Urban to Rural Shifts: Quantifying the Time Lag of SARS-CoV-2 between the Bay Area and Central Valley through Wastewater-Based Epidemiology

De'Liz Amador[1], Colleen C. Naughton[1], Jonathan Chavez[1], Marco Nava[1], Miriam Nuño[2], Maria L. Daza-Torres[2], Jose Cricelio Montesinos-Lopez[2], Alexandria B. Boehm[3], Marlene K. Wolfe[4], Heather N. Bischel[2]

[1]University of California, Merced; [2]University of California, Davis; [3]Stanford University; [4]Emory University

WASTEWATER SCAN — Stanford University, Emory University, Verily, National League of Cities, Coalition for Aligning Science, Sergey Brin Family Foundation

HEALTHY CENTRAL VALLEY TOGETHER — Wastewater testing for public health action

Introduction

- Wastewater-based epidemiology (WBE) can be an early indicator to clinical COVID-19 cases[1].

45% US population covered by National Wastewater Surveillance Systems (NWSS)[2]

2021[3]: 15% of wastewater treatment plants (WWTP) monitoring in California (CA) for SARS-CoV-2 located in rural communities

2021[3]: 8.2% of Central CA WWTPs covered
2023[3-4]: 15.6% of Central CA WWTPs covered

- Urban areas often prioritized due to:
  - Population served
  - Sewer connectivity
  - Funding
- Disease prevalence of SARS-CoV-2 not fully captured in rural communities
  - Greater distance to nearest hospital or testing center
  - Only test when symptoms occur
  - Increased at-home testing not reported
- Equitable monitoring efforts needed
  - Healthy Central Valley Together (HCVT) helped expand WBE in the Central Valley, CA[5]
- **Current literature:**
  - April 2020: clinical cases spread from urban to rural United States[6]
  - Within sewersheds: disadvantaged neighborhoods often overshadowed by wealthier neighborhoods in Boston, MA[7]
  - Visualization of wastewater viral concentrations and trends across different sampling locations[6-9]
- **Research Gap:** lack of inter-city statistical analysis of SARS-CoV-2 wastewater trends
- **Motivation**: Merced and Stanislaus County Local Health Departments noted at monthly HCVT meetings that they saw a potential lag in COVID-19 cases and wastewater signals from more urban, Bay Area counties to the Central Valley.
- **Hypothesis:** More urban, Bay Area wastewater concentrations will peak before more rural, Central Valley wastewater concentrations.
- **Goal:** investigate spatial and temporal trends of SARS-CoV-2 from urban to rural areas in California.
  - Potentially provide local health departments an expected lead time from urban area spread

Methodology

Wastewater Data[4, 10-11]
- R Version 4.3.1
- 9 select WWTPS: (Central Valley) Merced, Modesto, Los Banos; (Bay Area) Oceanside, Silicon Valley, Southeast San Francisco, Palo Alto, Sunnyvale, & San Jose (Figure 1)
- Parameters:
  - Monitoring Duration: > 6 months
  - Wastewater solids analyzed as part of WastewaterSCAN[10]
  - SARS-CoV-2 Gene tested: N (PMMoV normalized)
  - Period of Study: October 21, 2021 to October 31, 2023
  - Same samplings dates between plants

Clinical Data[12]
- 5 selected counties: Merced and Stanislaus (Central Valley); San Francisco, San Mateo, & Santa Clara (Bay Area)
- Confirmed COVID-19 hospitalizations
- 4 manually identifiable waves (12/02/2021 – 07/31/2023)

Smoothing:
- LOESS[13] – local polynomial regression fitting for peak identification
- 10-day moving average – used in Wavelet analysis

Wavelet Analysis[14-15] :
- Break down of signals into patterns and compares the synchrony across time and frequency
- Used to identify similar periodicities and quantify lag time

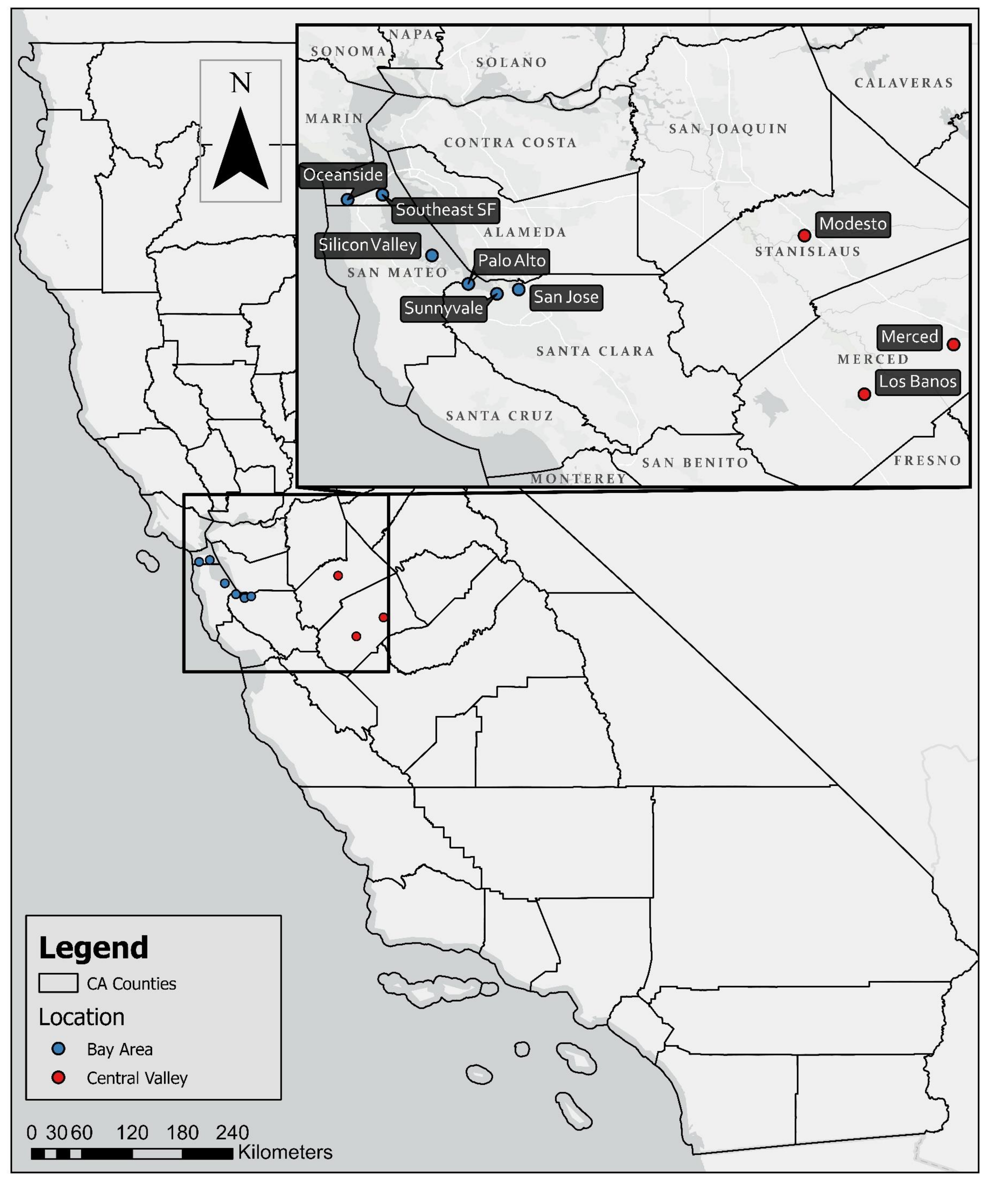

Figure 1. Locations of the Bay Area (blue) and Central Valley (red) WWTPs in California. Bay Area WWTPs include: Oceanside, Southeast San Francisco (SF), Silicon Valley, Palo Alto, Sunnyvale, and San Jose. Central Valley WWTPs include: Modesto, Merced, and Los Banos.

Selected Results

Table 1. Quantified Time Lags

Central Valley WWTP	Bay Area WWTP	Period (days)	Lag (days)
Merced	San Jose	190	-13.0
Merced	Palo Alto	NA	NA
Merced	Silicon Valley	NA	NA
Merced	Sunnyvale	82	NA
Merced	Oceanside	84	NA
Merced	Southeast SF	213	-16.0
Modesto	San Jose	165	-6.0
Modesto	Palo Alto	163	-9.6
Modesto	Silicon Valley	166	-6.0
Modesto	Sunnyvale	NA	NA
Modesto	Oceanside	165	-9.5
Modesto	Southeast SF	NA	NA
Los Banos	San Jose	151	-8.6
Los Banos	Palo Alto	150	-14.0
Los Banos	Silicon Valley	213	-17.0
Los Banos	Sunnyvale	78	NA
Los Banos	Oceanside	140	-9.0
Los Banos	Southeast SF	78	2.5
Los Banos	Southeast SF	150	-0.2

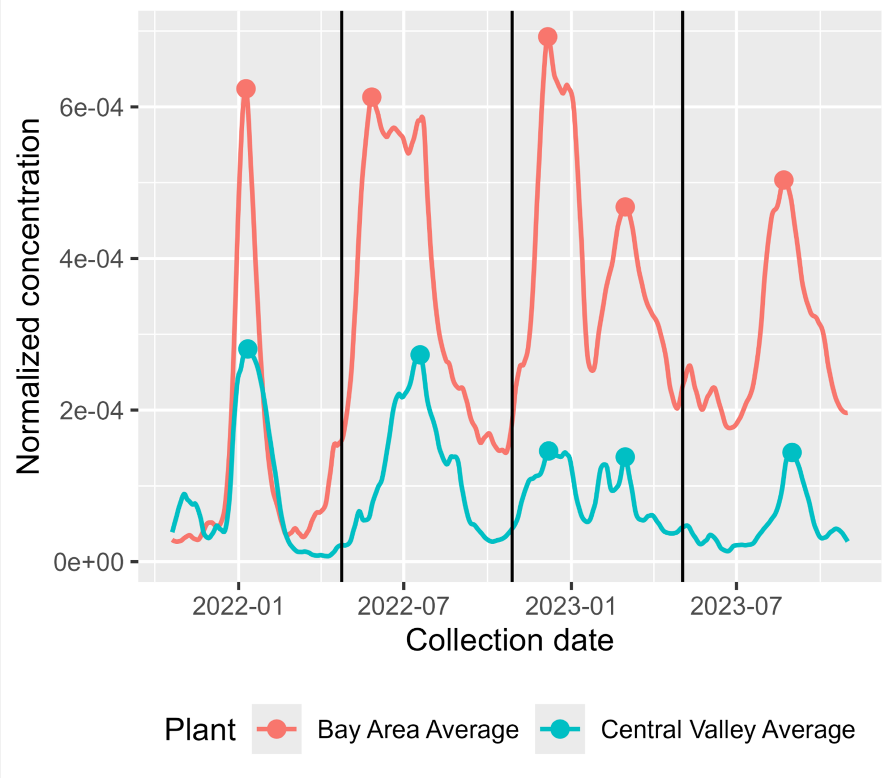

Figure 2. Loess-smoothed normalized wastewater signals for the aggregated Bay Area Average (red) and Central Valley Average (blue). The peaks for each wave (dots) and 187-day period (black lines) are also shown.

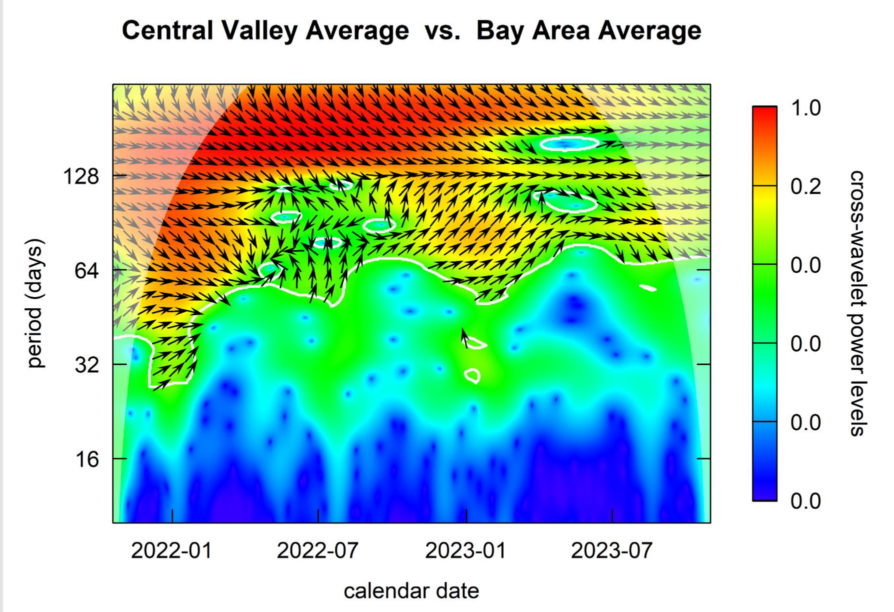

Figure 3. Coherence Wavelet plot for the aggregated wastewater data for the Bay Area Average and Central Valley Average. The cross-wavelet power levels in red indicates a high trend correlation between the signals at specific periods. Arrows pointing southeast show that the Bay Area leading over the Central Valley. Statistical significance is within the white boundary.

Discussion

- On average, the Bay Area wastewater signals leads Central Valley by 12 days.
- Early warning signals from the Bay Area may inform public health planning in the Central Valley, though the spread of COVID-19 to the Central Valley is likely influenced by other locations as well.
- Leading signal switched amongst WWTPs, indicating that regional analysis may provide more robust early indicators for rural forecasting.
- Analysis agrees with previous literature[6-9]:
  - Urban areas have higher SARS-CoV-2 wastewater concentration before the surrounding, less urban, areas
- Hospitalization waves correlated with different SARS-CoV-2 variants[16]:
  - *Wave 1* (12/01/2021 - 03/21/2022) –B.1.1
  - *Wave 2* (04/01/2022 - 10/21/2022) –BA.2 & BA.5
  - *Wave 3* (11/01/2022 - 01/31/2023) – BQ.1
  - *Wave 4* (02/01/2023 - 07/31/2023) – XBB.1.5

Significance

1. Inter-city analysis reveals overall temporal trends of SARS-CoV-2 WW peak concentrations in urban areas leading rural areas
   - There are some exceptions when rural areas may lead urban areas or have no trend
2. Time lag quantification between wastewater signals/peaks can be used as a complementary public health tool
3. Need for additional predictive tools to mitigate future COVID-19 surges in rural and underserved areas

References

1 M. Kumar, et al. (2022). Lead time of early warning by wastewater surveillance for COVID-19: Geographical variations and impacting factors. *Chemical Engineering Journal*, **441**.
2 CDC, About CDC's National Wastewater Surveillance System (NWSS), https://www.cdc.gov/nwss/about.html
3 C. Y. Medina, et al (2022). The need of an environmental justice approach for wastewater based epidemiology for rural and disadvantaged communities: A review in California. *Current Opinion in Environmental Science & Health*, **27**.
4 COVID-19 Wastewater Surveillance Data. California - California Open Data, https://data.ca.gov/dataset/covid-19-wastewater-surveillance-data-california.
5 Healthy Central Valley Together - Wastewater Testing, https://healthycvtogether.org/
6 R. Paul, et al (2020). Progression of COVID-19 From Urban to Rural Areas in the United States: A Spatiotemporal Analysis of Prevalence Rates. *J. Rural Health*, **36 (4)**.
7 T. L. Cowger, et al (2023). Visualizing Neighborhood COVID-19 Levels, Trends, and Inequities in Wastewater: An Equity-Centered Approach and Comparison to CDC Methods. *J. Public Health Manag. Pract.*, **31 (2)**.
8 G. Li, et al (2023). A spatio-temporal framework for modelling wastewater concentration during the COVID-19 pandemic. *Environ. Int.*, **172**.
9 V. B. Barua, et al (2022). Tracking the temporal variation of COVID-19 surges through wastewater-based epidemiology during the peak of the pandemic: A six-month long study in Charlotte, North Carolina. *Sci. Total Environ.*, **814**.
10 A. B. Boehm, et al (2023). Human viral nucleic acids concentrations in wastewater solids from Central and Coastal California USA. *Sci Data,* **10 (1)**.
11 K. F. Kadonsky, et al (2023). Expansion of wastewater-based disease surveillance to improve health equity in California's Central Valley: sequential shifts in case-to-wastewater and hospitalization-to-wastewater ratios, *Front. Public Health*, **11**.
12 COVID-19 Hospital Data (ARCHIVED) - California Open Data, https://data.ca.gov/dataset/covid-19-hospital-data-archived
13 X. Wang, fANCOVA: Nonparametric Analysis of Covariance.
14 A. Roesch and H. Schmidbauer, *WaveletComp 1.0: A guided tour through the R-package*, 2014.
15 M. L. Daza-Torres, et al (2024). Optimizing spatial distribution of wastewater-based epidemiology to advance health equity, *Epidemics*, **49**.
16 CDC, COVID Data Tracker, https://covid.cdc.gov/covid-data-tracker

Acknowledgements:

The analyses conducted through WastewaterSCAN was supported by gifts from the CDC Foundation and the Sergey Brin Family Foundation. Additional research support for Healthy Central Valley Together was provided through a philanthropic gift to the University of California, Davis.

This work and research would not be possible without our WWTP (Merced, Modesto, and Los Banos) and public health partners (Merced County Department of Public Health, Stanislaus County Department of Public Health, Yolo County Department of Public Health, and California Department of Public Health). We also thank the staff of our commercial lab partners.