

Title: Evolving Relationship Between Wastewater Levels of SARS-CoV2 and COVID-19 Hospitalizations in Marin County, California

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Objective: Throughout the COVID-19 pandemic, the average disease severity has decreased due to changes in immunity, the availability of treatments, and possible changes in virulence. Planning for healthcare-related surge response, and formulating appropriate policy, relies on an understanding of the association between infection and severe outcomes. Wastewater-based epidemiology (WBE) has replaced clinical testing to measure COVID-19 community transmission. To better understand the evolving dynamics of infection severity and wastewater levels, we examined the association between SARS-CoV-2 levels in wastewater and county-level COVID-19 hospitalizations across successive variant waves.

Methods: The 7-day average COVID-19 associated hospitalization rate among Marin County residents was calculated using data from mandated reporting of hospital admissions among those who test positive for COVID-19. Wastewater concentration data were obtained from Verily's WastewaterSCAN program, with data for sewersheds covering an estimated 85% of Marin's residents. The raw copies of SARS-CoV-2 RNA from the nucleocapsid gene per gram of dried solid from the six collection sites in Marin County were weighted by population coverage and aggregated to measure the 7-day average concentration in all six sites combined.

The association between the SARS-CoV-2 wastewater concentration and hospitalization rate was evaluated using Pearson's correlation coefficient during successive variant waves. Variant prevalence was obtained from the California Department of Public Health based on clinical samples submitted for sequencing. The start date for a variant wave was defined as the week of collection when a variant accounted for $\geq 50\%$ of all samples collected, and the end date was the week of collection where the variant was $< 50\%$.

Results: The correlation between the hospitalization rate and SARS-CoV-2 wastewater concentration decreased progressively from 8/29/2021 to 10/31/2023. The time interval with the highest correlation (12/12/2021 to 2/27/2022, $r=0.82$), was when Omicron B.1.1 and BA.1 were the dominant strains, and the lowest was 7/9/2023 to 10/8/2023, when XBB.1.16 was dominant ($r=0.40$).

Conclusions: The association between SARS-CoV-2 wastewater concentration and hospitalization admissions has weakened over successive variant intervals. This decoupling indicates a progression toward decreased average severity of COVID-19 infection over time, and suggests that predictive models of COVID-19 hospitalization based on wastewater need to account for progressive change in severity. Next steps include fitting a time series model that accounts for this evolving association to examine how wastewater data can inform healthcare resource planning and public health policy.