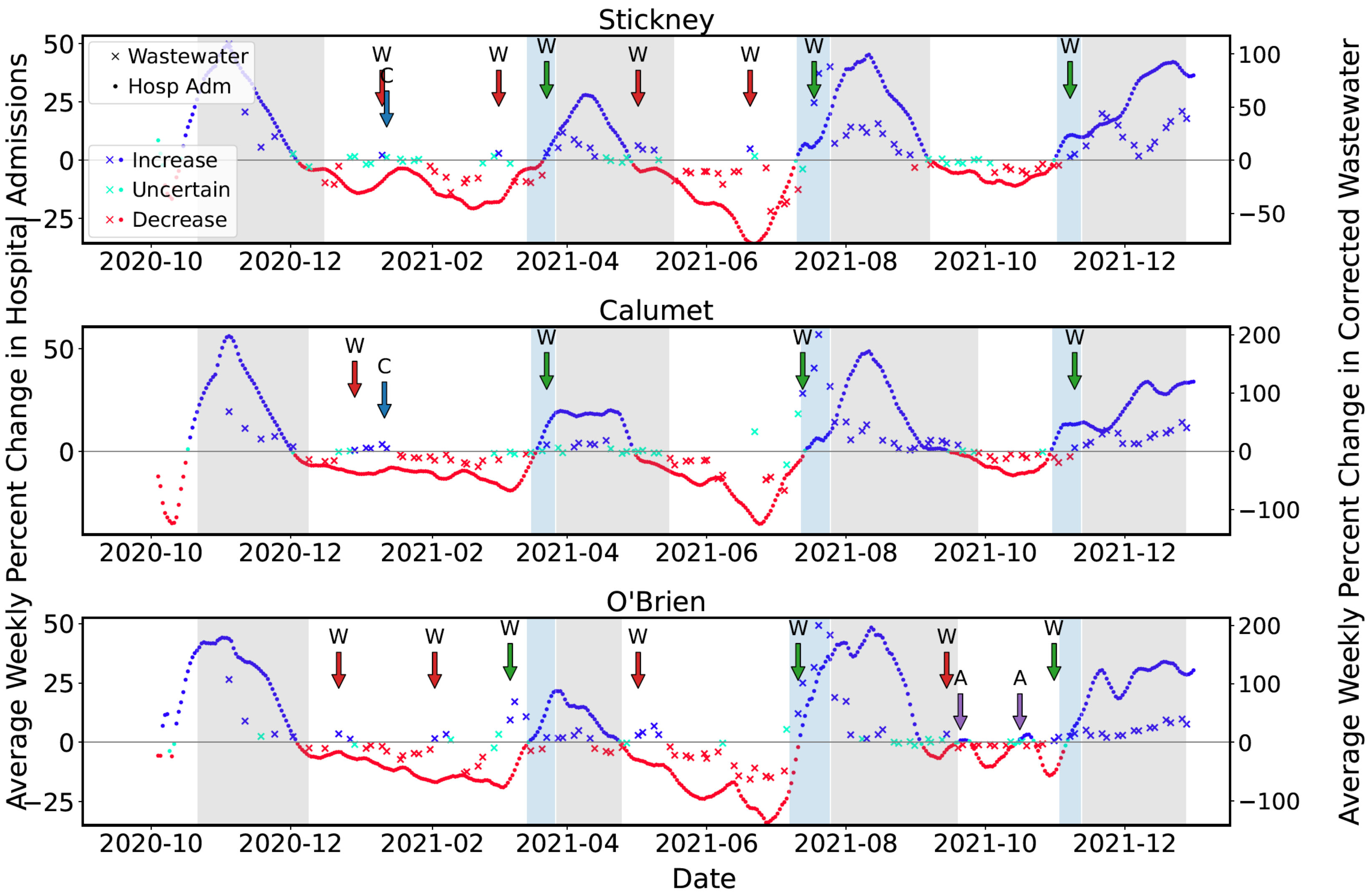
- Power-law model improves overall correlation by 4-15%
- Extend to other locations?

RNA in wastewater correlates with hospitalization data





RNA in wastewater detects all major surges



4-week trend analysis

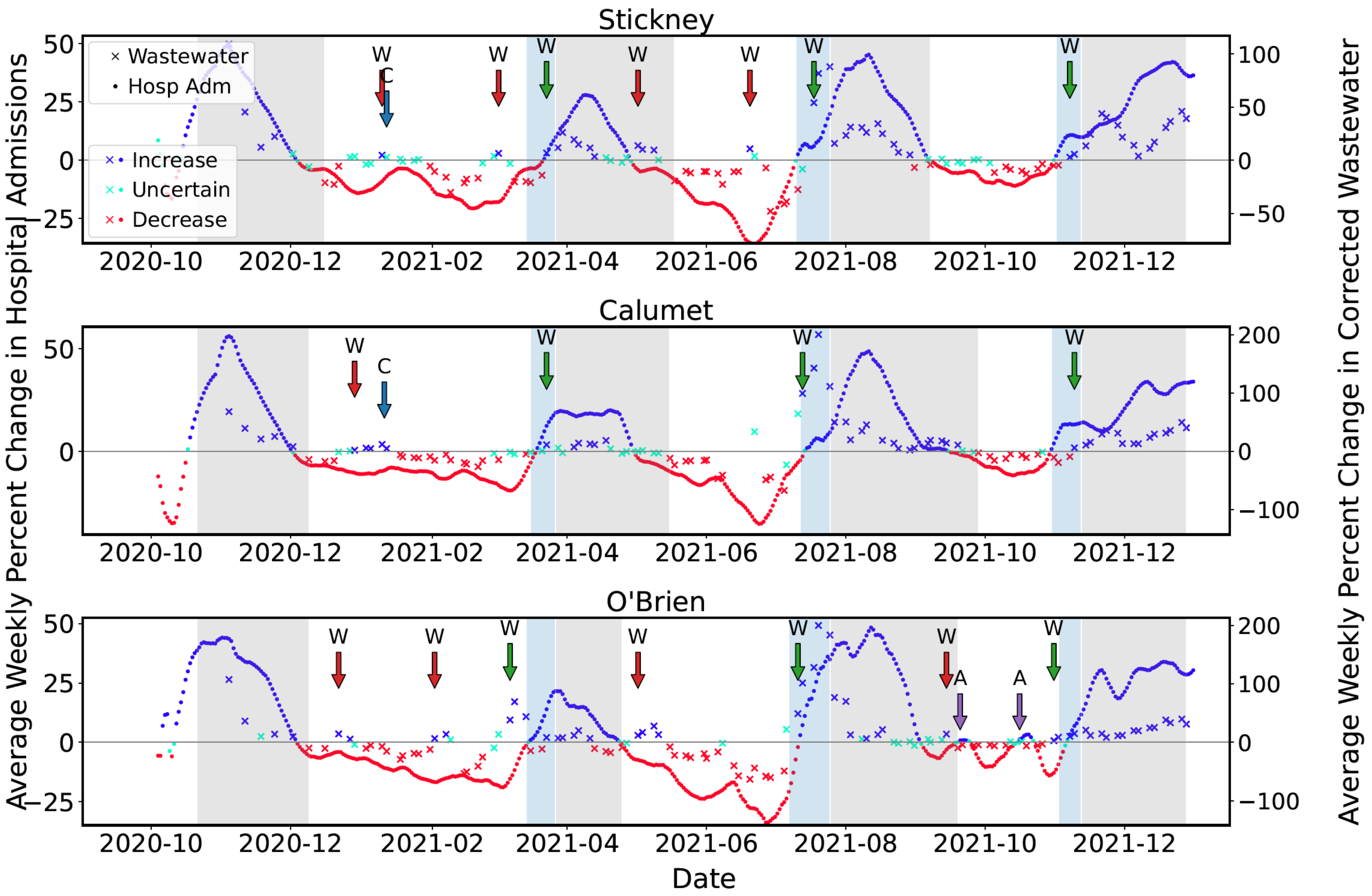
- Hospital admissions
- RNA detected in wastewater

Likely increase indicates >66% confidence of increasing slope

Likely increase indicates >66% confidence of decreasing slope

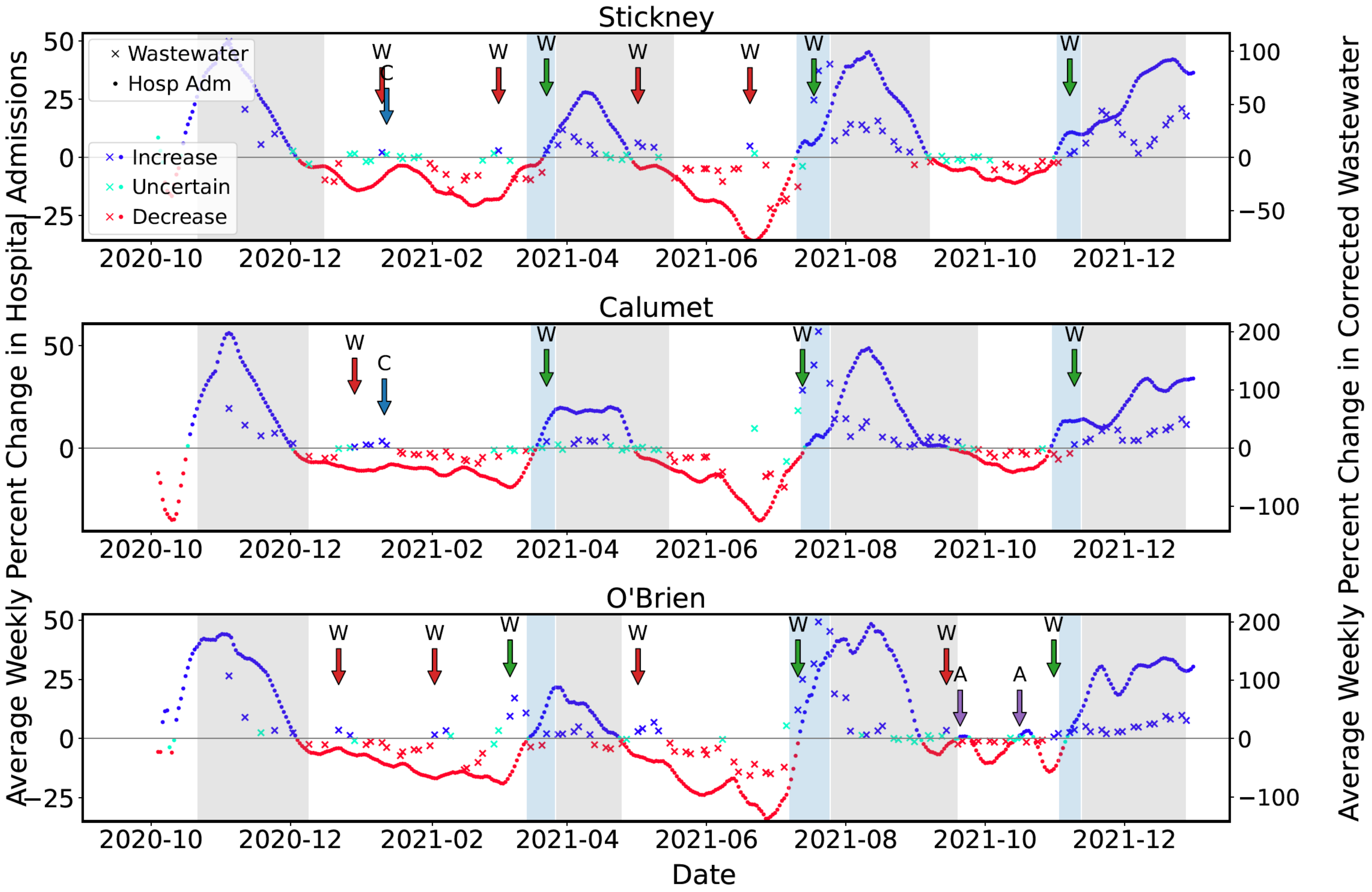
Uncertain is <66% confidence in slope change

RNA in wastewater detects all major surges



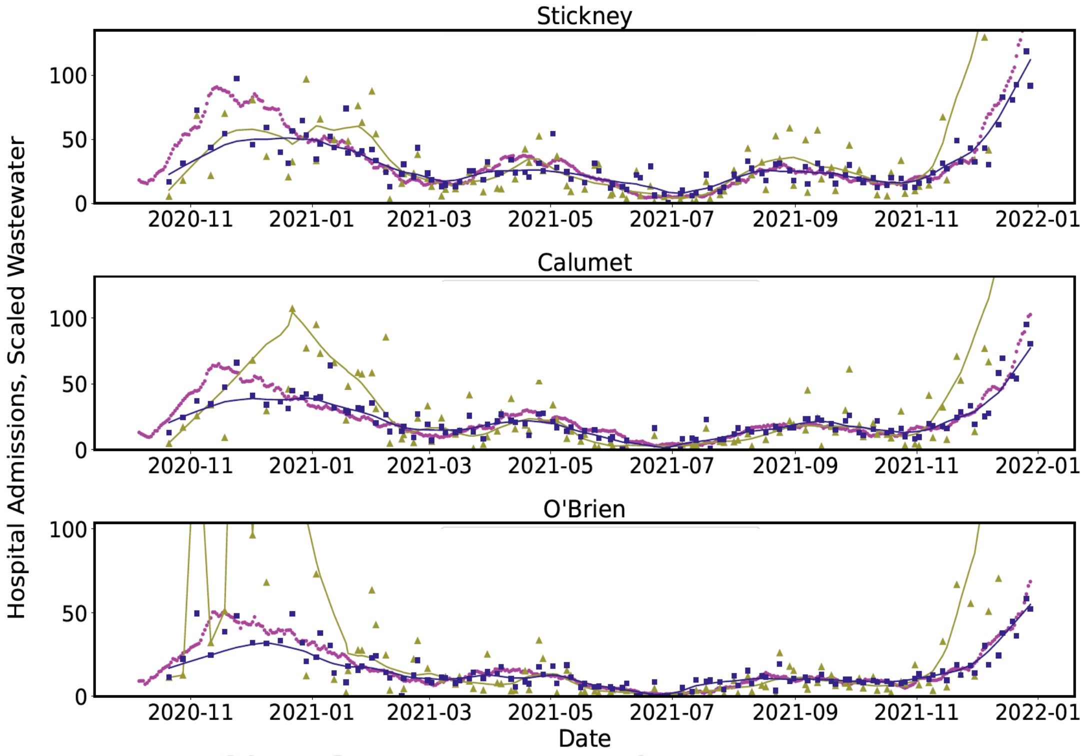
- Trend analysis identifies 18 likely increase in RNA wastewater measurements
- RNA in wastewater identifies all 9 major surges

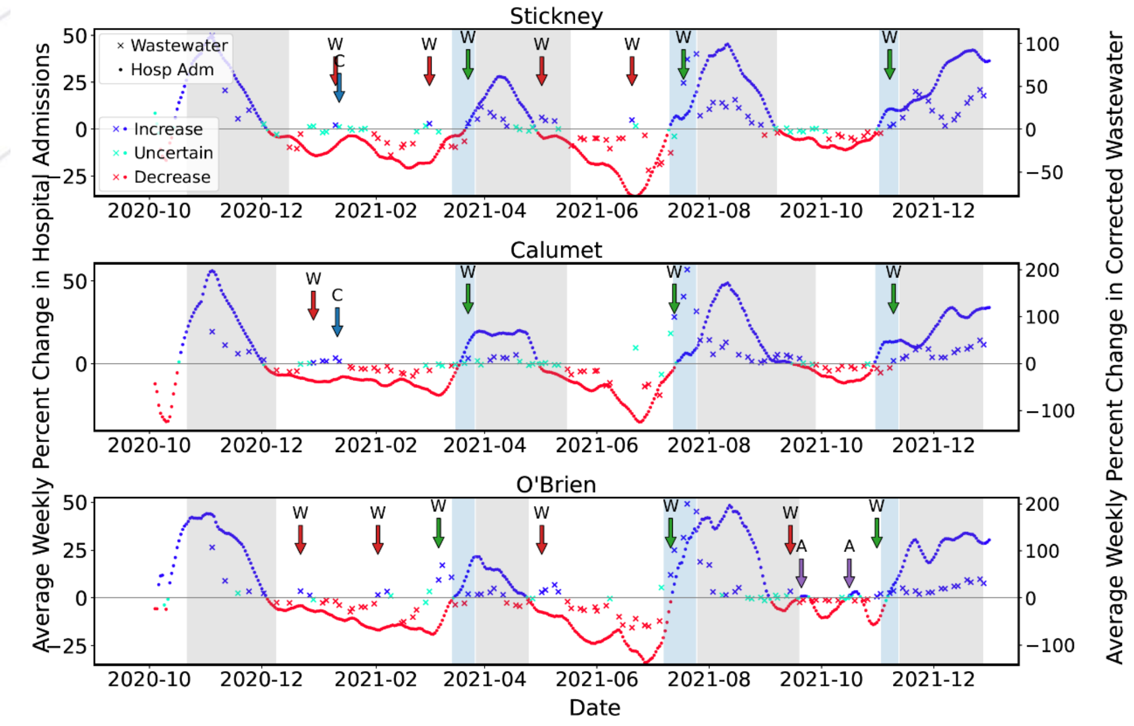
RNA in wastewater detects all major surges



- Trend analysis identifies 18 likely increase in RNA wastewater measurements
- RNA in wastewater identifies all 9 major surges
- 4 other likely increases in RNA wastewater correspond to increase in other indicators
- 5 unsupported likely increases

Punchline: RNA measurements in wastewater correlate with other public health indicators





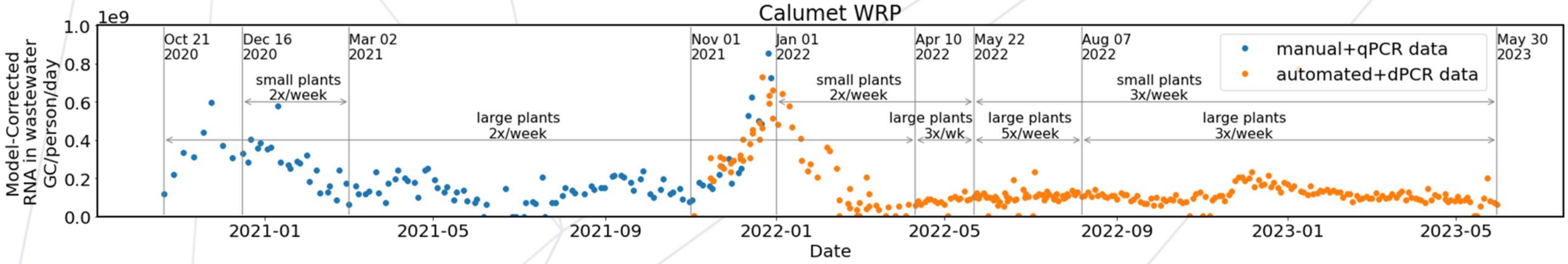
Over the course of outbreak dynamics!

Specifically in capturing new surges!

Modeling improves these correlations & has been integrated into our public health reporting

Northwestern

Transfer Model to high-throughput data



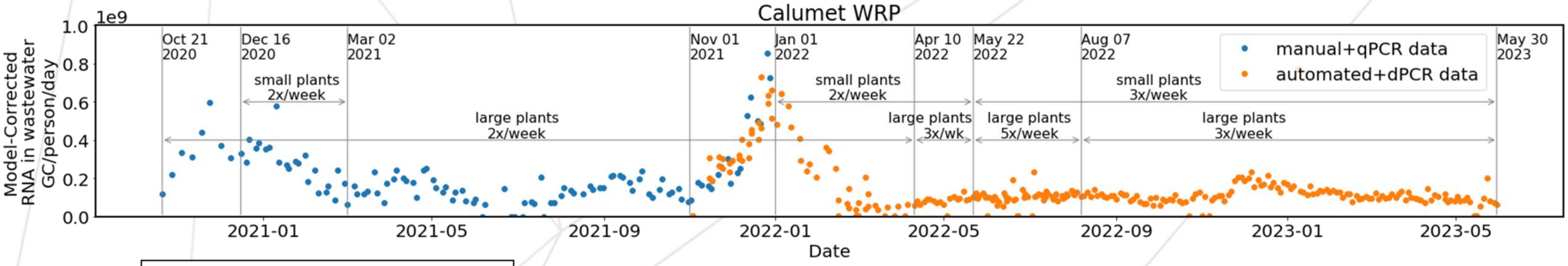
Low-throughput

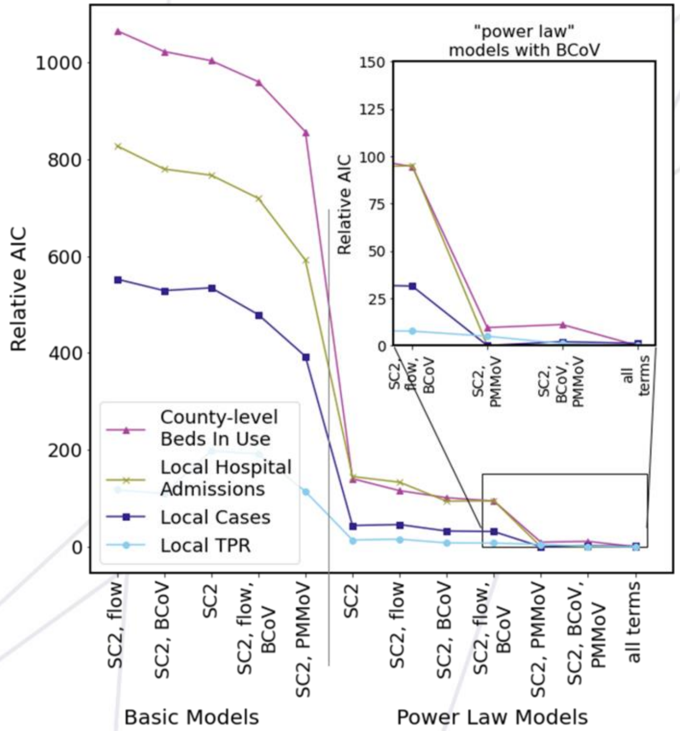
- **by hand**
- **qPCR quantification**
- **lower sensitivity**
- **Larger sample**

High-throughput

- **Robots**
- **dPCR quantification**
- **higher sensitivity**
- **Smaller sample**

Transfer Model to high-throughput data





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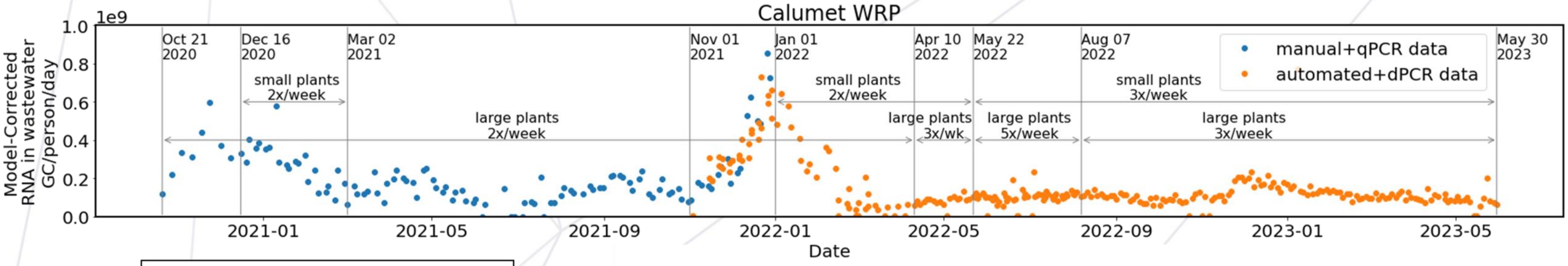

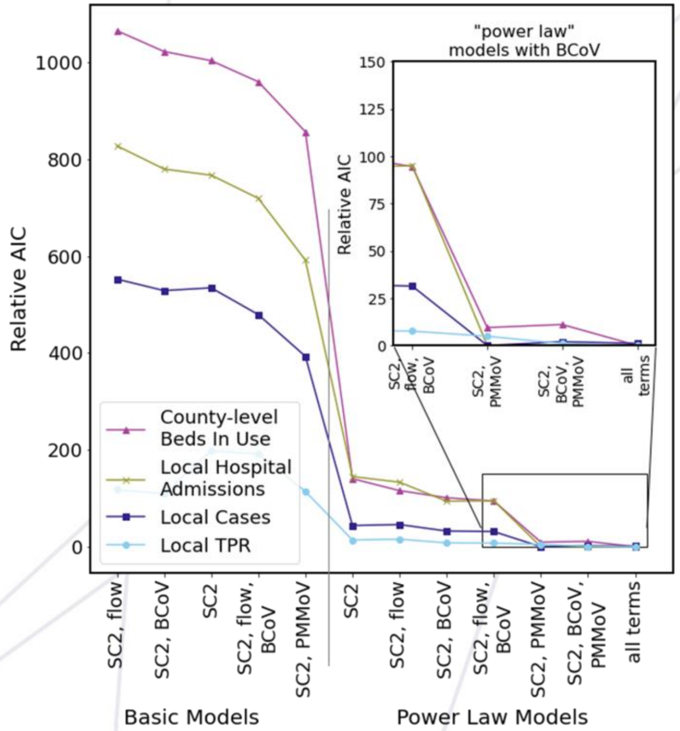

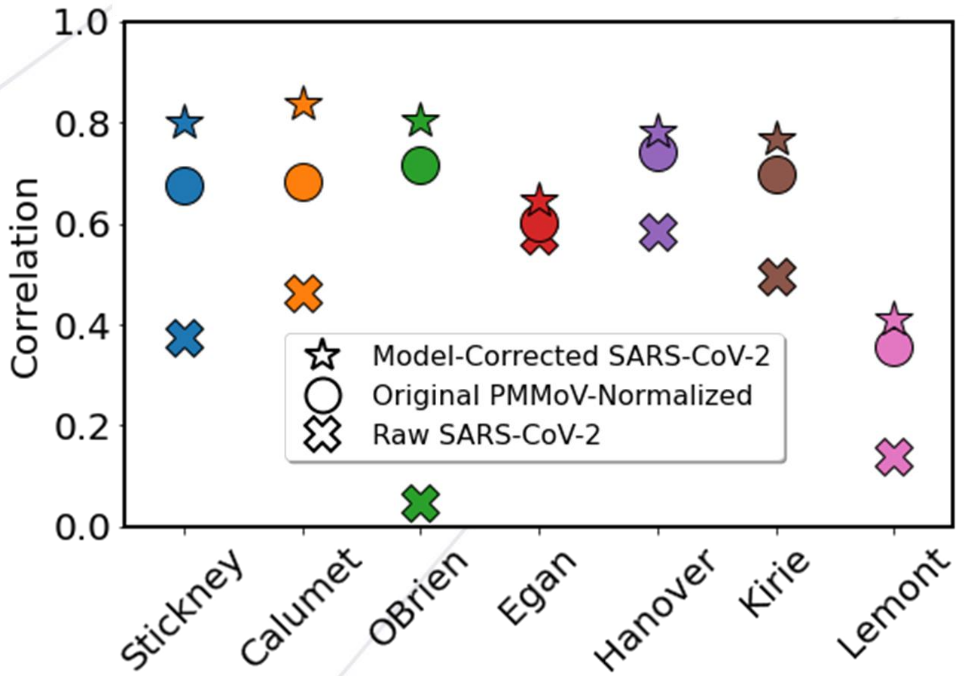

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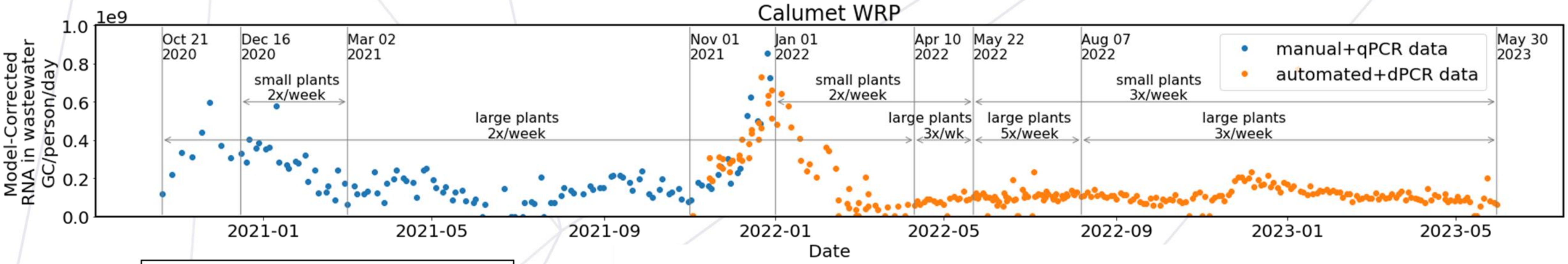
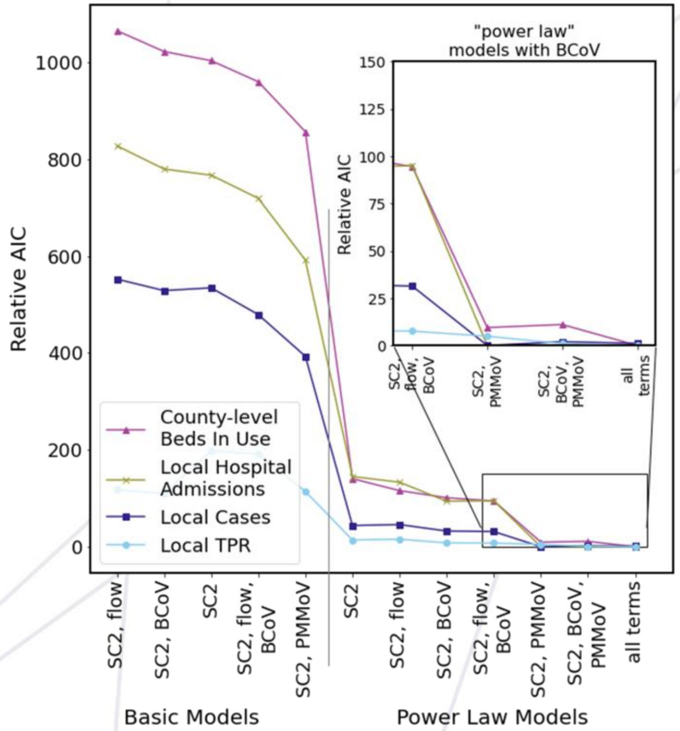
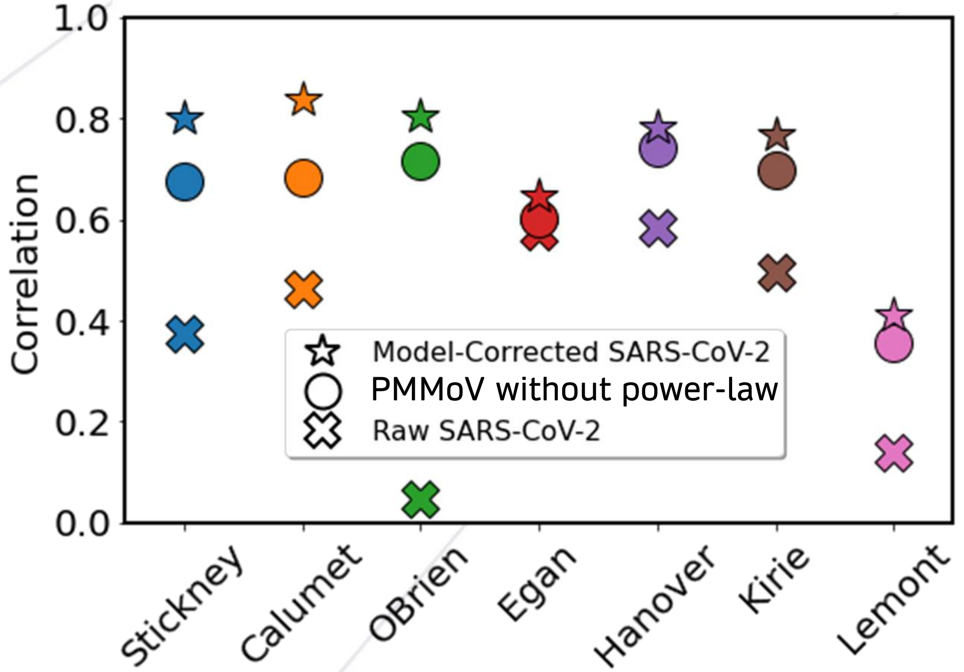


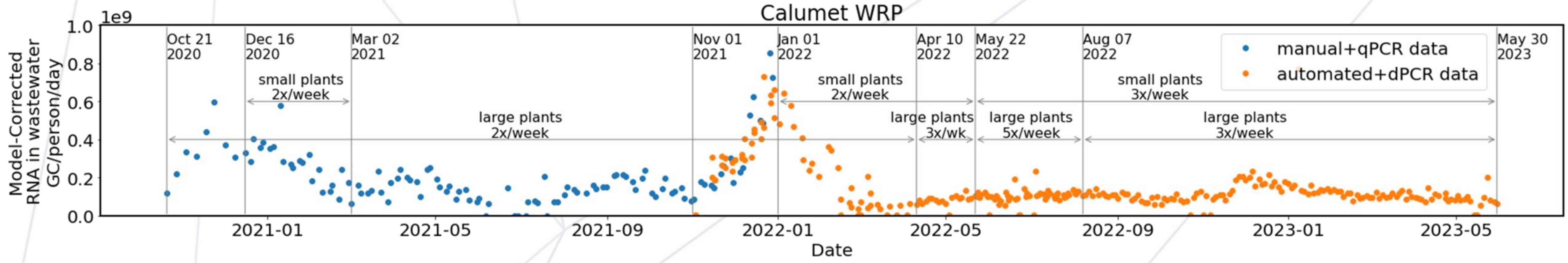


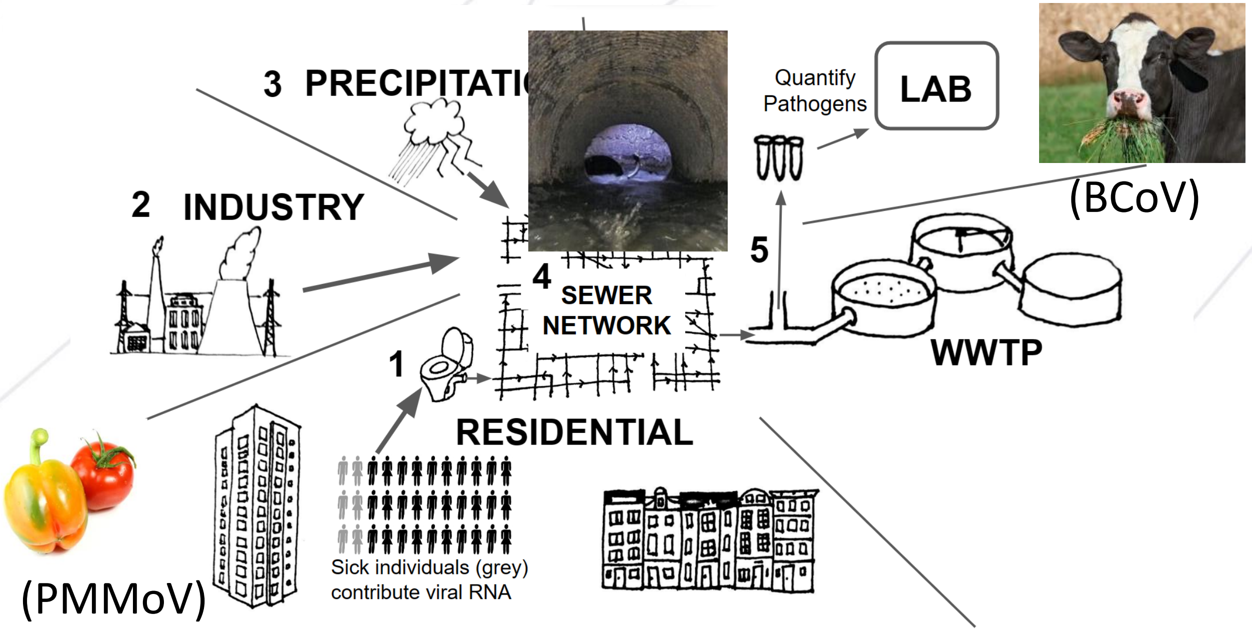


	Experimental throughput	
	low	high
a (SARS-CoV-2)	0.548	0.369
b (PMMoV)	0.152	0.255
c (BCoV)	0.224	0.018
d (Flow Rate)	-0.096	-0.169

Model parameters change
PMMoV becomes more important!

Transfer Model to high-throughput data





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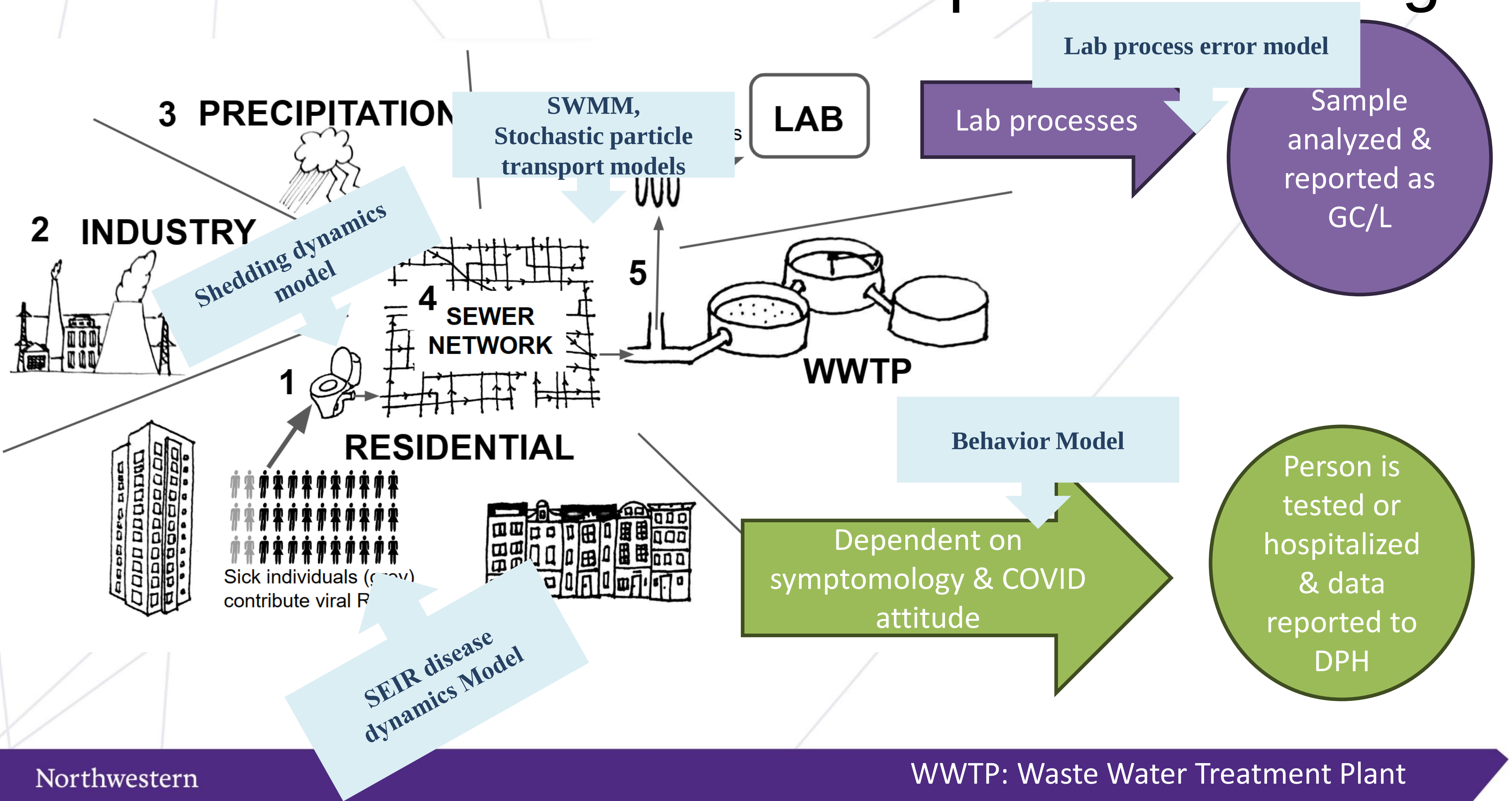
Current/Future work: improve modeling



WWTP: Waste Water Treatment Plant

Thank you!