

Predicting COVID-19 Incidence Using Wastewater Surveillance Data, Denmark, October 2021–June 2022

Oliver McManus, Lasse Engbo Christiansen, Maarten Nauta, Lene Wulff Krogsgaard, Naja Stolberg Bahrenscheer, Lene von Kappelgaard, Tobias Christiansen, Mikkel Hansen, Nicco Claudio Hansen, Jonas Kähler, Anders Rasmussen, Stine Raith Richter, Lasse Dam Rasmussen, Kristina Træholt Franck, Steen Ethelberg

Analysis of wastewater is used in many settings for surveillance of SARS-CoV-2, but it remains unclear how well wastewater testing results reflect incidence. Denmark has had an extensive wastewater analysis system that conducts 3 weekly tests in ≈200 sites and has 85% population coverage; the country also offers free SARS-CoV-2 PCR tests to all residents. Using time series analysis for modeling, we found that wastewater data, combined with information on circulating variants and the number of human tests performed, closely fitted the incidence curve of persons testing positive. The results were consistent at a regional level and among a subpopulation of frequently tested healthcare personnel. We used wastewater analysis data to estimate incidence after testing was reduced to a minimum after March 2022. These results imply that data from a large-scale wastewater surveillance system can serve as a good proxy for COVID-19 incidence and for epidemic control.

The COVID-19 pandemic has shown the need for accurate surveillance data. Incidence rate data, commonly collected as part of human surveillance, can only be interpreted with the understanding that local testing strategies vary over time. COVID-19 surveillance using wastewater testing, in which SARS-CoV-2

RNA fragments shed in the feces of infected persons are quantified, has been implemented in many countries (1–5). Wastewater data have been suggested as a complement to or even a substitute for human surveillance data, particularly in times of low human testing activity. The association between wastewater concentrations and incidence has been demonstrated in multiple settings, but few studies have succeeded in predicting incidence through wastewater surveillance, and the direct value of wastewater testing for epidemic control remains debatable (1).

In response to the pandemic, Denmark set up an extensive wastewater surveillance system, which was implemented in July 2021 and fully rolled out in October 2021. During the study period, the system included 201 wastewater treatment plant (WWTP) inlets, which were sampled 3 times a week and covered 85% of the population. Denmark has also had exceptionally high COVID-19 testing capacity, offering unlimited, free reverse transcription PCR (RT-PCR) testing through public testing stations (6,7; M.A. Gram et al., unpub. data, <http://medrxiv.org/lookup/doi/10.1101/2023.02.06.23285556>). The per capita testing rate has been among the highest in the world during some periods of the pandemic; the country tested up to 27% of the population per week in December 2021 and was capturing an estimated 70% of active COVID-19 cases at the start of 2022 (M.A. Gram et al., unpub. data). However, testing activity was scaled down in early 2022, to <1% per week by June 2022 (8,9).

Given the variation in testing rates, wastewater concentrations should not be directly compared with observed incidence. Instead, models should include information on changing testing rates over time.

Author affiliations: European Centre for Disease Prevention and Control, Solna, Sweden (O. McManus); Statens Serum Institut, Copenhagen, Denmark (O. McManus, L.E. Christiansen, M. Nauta, L.W. Krogsgaard, N.S. Bahrenscheer, L. von Kappelgaard, T. Christiansen, M. Hansen, N.C. Hansen, J. Kähler, A. Rasmussen, S.R. Richter, L.D. Rasmussen, K.T. Franck, S. Ethelberg); University of Copenhagen, Copenhagen, Denmark (S. Ethelberg)

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Another strategy is to look at a subgroup of regularly tested persons, where the effect of fluctuations in testing patterns should be less pronounced. Such a subgroup exists in Denmark, where recommendations were made for regular screening tests for certain care personnel (10).

The association between wastewater data and incidence might be affected by the SARS-CoV-2 variants in circulation, because those variants could have different fecal shedding patterns. Viral load for oropharyngeal samples has been shown to be higher for Delta than previous variants (B. Li et al., unpub. data, <https://www.medrxiv.org/content/10.1101/2021.07.07.21260122v2>), but how fecal shedding differs among variants is not known (11). Other variables, such as temperature and traveling time of SARS-CoV-2 in sewers, dilution by precipitation or wastewater from industry, and inhibitors of laboratory analyses, might affect viral quantification, (12,13).

We used the results of wastewater surveillance to predict the observed incidence of SARS-CoV-2 infections in Denmark. We performed the analysis at the national and regional level and among a subgroup of healthcare personnel.

Methods

Overview

We conducted a time-series analysis, constructing a model to explain observed incidence by wastewater concentrations. Besides the main national-level analysis, we also tested the model at a regional level and on a subpopulation of healthcare personnel. We used the human testing rate as a covariate in our model and considered interactions between wastewater concentrations and the proportion of circulating Omicron versus Delta variants and between wastewater concentrations and wastewater temperature. The study period was September 27, 2021–June 26, 2022.

Data Sources

Wastewater

Throughout the study period, 24-hour composite samples were taken 3 times a week from 202 WWTP inlets across Denmark. Sampling started on Mondays, Tuesdays, and Thursdays. Where possible, the samples were flow-proportional, which enabled sampling of more water at times of heavy flow, providing a more representative sample of the 24-hour water flow. Otherwise, samples were time-proportional, sampling a fixed amount of water at fixed time intervals.

Samples were purified and analyzed using quantitative real-time RT-PCR at Eurofins Miljø, a central commercial laboratory in Vejen, Denmark. We measured cycle threshold (Ct) values for 2 SARS-CoV-2 genes (the N2 region of the nucleocapsid gene and the RNA-dependent RNA polymerase [RdRp]) and converted them to concentrations (copies/L). We calculated limits of detection (LOD) and limits of quantification (LOQ) for each gene in each sample. We imputed values <LOD as LOD/2, and <LOQ as (LOD + LOQ)/2. Starting in 2022, we also measured the concentrations of 2 indicators of fecal concentration: crAssphage and pepper mild mottle virus (14,15). For consistency with 2021 data, we used those measurements as data quality indicators but not to normalize SARS-CoV-2 concentrations.

For each sample, utility companies reported the volume of wastewater that entered WWTPs over the 24-hour sampling window and the temperature of wastewater upon entry. Utility companies also provided geographic information, which we used to calculate the resident population of each catchment area by linking to the Danish Civil Registration System (16).

Incidence

In-person PCR COVID-19 testing was available for free to all residents throughout our study period; results were collected centrally in the Danish Microbiology Database (17). Testing recommendations changed throughout the study period; the most substantial change occurred on March 10, 2022. After that date, tests for the general population were recommended only for symptomatic persons in groups at high risk (9). We extracted data on daily incidence of PCR-confirmed COVID-19 cases and weekly PCR testing rate from Denmark's official COVID-19 statistics (18) for its 5 administrative regions.

Care Personnel

We used data on healthcare personnel, consisting of care home staff and in-home caretakers, for a secondary analysis. During September 4, 2021–April 28, 2022, weekly PCR tests were recommended for healthcare personnel for screening purposes. After this time and until the end of the study period, the recommendation was 1 test every 2 weeks (10). Because of those recommendations, we believed incidence in this group might be less affected by testing patterns and therefore a better measure of actual community incidence than observed incidence among the general population. Information on this group came from Denmark's centrally collected data on COVID-19

tests and results, linked to employment information through the Civil Registration System (16,19).

Variants

Denmark had extensive whole-genome sequencing to monitor SARS-CoV-2 variants, sequencing up to 15,000 samples/week (20,21). We calculated the weekly proportion of sequences belonging to the Delta and Omicron variants through the start of June 2022, excluding other variants that were present in negligible amounts.

Data Processing

Our wastewater measure for each sample is expressed as the average number of SARS-CoV-2 RNA copies shed per person living in the WWTP catchment area during a 24-hour sampling period. We calculated this value using the equation

$$X = \frac{C \times V}{P}$$

where C is the geometric mean of the N_2 and $RdRp$ gene concentrations (in copies/L) and is log-normally distributed, V is the volume of wastewater (in liters) that entered the WWTP in a 24-hour measurement period, and P is the population size of the catchment area. We removed outliers of wastewater volume measurements, defined as being >1.5 times the interquartile range from the 25th or 75th percentile, and then truncated values at 1.96 SDs from the mean on the log scale.

We aggregated all data into weekly observations: incidence was weekly cases per 100,000 population; testing rate was weekly tests per 1,000 population; wastewater concentrations were the weekly weighted median of all average copies per person measurements (≈ 600 values of X per week), using the \log_{10} -transformed population size of each WWTP catchment area as the weights (the choice of weight being a compromise between equal weighting because of the uncertainty of individual measurements and weighting according to population size); wastewater temperature was similarly the weekly weighted median. Wastewater concentrations were log-normally distributed, and the variance of incidence and testing rates increases with the values, so we used \log_{10} -transformed versions of those variables in our models, using the same transformation for all to ease interpretation.

Exclusions

Because great fluctuations in the fecal load of wastewater are not expected, finding such a fluctuation in

measurements of the fecal indicators pepper mild mottle virus and crAssphage indicated a likely failure in sampling or laboratory analysis. We therefore excluded samples with missing or extreme concentrations of these fecal indicators, defined as concentrations ≥ 3 SDs from the mean for each WWTP, on the log scale. We also excluded samples that the laboratory received on unexpected days of the week. Such samples might not have been comparable to others because more time had passed in which RNA content could have degraded during transit. Furthermore, we excluded samples with missing values for the volume of wastewater entering the WWTP over a 24-hour sampling period. Finally, we excluded samples from WWTPs where we had no geographic information defining the catchment area, which we needed to define the population served by each WWTP. We also discarded wastewater temperature data reported as $< 1^\circ\text{C}$ or $> 30^\circ\text{C}$, but we did not exclude other data for those samples from the analysis.

Statistical Analysis

First, we plotted the national incidence and wastewater concentrations to compare patterns visually. Second, we fitted a model to see whether wastewater results were a predictor of national incidence. We split the data into a training and testing set. We used training data from before June 9, 2022, to select and estimate our models. We reserved data from June 9, 2022, onward (7 weekly datapoints) as an out-of-sample test dataset for model validation. We constructed an ARIMAX (autoregressive integrated moving average with exogenous variables) model, using incidence as the dependent variable and wastewater concentrations and testing rate as the explanatory variables. We tested including the interaction between wastewater concentrations and the circulating variant (expressed as proportion of Delta sequences) and the interaction between wastewater concentration and wastewater temperature. We only included temperature as an interaction with the wastewater concentration to restrict it to describe degradation of RNA and not the overall seasonal effect on incidence. Likewise, the proportion of Delta was included as an interaction with the wastewater concentration to adjust for different shedding patterns for the different variants. We selected which covariates to include based on the Akaike information criterion. For consistency, we used the terms selected for the national model in the secondary models as well. Third, we also estimated the model allowing for a time delay between wastewater results and incidence. We examined lag times of 0, 1, and 2 weeks in each direction, comparing the resulting models by

the Akaike information criterion. Fourth, we validated the model on the out-of-sample dataset not used in the model estimation, using the root mean squared error. Fifth, we repeated the modeling steps in 2 secondary analyses: reestimating the main model independently for each region and for the subpopulation of care personnel only. For the care personnel model, we used both incidence and testing rate specific to care personnel. Sixth, we used the national model to predict the incidence that would have been observed had the testing rate remained stable throughout the study period by generating model predictions where we fixed the testing rate at a constant value. We used the highest recorded testing rate in the study period for this. We used R version 4.1.3 (The R Project for Statistical Computing, <https://cran.r-project.org>) for statistical analyses (Appendix, <https://wwwnc.cdc.gov/EID/article/29/8/22-1634-App1.pdf>).

Results

Description of Data

We included 18,737 wastewater samples from 202 WWTPs in the study (Appendix Table 1). Our initial dataset consisted of 21,069 samples, but we excluded 2,361 samples (29 for extreme concentrations of fecal indicators, 301 from WWTPs with unknown populations, 81 that arrived on unexpected days of the week, 919 missing data on wastewater flow in the sampling period, and 1,031 with sampling method not listed as flow-proportional or time-proportional). Of the included samples, 15,801 were flow-proportional and 2,764 were time-proportional. After aggregating by week at national level, we had 39 wastewater data points. We included a median of 515 (interquartile range 480.5–532.5) weekly samples.

Wastewater concentrations and incidence followed similar patterns, increasing until early 2022,

decreasing until late May, and then increasing again (Figure 1). Testing rates remained fairly stable during November 2021–February 2022, after which they decreased to low levels. Per person, on average 2.6 times as many weekly tests occurred among healthcare personnel as occurred among the general population.

Incidence followed a similar pattern in all regions (Appendix Figure 1), although slightly offset in time. Numbers throughout 2021 were slightly higher in the Capital region and neighboring Zealand region than in the other 3 regions. The pattern of testing rate over time also did not differ greatly by region (Appendix Figure 2).

Until late November 2021, nearly all human isolates sequenced were the Delta variant. Omicron quickly took over in December, reaching $\approx 50\%$ half-way through the month and $>95\%$ in the first week of January 2022. After that, nearly all samples were Omicron (Appendix Figure 3).

Model Results

Our final models were based on wastewater concentration, testing rate, and the interaction of wastewater concentration with circulating variants (percentage Delta). They did not include the interaction between wastewater results and wastewater temperature, because it did not improve the model (Appendix). The model performed best with no lead or lag time between wastewater results and incidence.

The pattern of the model fit and validation estimates follows the pattern of observed incidence well (Figure 2; Appendix Figure 4). However, only 43% of validation points were covered by the 95% prediction intervals in the national model (Appendix Table 3).

The coefficients for wastewater results were generally 0.4–0.5 during Omicron; coefficients were lower during Delta by ≈ 0.15 –0.20 (Table). The coefficient for wastewater was higher in the care personnel model

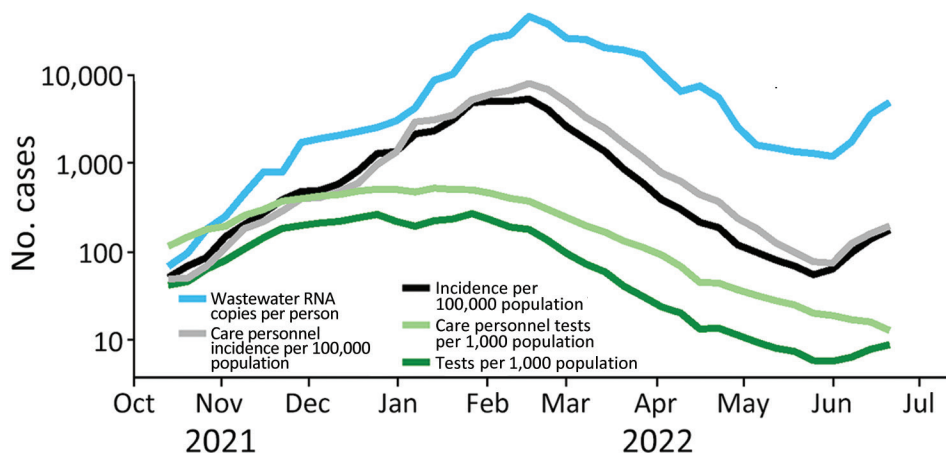


Figure 1. Comparison of results of COVID-19 wastewater surveillance with incidence and testing rate (both national and for care personnel) over time, Denmark, illustrating the agreement between wastewater concentrations and incidence. Wastewater concentrations are based on 18,565 individual samples. Testing rates were high during November 2021–February 2022 and decreased after that time.

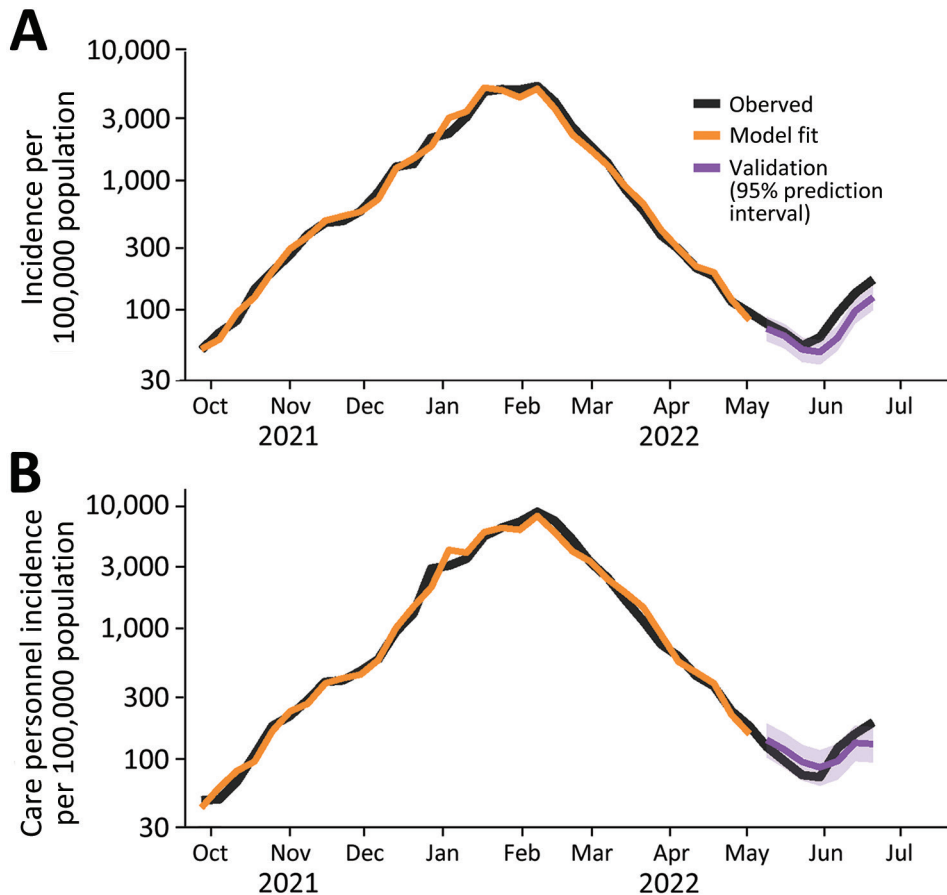


Figure 2. Model fit and forecasts for the national model (A) and the care personnel model (B) used in study of predicting COVID-19 incidence using wastewater surveillance data, Denmark. The fitted values (orange) are seen to follow the observed incidence (black) during the training period. The forecasts in the test period (purple) are also shown against the observed incidence (black).

(0.52 [95% CI 0.46–0.59] during Omicron) than in the main national model (0.40 [95% CI 0.34–0.46]). At a regional level, the wastewater coefficient was lower for the Capital region than other regions (0.31 [95% CI 0.24–0.38] during Omicron).

Predicted Incidence at Stable Testing

We used the national model to estimate the COVID-19 incidence that would have been observed if the testing rate had remained constant (Figure 3). We used the highest testing rate in our study period (270 weekly tests/1,000 persons, as in the week of January 17, 2022). The difference between the model predictions and the observed incidence can be used as a measure of underreporting. Given the estimate from serologic studies that 70% of actual cases were captured in early 2022, we estimate that $\approx 15\%$ of actual cases were captured by the national PCR testing system from April 2022 on.

Discussion

We constructed a model to explain the observed incidence of COVID-19 in Denmark using wastewater data, information on the circulating variants, and

the number of human tests performed as predictors. We found that we could accurately reconstruct the observed incidence curve. Results were consistent at a regional level and among the subgroup of frequently tested care personnel. Using data from a country with extensive wastewater and human testing systems, we demonstrated that predicting incidence based on wastewater surveillance is possible. We used these results to predict the incidence that could have been observed in Denmark if testing activity had remained high. In Denmark, after mass-testing programs were rolled back in the spring of 2022, wastewater analysis became a key source of information for the healthcare system in its handling of the COVID-19 pandemic.

The steeper association between wastewater and incidence during the Omicron period than in the Delta period might indicate that shedding dynamics differ between variants. However, the transition from Delta to Omicron coincided with the peak of rollout of vaccine booster doses (22). Information is lacking on how vaccination affects fecal shedding, but nasopharyngeal viral loads appear lower among vaccinated persons (2). Further studies are needed on how

fecal shedding is affected by SARS-CoV-2 variants and vaccination status.

The model fit at the regional level was generally very similar to that for national results, although wastewater concentrations had less effect in the model for the Capital region. A likely factor is that the Capital region is dominated by 4 very large catchment areas, and correlations between wastewater concentration and incidence are poorer in larger catchment areas (1). Commuting across catchment areas, which is typical for the densely populated Capital region, might also have played a role.

We performed a subanalysis of healthcare personnel, who were consistently tested at a higher rate than the general population for screening purposes. We reasoned that the incidence of healthcare personnel would be less dependent on testing rates than the observed incidence in the general population. In fact, testing among this group followed a similar pattern over time to that of the general population and gave

similar model results, possibly because the overall testing rate in Denmark was so high.

We used the national model to estimate what observed incidence would have been if the testing rate had remained at its maximum. We estimated that the proportion of actual cases identified had fallen to ≈15% by April 2022. However, if tests became more targeted over time as recommendations for regular screening tests were relaxed, the percentage of cases identified could be higher.

SARS-CoV-2 is known to decay faster at higher temperatures (12,13), but including an interaction term between wastewater results and temperature did not improve our model fit. The effect of temperature might have been outweighed by other unmeasured factors that affect SARS-CoV-2 decay, such as retention time in the sewage system or other chemical components of wastewater.

Unlike other studies (1), we did not find wastewater results to be a leading indicator of incidence. That

Table. Estimated coefficients from the national model, care personnel model, and regional model in study using wastewater surveillance data to predict COVID-19 incidence, Denmark, October 2021–June 2022*

Model	Term	Estimate (95% CI)	p value	
National	AR (1)	0.46 (0.16–0.76)	0.004	
	Wastewater concentration	0.4 (0.34–0.46)	<0.001	
	Testing rate	0.87 (0.81–0.94)	<0.001	
	Wastewater concentration × Delta (%)	-0.15 (-0.19 to -0.11)	<0.001	
	Intercept	-0.14 (-0.32 to 0.04)	0.12	
Care personnel	AR (1)	0.32 (-0.06 to 0.70)	0.1	
	Wastewater concentration	0.52 (0.46–0.59)	<0.001	
	Testing rate (care personnel)	0.84 (0.73–0.94)	<0.001	
	Wastewater concentration × Delta (%)	-0.17 (-0.21 to -0.13)	<0.001	
	Intercept	-2.45 (-2.83 to -2.07)	<0.001	
Regional	Capital Region	AR (1)	0.31 (-0.07 to 0.70)	0.12
		Wastewater concentration	0.31 (0.24–0.38)	<0.001
		Testing rate	1.03 (0.94–1.11)	<0.001
		Wastewater concentration × Delta (%)	-0.15 (-0.19 to -0.12)	<0.001
		Intercept	-0.11 (-0.34 to 0.12)	0.3
	Central Denmark	AR (1)	-0.19 (-0.56 to 0.18)	0.3
		Wastewater concentration	0.48 (0.45–0.52)	<0.001
		Testing rate	0.88 (0.84–0.92)	<0.001
		Wastewater concentration × Delta (%)	-0.14 (-0.16 to -0.12)	<0.001
		Intercept	-0.48 (-0.60 to -0.36)	<0.001
	North Denmark	AR (1)	-0.09 (-0.46 to 0.28)	0.6
		Wastewater concentration	0.47 (0.43–0.51)	<0.001
		Testing rate	0.91 (0.86–0.96)	<0.001
		Wastewater concentration × Delta (%)	-0.16 (-0.19 to -0.13)	<0.001
		Intercept	-0.49 (-0.64 to -0.33)	<0.001
	Southern Denmark	AR (1)	0.16 (-0.19 to 0.51)	0.4
		Wastewater concentration	0.48 (0.44–0.52)	<0.001
		Testing rate	0.83 (0.78–0.88)	<0.001
		Wastewater concentration × Delta (%)	-0.15 (-0.17 to -0.12)	<0.001
		Intercept	-0.39 (-0.52 to -0.26)	<0.001
Zealand	AR (1)	0.07 (-0.34 to 0.47)	0.7	
	Wastewater concentration	0.42 (0.37–0.48)	<0.001	
	Testing rate	0.8 (0.73–0.86)	<0.001	
	Wastewater concentration × Delta (%)	-0.14 (-0.17 to -0.11)	<0.001	
	Intercept	-0.11 (-0.26 to 0.04)	0.2	

*The response variable incidence, wastewater concentration, and testing rate are included after log₁₀-transformation. AR (1) denotes the first-order autoregressive term.

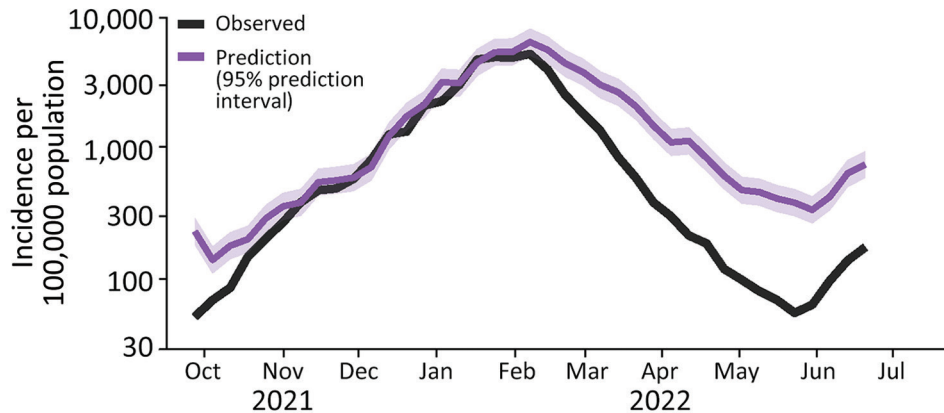


Figure 3. Predicted COVID-19 incidence at a constant testing rate (purple) based on the national model, compared with observed incidence (black), in study of wastewater surveillance data as a predictor of COVID-19 incidence, Denmark. The prediction is an estimate of the true incidence. The proportion of estimated true cases captured decreased from >80% to \approx 20% during 2022.

difference might be because our analysis was based on weekly data, so we could only assess lag times in 7-day intervals. However, a lag of <1 week would likely have limited effects on public health action in practice. In addition, extensive human testing occurred during most of the study period, so infections might have been detected earlier than in other settings.

In our models, the coefficient for wastewater concentrations was <1. This result might seem surprising, because it means that a doubling in wastewater concentrations is not associated with a doubling in incidence (after adjusting for testing rate). Several explanations exist for this finding. First, the variability in the number of viral copies shed is best described by a log-normal distribution (23,24). The cumulative number of copies shed by a population will therefore follow a highly skewed distribution (24,25), which in itself is expected to lead to a coefficient <1, as seen in simulation models generating the relationship between the number of infected persons in the population and concentration of RNA in sewage (26). Second, observed incidence depends on the testing pattern; specifically, the probability that an infected person will be tested and have a positive result. The testing rate that we included in our models is an imperfect measure of this probability. Third, testing rate itself is influenced by incidence. Testing rates were highest, on average, when incidence was high. This factor might have increased the predictive power of testing rate in our models and therefore disadvantaged wastewater as a predictor. This interpretation is supported by the fact that the coefficient for testing rate in the national model (0.87 [95% CI 0.81–0.94]) is higher than the 0.7 that was found in Denmark's method for estimating the reproduction number in the fall of 2020 (27). The secondary analysis of healthcare personnel provides further support. We expected observed incidence in this population to be a closer reflection of

actual incidence (compared to national observed incidence numbers) because the testing rate was more stable. That expectation is consistent with our results: a larger coefficient for wastewater concentrations and marginally smaller (though with overlapping 95% CIs) coefficient for testing rate.

The first limitation of our model is that testing rate is influenced by incidence and changes in recommendations. However, this effect was likely smaller in our setting than in most others because there were high numbers of screening tests for asymptomatic people for much of the study period. Another limitation is that the performance of the model on the validation data was mixed. Validation model estimates clearly followed the same pattern as the observed incidence, but they were lower than the observed data; most of the 95% prediction intervals did not include the observed data. This discrepancy is likely because of the changes in recommendations in the first half of 2022, in which a gradual shift occurred toward less testing for screening purposes and a larger share of diagnostic testing of symptomatic persons. Finally, we could not incorporate the unknown effect of immunity (through vaccination or previous infection) on fecal shedding.

This study benefited from copious wastewater testing data because of the extensive surveillance system in Denmark. One remaining question is how well wastewater data perform in less developed surveillance systems. Denmark's surveillance was scaled down after this study period to incorporate fewer WWTPs and fewer weekly samples. Repeating this analysis once enough data has been collected under the new system might help answer that question.

In conclusion, we performed a large-scale study of the association between wastewater results and observed incidence of COVID-19. Our relatively simple model makes it easy to specifically examine the

association between wastewater results and incidence. We found that wastewater testing results can be used to accurately model the observed incidence of COVID-19, in combination with data on human tests. This finding implies that wastewater testing can serve as a proxy for incidence in the context of little to no human testing. The link between wastewater concentrations and incidence has been stronger since Omicron has been dominant. We found no effect of temperature on the association. For a wastewater surveillance system as extensive as that of Denmark, we believe wastewater results are a trustworthy indicator of actual incidence, especially in a situation in which human testing rates continue to decline.

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Data used for this study are available at <https://github.com/oloverm/ww-incidence> and <https://zenodo.org/record/8060977>.

About the Author

Mr. McManus is an epidemiologist at Denmark's national public health institute, Statens Serum Institut, and a fellow of the European Programme for Intervention Epidemiology Training. His primary research interest is wastewater surveillance of COVID-19.

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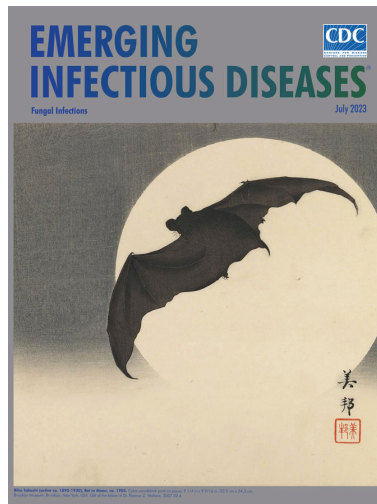
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Address for correspondence: Steen Ethelberg, Department of Infectious Disease Epidemiology and Prevention, Statens Serum Institut, Artillerivej 5, 2300 Copenhagen, Denmark; e-mail: set@ssi.dk

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Predicting COVID-19 Incidence Using Wastewater Surveillance Data, Denmark, October 2021–June 2022

Appendix

R Session Info

```
— Session info —————  
setting value  
version R version 4.2.3 (2023-03-15)  
os      macOS Monterey 12.3.1  
system  aarch64, darwin20  
ui      X11  
language (EN)  
collate en_US.UTF-8  
ctype   en_US.UTF-8  
tz      Europe/London  
date    2023-04-19  
pandoc  2.19.2 @  
/Applications/RStudio.app/Contents/Resources/app/quarto/bin/tools/ (via rmarkdown)
```

```
— Packages —————  
package      * version      date (UTC) lib source  
abind         1.4-5         2016-07-21 [1] CRAN (R 4.2.0)  
anytime      0.3.9         2020-08-27 [1] CRAN (R 4.2.0)  
assertthat   * 0.2.1         2019-03-21 [1] CRAN (R 4.2.0)  
backports    1.4.1         2021-12-13 [1] CRAN (R 4.2.0)  
base64enc    0.1-3         2015-07-28 [1] CRAN (R 4.2.0)
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broom.helpers	1.13.0	2023-03-28	[1]	CRAN	(R 4.2.0)
bslib	0.3.1	2021-10-06	[1]	CRAN	(R 4.2.0)
cachem	1.0.7	2023-02-24	[1]	CRAN	(R 4.2.0)
cellranger	1.1.0	2016-07-27	[1]	CRAN	(R 4.2.0)
checkmate	2.1.0	2022-04-21	[1]	CRAN	(R 4.2.0)
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cli	* 3.6.1	2023-03-23	[1]	CRAN	(R 4.2.0)
clipr	0.8.0	2022-02-22	[1]	CRAN	(R 4.2.0)
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cluster	2.1.4	2022-08-22	[1]	CRAN	(R 4.2.3)
colorspace	2.0-3	2022-02-21	[1]	CRAN	(R 4.2.0)
conflicted	* 1.2.0	2023-02-01	[1]	CRAN	(R 4.2.0)
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curl	4.3.2	2021-06-23	[1]	CRAN	(R 4.2.0)
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DBI	1.1.3	2022-06-18	[1]	CRAN	(R 4.2.0)
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desc	1.4.2	2022-09-08	[1]	CRAN	(R 4.2.0)
details	* 0.3.0	2022-03-27	[1]	CRAN	(R 4.2.0)
digest	0.6.29	2021-12-01	[1]	CRAN	(R 4.2.0)
distributional	0.3.2	2023-03-22	[1]	CRAN	(R 4.2.0)
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e1071	1.7-13	2023-02-01	[1]	CRAN	(R 4.2.0)
ellipsis	0.3.2	2021-04-29	[1]	CRAN	(R 4.2.0)
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fastmap	1.1.0	2021-01-25	[1]	CRAN	(R 4.2.0)

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generics	0.1.2	2022-01-31	[1]	CRAN	(R 4.2.0)
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ggthemes	* 4.2.4	2021-01-20	[1]	CRAN	(R 4.2.0)
glue	* 1.6.2	2022-02-24	[1]	CRAN	(R 4.2.0)
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gt	0.9.0	2023-03-31	[1]	CRAN	(R 4.2.0)
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gtools	3.9.4	2022-11-27	[1]	CRAN	(R 4.2.0)
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ISOweek	* 0.6-2	2011-09-07	[1]	CRAN	(R 4.2.0)
janitor	* 2.2.0	2023-02-02	[1]	CRAN	(R 4.2.0)
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jsonlite	1.8.0	2022-02-22	[1]	CRAN	(R 4.2.0)
KernSmooth	2.23-20	2021-05-03	[1]	CRAN	(R 4.2.3)
knitr	1.39	2022-04-26	[1]	CRAN	(R 4.2.0)
labeling	0.4.2	2020-10-20	[1]	CRAN	(R 4.2.0)
lattice	0.20-45	2021-09-22	[1]	CRAN	(R 4.2.3)
lifecycle	1.0.3	2022-10-07	[1]	CRAN	(R 4.2.0)

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minqa	1.2.5	2022-10-19	[1]	CRAN	(R 4.2.0)
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pacman	0.5.1	2019-03-11	[1]	CRAN	(R 4.2.0)
patchwork	* 1.1.2	2022-08-19	[1]	CRAN	(R 4.2.0)
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png	0.1-8	2022-11-29	[1]	CRAN	(R 4.2.0)
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proxy	0.4-27	2022-06-09	[1]	CRAN	(R 4.2.0)
purrr	* 0.3.4	2020-04-17	[1]	CRAN	(R 4.2.0)
quadprog	1.5-8	2019-11-20	[1]	CRAN	(R 4.2.0)
Quandl	2.11.0	2021-08-11	[1]	CRAN	(R 4.2.0)
quantmod	* 0.4.22	2023-04-07	[1]	CRAN	(R 4.2.0)
R6	2.5.1	2021-08-19	[1]	CRAN	(R 4.2.0)
RColorBrewer	1.1-3	2022-04-03	[1]	CRAN	(R 4.2.0)
Rcpp	1.0.10	2023-01-22	[1]	CRAN	(R 4.2.0)
readr	* 2.1.2	2022-01-30	[1]	CRAN	(R 4.2.0)
readxl	* 1.4.0	2022-03-28	[1]	CRAN	(R 4.2.0)

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rmarkdown	2.14	2022-04-25	[1]	CRAN	(R 4.2.0)
rpart	* 4.1.19	2022-10-21	[1]	CRAN	(R 4.2.3)
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rstudioapi	0.13	2020-11-12	[1]	CRAN	(R 4.2.0)
sass	0.4.5	2023-01-24	[1]	CRAN	(R 4.2.0)
scales	* 1.2.1	2022-08-20	[1]	CRAN	(R 4.2.0)
sessioninfo	1.2.2	2021-12-06	[1]	CRAN	(R 4.2.0)
sf	* 1.0-12	2023-03-19	[1]	CRAN	(R 4.2.0)
snakecase	0.11.0	2019-05-25	[1]	CRAN	(R 4.2.0)
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spatstat.data	* 3.0-1	2023-03-12	[1]	CRAN	(R 4.2.0)
spatstat.explore	* 3.1-0	2023-03-14	[1]	CRAN	(R 4.2.0)
spatstat.geom	* 3.1-0	2023-03-12	[1]	CRAN	(R 4.2.0)
spatstat.linnet	* 3.1-0	2023-04-14	[1]	CRAN	(R 4.2.0)
spatstat.model	* 3.2-1	2023-02-15	[1]	CRAN	(R 4.2.0)
spatstat.random	* 3.1-4	2023-03-13	[1]	CRAN	(R 4.2.0)
spatstat.sparse	3.0-1	2023-03-12	[1]	CRAN	(R 4.2.0)
spatstat.utils	3.0-2	2023-03-11	[1]	CRAN	(R 4.2.0)
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stringr	* 1.4.0	2019-02-10	[1]	CRAN	(R 4.2.0)
tensor	1.5	2012-05-05	[1]	CRAN	(R 4.2.0)
tibble	3.2.1	2023-03-20	[1]	CRAN	(R 4.2.0)
tidylog	1.0.2	2020-07-03	[1]	CRAN	(R 4.2.0)
tidyquant	* 1.0.7	2023-03-31	[1]	CRAN	(R 4.2.0)
tidyr	* 1.2.0	2022-02-01	[1]	CRAN	(R 4.2.0)
tidyselect	1.2.0	2022-10-10	[1]	CRAN	(R 4.2.0)
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TTR	* 0.24.3	2021-12-12	[1]	CRAN	(R 4.2.0)
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units	0.8-1	2022-12-10	[1]	CRAN	(R 4.2.0)
urca	1.3-3	2022-08-29	[1]	CRAN	(R 4.2.0)
utf8	1.2.2	2021-07-24	[1]	CRAN	(R 4.2.0)

vctr	0.6.2	2023-04-19	[1]	CRAN	(R 4.2.3)
weights	1.0.4	2021-06-10	[1]	CRAN	(R 4.2.0)
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writexl	* 1.4.2	2023-01-06	[1]	CRAN	(R 4.2.0)
xfun	0.38	2023-03-24	[1]	CRAN	(R 4.2.0)
xml2	1.3.3	2021-11-30	[1]	CRAN	(R 4.2.0)
xts	* 0.13.1	2023-04-16	[1]	CRAN	(R 4.2.0)
yaml	2.3.5	2022-02-21	[1]	CRAN	(R 4.2.0)
zoo	* 1.8-12	2023-04-13	[1]	CRAN	(R 4.2.0)

[1] /Library/Frameworks/R.framework/Versions/4.2-arm64/Resources/library

Model Selection

We tested the following model specifications to model national incidence. Model 5 is the model that we ultimately selected.

1. wastewater concentration + AR(1)
2. wastewater concentration + testing rate + AR(1)
3. wastewater concentration + testing rate + wastewater concentration * wastewater temperature + AR(1)
4. wastewater concentration + testing rate + wastewater concentration * wastewater temperature + wastewater concentration * Delta (%) + AR(1)
5. wastewater concentration + testing rate + wastewater concentration * Delta (%) + AR(1)
6. wastewater concentration + wastewater concentration * Delta (%) + AR(1)
7. testing rate + AR(1)
8. wastewater concentration + testing rate + wastewater concentration * Delta (%) + testing rate * Delta (%) + AR(1)

The log-likelihood, AIC, and BIC measures for each tested model are in Appendix Table 2.

Model Equations

In the national model, incidence (I) is modeled as:

$$I = 10^{0.43 \cdot \log_{10}(WW) + 0.86 \cdot \log_{10}(T) - 0.16 \cdot \log_{10}(WW) \cdot P_D + 0.43 \cdot AR(1) - 0.14}$$

WW = weekly wastewater result (copies per person)

T = weekly testing rate (tests / 1,000 population)

P_D = proportion of human samples that were of the Delta variant (%)

$AR(I)$ = autoregressive coefficient of order 1

The care personnel and regional models follow the same structure.

Appendix Table 1. Wastewater treatment plant characteristics

Treatment plant	Population	Samples included	RNA copies per liter ¹		24-h flow (liters) ¹		Temperature ²	
			Median	IQR	Median	IQR	Median	IQR
Region Hovedstaden								
Dragør	14,582	74	4.26	1.28	3.73	0.20	4.00	1.00
Fredensborg/Lønholt	10,272	98	4.32	0.88	3.41	0.13	10.40	4.70
Frederikssund	20,767	89	4.07	0.83	3.77	0.14	1.00	0.00
Gilleleje	8,383	73	3.97	0.71	3.56	0.24	11.60	5.35
Halsnæs (Melby)	30,110	98	4.17	0.92	3.95	0.17	10.70	4.90
Helsingø	13,585	74	4.10	0.84	3.79	0.16	11.80	5.80
Helsingør	30,752	92	4.46	0.60	3.80	0.12	13.20	3.43
Hillerød	39,918	104	4.00	0.73	4.27	0.24	10.25	4.88
Humblebæk/Nivå	18,330	94	4.46	0.75	3.62	0.18	11.90	4.30
Hvidovre (Avedøre)	252,811	93	4.00	1.05	4.79	0.14	4.00	2.00
København (Damhusåen)	290,219	97	4.40	0.65	4.82	0.22	5.00	2.20
Lillerød	17,447	94	4.31	0.85	3.66	0.11	10.70	4.97
Lynetten (nordre tilløb)	211,322	99	4.40	0.61	4.77	0.19	4.00	7.20
Lynetten (søndre tilløb)	430,548	92	4.47	0.59	4.94	0.07	4.00	4.10
Lyngby-Taarbæk	55,224	92	4.23	0.64	4.45	0.17	12.00	7.00
Lynge	4,709	98	4.01	0.94	2.99	0.25	9.45	5.95
Måløv	50,072	99	4.35	0.76	3.96	0.19	11.50	5.10
Neder Dråby	3,554	87	2.12	1.15	2.92	0.22	1.00	0.00
Nexø	4,714	105	3.39	1.17	3.58	0.40	9.85	5.35
Nordkysten	12,122	102	4.04	0.82	3.72	0.28	10.00	4.00
Ølstykke	16,622	96	4.12	1.01	3.53	0.16	1.00	0.00
Rønne	18,640	108	3.78	0.99	3.91	0.29	11.45	4.02
Sjælsø	13,262	104	4.09	1.00	3.50	0.30	11.00	4.63
Slangerup	7,465	87	3.20	1.62	3.20	0.18	1.00	0.00
Stavnsholt	20,554	91	4.41	0.87	3.51	0.10	12.70	4.75
Stenløse	12,167	92	4.46	0.83	3.28	0.16	1.00	0.00
Sydkysten	18,485	100	3.95	0.89	3.78	0.18	10.45	4.70
Tårnby	42,415	83	4.22	0.69	4.08	0.25	12.70	4.25
Tejn	2,549	105	3.48	1.26	3.37	0.42	7.85	5.50
Tørslev	3,852	91	4.08	1.19	3.13	0.20	1.00	0.00
Usserød	35,488	93	3.92	1.09	3.97	0.15	11.30	4.40
Vedbæk	11,926	103	4.13	0.96	3.69	0.21	10.50	4.45
Region Midtjylland								
Aarhus (Åby)	59,770	106	4.20	1.10	4.10	0.24	12.90	4.70
Aarhus (Egå)	86,360	103	4.14	1.15	4.25	0.16	12.00	3.50
Aarhus (Marselisborg)	122,064	102	4.19	1.24	4.40	0.14	14.20	4.00
Aarhus (Viby)	79,099	108	4.09	1.05	4.25	0.28	10.85	4.23
Aulum	5,751	105	3.93	1.59	3.26	0.25	9.50	4.00
Bjerringbro	11,328	93	3.85	1.29	3.74	0.16	10.30	4.50

Treatment plant	Population	Samples included	RNA copies per liter ¹		24-h flow (liters) ¹		Temperature ²	
			Median	IQR	Median	IQR	Median	IQR
Boeslum	7,984	93	4.14	0.87	3.33	0.08	5.00	2.00
Brædstrup	10,415	102	4.02	1.11	3.44	0.31	8.85	4.90
Brande	8,190	109	3.39	1.30	3.65	0.18	12.00	3.30
Drøsbro	2,103	25	3.80	1.14	2.86	0.12	10.10	3.30
Fornæs	21,348	107	3.15	1.36	4.09	0.18	11.17	3.62
Hadsten	10,389	33	3.91	1.47	3.50	0.28	9.40	5.50
Hammel	8,994	31	4.49	1.35	3.21	0.19	9.45	5.15
Harboøre	5,194	99	3.98	1.31	3.38	0.16	16.00	5.00
Harre-Vejle	3,134	101	3.20	1.34	3.31	0.25	8.60	4.30
Hedensted	20,286	100	3.77	1.00	3.90	0.15	11.00	4.00
Herning	55,728	103	3.92	1.00	4.39	0.29	11.00	3.50
Hinnerup	13,717	33	4.48	1.17	3.48	0.18	9.90	3.80
Holstebro øst	11,480	100	4.03	1.05	3.84	0.14	11.30	3.62
Holstebro vest	30,431	92	3.47	1.27	3.74	0.09	15.20	3.40
Hørning	8,917	78	4.25	0.83	3.26	0.28	9.90	4.30
Horsens	78,844	96	4.14	0.87	4.39	0.14	14.05	3.93
Hvide Sande	2,987	85	3.62	1.67	3.18	0.38	9.30	4.87
Ikast	22,195	107	4.03	1.03	3.88	0.26	8.00	5.80
Juelsminde	8,161	95	4.18	1.03	3.38	0.16	10.00	4.50
Karup	5,121	37	3.03	2.01	3.31	0.38	11.10	5.80
Kjellerup	9,235	98	4.06	1.04	3.47	0.25	9.35	5.27
Langå	7,522	64	3.19	1.54	2.98	0.15	11.10	4.75
Lemvig	11,592	97	3.76	0.88	3.60	0.22	10.30	3.60
Mørke	8,936	107	4.00	0.93	3.37	0.27	10.15	4.92
Nørre Snede	4,991	102	4.00	0.63	3.02	0.18	10.15	3.52
Odder	20,050	102	4.14	0.96	3.69	0.18	10.65	4.95
Randers Nord	29,990	100	4.11	1.02	3.78	0.15	12.00	3.95
Randers Syd	38,651	106	4.15	1.11	3.90	0.15	9.20	4.00
Randers Vest	21,472	94	3.93	0.97	3.64	0.23	9.95	4.28
Ringkøbing	13,518	22	3.95	1.86	3.81	0.15	7.20	5.70
Ry	7,876	83	4.42	0.93	3.11	0.24	10.50	5.00
Skanderborg	24,918	79	4.12	0.92	3.75	0.19	11.70	4.10
Skive	33,048	107	3.75	1.04	4.19	0.27	9.00	3.75
Skjern/Tarm	17,248	104	3.81	1.52	3.91	0.18	13.12	4.28
Skovby	14,646	81	3.89	0.85	3.66	0.38	9.40	4.60
Søholt	59,148	91	4.30	0.94	4.18	0.10	11.50	3.90
Struer	14,961	103	4.08	0.88	3.66	0.20	10.90	4.70
Sunds	5,195	104	3.66	1.39	3.61	0.18	10.00	2.70
Them	5,296	95	3.83	1.03	3.24	0.11	11.70	4.60
Trehøje Øst	5,545	106	3.63	1.59	3.45	0.26	9.50	3.50
Truust	4,823	93	3.94	0.97	3.15	0.15	9.00	4.30
Viborg	48,974	88	4.19	0.98	4.03	0.21	10.55	4.50
Videbæk	7,078	105	3.94	1.11	3.37	0.27	9.50	3.50
Vinderup	5,097	101	3.93	1.29	3.45	0.24	9.80	4.00
Region Nordjylland								
Aalborg Øst	68,413	104	4.00	0.75	4.24	0.17	12.00	3.05
Aalborg Vest	141,626	102	3.97	0.83	4.65	0.16	11.25	3.27
Aars	9,972	107	4.01	1.05	3.57	0.08	5.00	0.00
Attrup	5,625	101	2.93	1.65	3.52	0.25	8.86	5.30
Brønderslev	16,246	85	3.92	0.74	3.72	0.22	10.00	2.00
Fjerritslev	5,622	100	3.93	1.11	3.33	0.19	9.44	4.50
Frederikshavn	30,415	107	3.97	1.06	4.12	0.20	11.60	4.88
Hanstholm	3,624	93	4.45	1.03	2.75	0.12	7.00	4.62
Hirtshals	10,394	109	3.82	1.38	3.82	0.21	9.70	4.30
Hjørring	33,814	102	4.11	1.03	4.04	0.28	9.85	4.15
Karby	1,039	91	3.17	1.87	3.11	0.19	8.40	5.45
Løgstør	6,580	104	3.63	1.18	3.50	0.15	5.00	0.00
Løkken (Nr. Lyngby)	3,404	103	3.61	1.23	3.30	0.21	9.50	4.40
Mariagerfjord	34,566	104	3.85	1.13	4.09	0.15	10.90	4.31
Nykøbing Mors	15,136	104	3.83	1.04	3.70	0.21	10.75	5.00
Sæby	11,987	94	3.71	1.24	3.83	0.11	14.80	4.75
Sigsgård	18,307	106	4.03	1.11	3.77	0.26	11.50	5.35

Treatment plant	Population	Samples included	RNA copies per liter ¹		24-h flow (liters) ¹		Temperature ²	
			Median	IQR	Median	IQR	Median	IQR
Sindal	4,839	108	3.63	1.37	3.25	0.19	9.15	3.97
Skagen	7,497	104	3.35	0.92	4.01	0.17	13.50	3.30
Stistrup	11,422	105	4.32	1.07	3.31	0.11	5.00	0.00
Sundby (Morsø)	687	90	2.98	1.84	2.43	0.40	9.00	3.00
Tåbel	6,746	107	3.51	0.91	3.49	0.40	9.40	4.07
Thisted	16,182	106	3.48	1.17	3.96	0.25	17.20	3.98
Vilsund	4,411	102	3.54	1.44	3.32	0.43	7.00	4.00
Region Sjælland								
Bjergmarken	64,493	92	2.78	1.27	4.19	0.18	13.50	4.00
Borup	5,662	106	3.86	0.81	3.35	0.33	9.40	5.68
Dalby	2,487	98	3.90	1.15	2.90	0.21	10.00	5.10
Fårevejle	10,969	98	3.92	0.97	3.48	0.14	11.50	4.97
Faxe	7,610	102	3.72	1.04	3.56	0.34	6.40	4.85
Fuglebjerg	5,816	102	4.08	1.15	3.09	0.33	9.60	4.90
Haslev	14,568	97	3.93	0.78	3.56	0.31	10.40	4.90
Holbæk	36,320	92	4.03	0.96	3.87	0.12	13.95	4.20
Holme Olstrup	7,656	106	4.00	0.98	3.34	0.39	9.95	5.20
Hvalsø	7,413	88	4.20	0.74	3.28	0.31	10.45	5.47
Jyllinge	13,332	100	4.38	0.88	3.32	0.11	12.75	5.60
Kalundborg	18,701	94	3.72	1.26	3.87	0.18	11.00	5.20
Køge	53,293	94	4.11	0.90	4.13	0.20	12.40	5.05
Korsør	20,474	74	4.24	0.67	3.66	0.14	11.65	4.77
Maribo (Hunseby)	17,296	108	3.96	1.20	3.81	0.35	10.30	4.30
Marielyst	4,321	65	4.43	0.80	3.22	0.15	7.60	1.30
Mosedede	47,491	99	4.34	0.74	4.12	0.19	11.70	4.60
Næstved	69,102	107	4.02	0.85	4.32	0.28	10.60	4.31
Nakskov	12,862	109	3.80	0.91	3.83	0.22	11.70	5.60
Nykøbing	5,890	106	3.73	0.99	3.25	0.30	12.35	3.70
Nykøbing Falster	26,505	70	4.26	0.95	3.94	0.29	7.60	1.30
Ornum	8,808	108	3.71	1.11	3.56	0.32	9.90	5.45
Præstø	4,623	103	3.84	1.16	3.37	0.31	9.90	6.20
Ringsted C	31,851	102	3.70	1.08	3.97	0.27	13.70	6.03
Rødbyhavn	3,537	94	3.34	1.51	3.24	0.22	10.80	4.70
Skælskør	8,005	98	4.12	1.03	3.36	0.16	13.34	4.93
Slagelse	35,911	92	4.17	1.07	4.01	0.15	13.46	4.28
Solrød	19,197	100	4.08	0.81	3.70	0.17	11.30	4.00
Sorø	13,798	1	2.15	0.00	3.28	0.00	18.00	0.00
Stege	5,104	102	3.53	1.42	3.35	0.25	11.05	6.10
Store Heddinge	4,935	98	3.95	1.39	2.97	0.18	10.25	6.65
Strøby	9,888	106	4.10	0.96	3.47	0.32	10.05	6.02
Tornved	8,195	92	3.98	0.63	3.41	0.23	10.40	5.30
Tysinge	9,272	88	4.18	0.97	3.55	0.38	9.10	4.80
Viby	5,798	102	4.10	0.96	3.28	0.31	10.45	5.77
Vordingborg	22,542	101	4.00	0.96	3.79	0.20	11.70	5.20
Region Syddanmark								
Å Strand	2,628	43	3.77	1.05	3.07	0.21	7.75	2.85
Ærøskøbing	1,921	66	4.30	1.49	2.84	0.19	9.00	2.00
Årup	4,561	46	3.73	1.57	3.29	0.27	7.40	2.38
Assens	8,204	43	3.48	1.37	3.49	0.16	10.75	3.15
Bogense	7,170	99	4.10	1.14	3.33	0.15	11.10	4.00
Bov	6,233	98	3.79	0.88	3.33	0.30	9.10	4.15
Bramming Nord	5,035	104	3.95	1.26	3.05	0.37	10.80	3.30
Brejning	12,850	101	3.91	1.21	3.54	0.23	10.40	4.12
Brørup	5,337	101	3.87	1.44	3.42	0.42	9.00	7.62
Christiansfeld	5,580	101	3.60	1.27	3.40	0.18	12.28	4.06
Egebjerg Syd	4,113	103	3.45	1.87	3.20	0.27	9.80	3.75
Egsmade	40,860	98	3.79	1.09	4.10	0.22	11.20	3.85
Esbjerg Øst	24,278	107	3.94	1.44	4.11	0.19	11.40	4.40
Esbjerg Vest	61,935	102	3.67	0.96	4.39	0.11	13.95	2.50
Fåborg	21,569	3	4.23	1.01	4.37	0.05	8.40	0.80
Fredericia	51,429	94	3.87	1.14	4.28	0.16	14.35	3.66
Gaardeby	6,786	105	3.69	1.05	3.47	0.24	9.90	4.50

Treatment plant	Population	Samples included	RNA copies per liter ¹		24-h flow (liters) ¹		Temperature ²	
			Median	IQR	Median	IQR	Median	IQR
Give	12,140	98	3.68	0.89	3.71	0.29	10.30	4.38
Gram	4,004	97	3.81	1.15	3.45	0.14	9.30	4.40
Grindsted/Billund	16,699	105	3.79	0.72	4.05	0.12	10.90	4.20
Haderslev	30,473	94	3.81	1.01	3.95	0.20	13.00	3.23
Haraldskær	15,179	100	3.86	0.80	3.58	0.19	11.80	4.67
Hårby	3,518	44	3.31	1.30	3.15	0.26	6.90	2.02
Hofmangave	718	70	2.16	1.11	3.05	0.22	9.20	4.20
Holsted by	7,902	100	3.51	0.96	3.70	0.28	8.80	6.60
Kerteminde/Munkebo	15,807	105	3.89	0.87	3.85	0.23	10.60	4.70
Kolding	72,474	96	4.01	0.83	4.33	0.20	12.30	4.15
Kollund	2,418	94	4.06	1.17	2.75	0.16	9.40	3.90
Kværndrup	1,966	3	3.77	1.15	3.14	0.14	12.60	1.00
Middelfart	22,818	106	4.02	0.94	3.89	0.25	11.60	4.10
Nr. Åby	5,502	104	2.56	1.77	3.45	0.25	10.70	4.05
Nr. Nebel	2,412	99	3.96	1.37	3.21	0.25	8.90	4.45
Nyborg	30,414	5	3.62	0.38	3.94	0.16	14.00	0.00
Odense (Ejby Mølle)	133,463	103	3.79	1.50	4.68	0.17	11.60	3.45
Odense (Nordøst)	17,351	98	4.07	1.16	3.74	0.13	11.70	3.45
Odense (Nordvest)	50,344	107	4.03	1.02	4.21	0.20	11.50	4.10
Ørbæk	3,660	100	3.72	1.08	3.13	0.20	11.95	4.90
Otterup	10,401	101	3.90	0.81	3.55	0.18	10.20	4.50
Outrup	1,403	94	3.28	1.47	2.87	0.21	8.25	5.10
Ribe	12,900	107	3.78	1.08	3.74	0.29	9.80	4.15
Ringe	7,600	90	3.50	1.17	3.41	0.16	12.20	4.10
Rødding	8,664	105	3.57	1.14	3.40	0.38	7.80	6.05
Rudkøbing	5,403	97	3.86	1.12	3.19	0.26	11.90	4.50
Sdr. Nærá	8,059	7	4.09	0.45	3.37	0.21	10.10	3.15
Skærbæk	3,972	85	3.84	1.31	3.37	0.22	10.50	5.10
Skovlund	8,151	106	3.54	1.32	3.54	0.24	10.05	3.50
Sønderborg (Broager)	5,518	99	3.64	1.35	3.28	0.22	14.00	1.50
Sønderborg (Gråsten)	6,540	97	3.79	1.23	3.41	0.15	14.00	0.00
Sønderborg (Himmark)	10,524	103	3.96	1.02	3.52	0.28	11.00	3.30
Sønderborg	44,201	102	3.74	0.92	4.14	0.18	15.00	3.50
Søndersø	9,756	101	3.67	1.18	3.54	0.24	9.15	3.93
Stegholt	28,818	102	3.81	0.92	4.02	0.22	11.30	4.10
Strandgården	2,509	100	3.81	1.07	3.02	0.28	9.20	5.27
Tønder	10,514	109	3.80	1.09	3.81	0.18	14.20	4.80
Vamdrup	11,565	107	3.74	1.26	3.57	0.18	10.25	3.97
Varde	20,785	107	3.90	1.06	3.97	0.24	10.90	3.85
Vejen	20,652	101	3.63	0.76	3.91	0.27	8.25	6.48
Vejle	70,939	99	3.92	0.71	4.42	0.19	11.40	4.05
Vojens	7,910	90	3.99	1.05	3.28	0.18	10.60	4.70

¹ Calculated on the log₁₀ scale.

² Contains missing values.

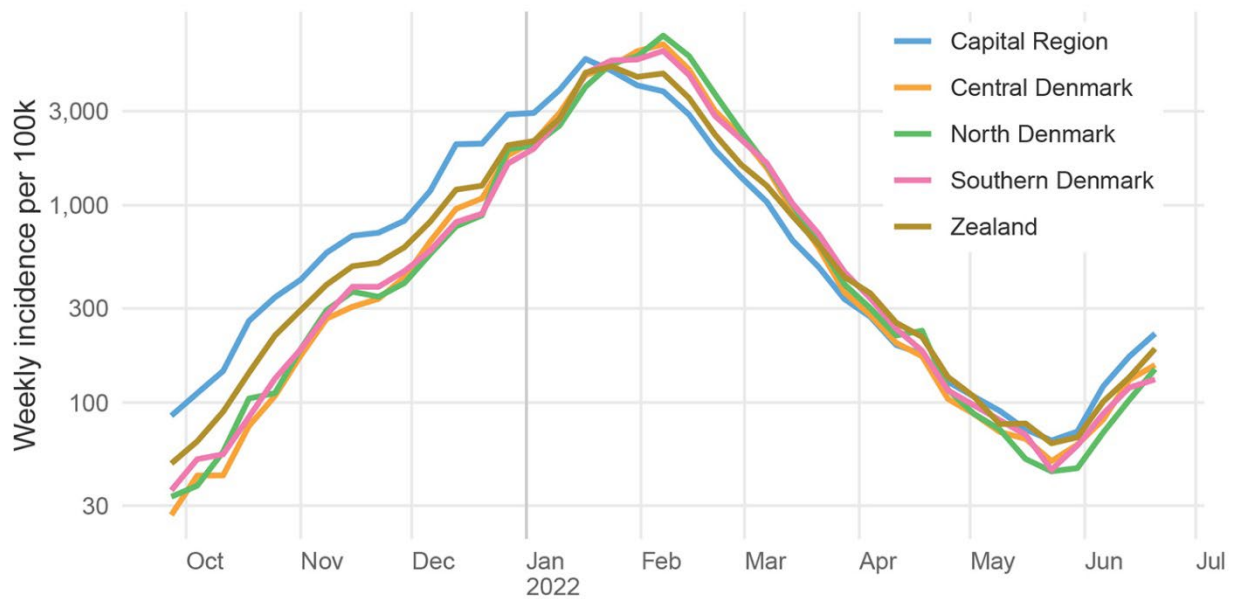
Appendix Table 2. Log-likelihood, AIC, and BIC measures for each tested model

Model	Log-likelihood	AIC	BIC
1	37.6	-67.3	-60.6
2	49.3	-88.6	-80.2
3	50.3	-88.6	-78.7
4	64.0	-113.9	-102.3
5	63.1	-114.2	-104.3
6	38.3	-66.6	-58.3
7	40.5	-73.0	-66.3
8	63.2	-112.3	-100.7

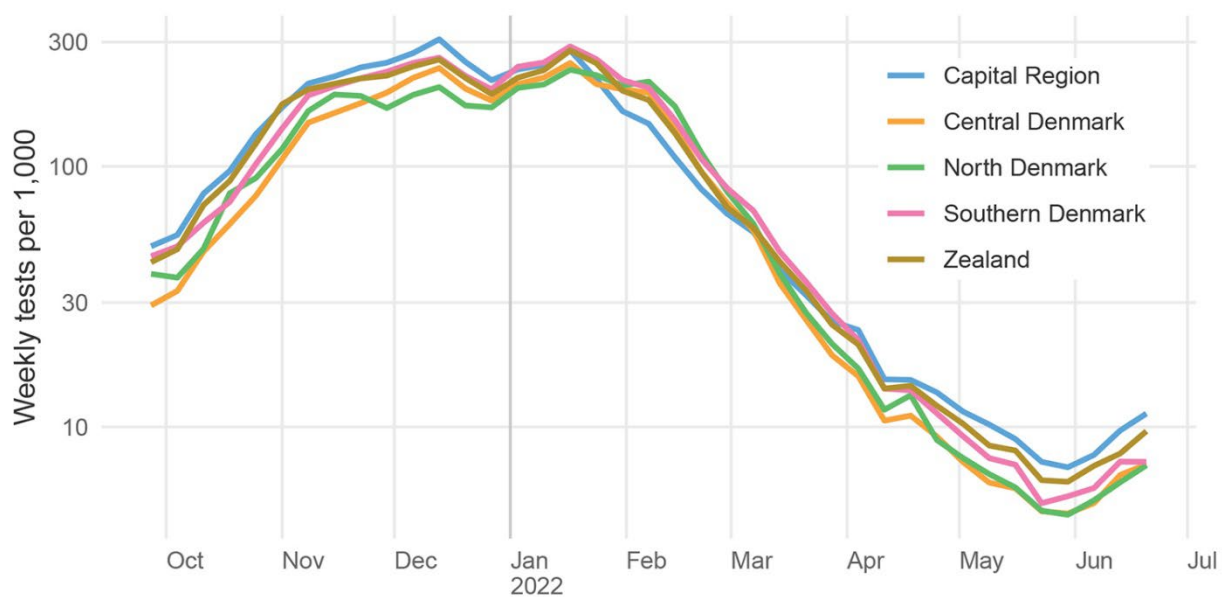
Appendix Table 3. Validation accuracy measures*

Model	Region	ME	RMSE	MAE	MPE	MAPE	ACF1	PI coverage
National	–	17.3	21.2	17.3	16.7	16.7	0.5	57%
Care personnel	–	-3.8	21.4	19.8	-7.5	17.7	0.1	100%
Regional	Capital Region	15.4	27.5	20.2	8.6	15.0	0.3	86%
Regional	Central Denmark	18.9	20.4	18.9	22.4	22.4	0.6	43%
Regional	North Denmark	16.6	21.1	16.6	18.9	18.9	0.4	57%
Regional	Southern Denmark	17.3	22.1	17.3	20.9	20.9	0.3	57%
Regional	Zealand	-1.0	14.9	10.6	0.3	9.8	-0.2	86%

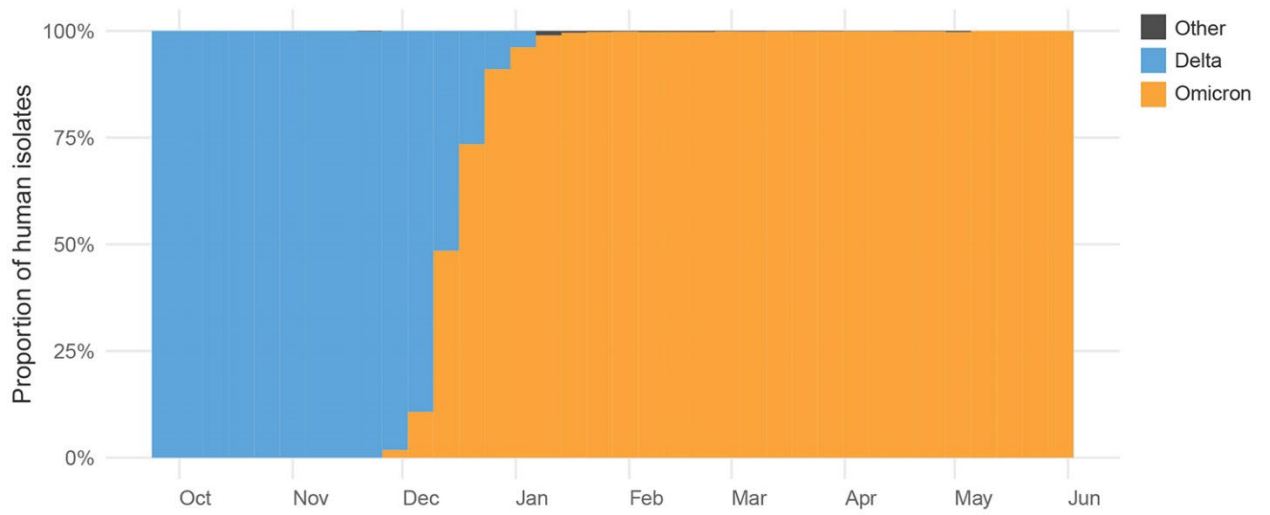
*ACF1, autocorrelation at lag 1; MAE, mean absolute error; MAPE, mean absolute percent error; ME, mean error; MPE, mean percent error; PI coverage, percentage of validation observations contained in 95% prediction interval; RMSE, root mean squared error.



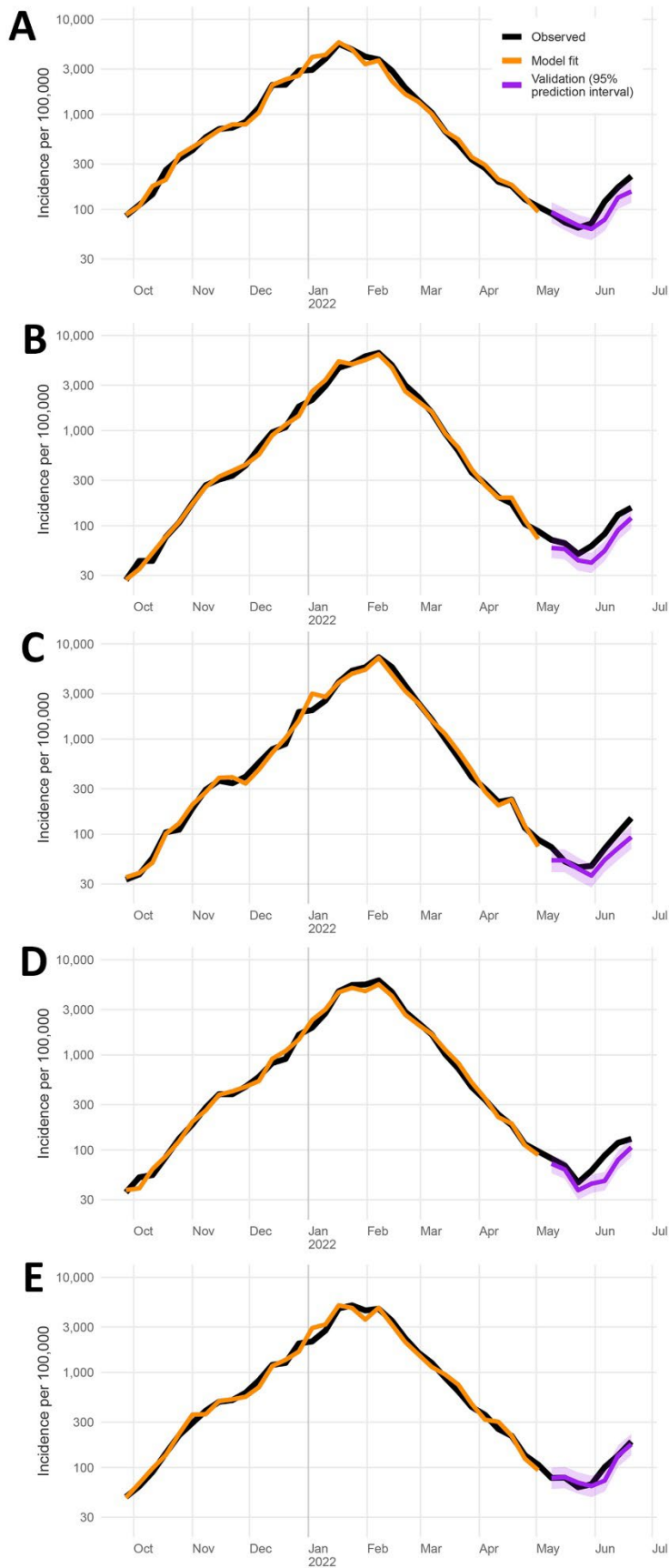
Appendix Figure 1. COVID-19 incidence over time by region



Appendix Figure 2. COVID-19 testing rate over time by region



Appendix Figure 3. Variant proportion over time, based on human samples



Appendix Figure 4. Model fit and forecasts based on the regional models. A) Capital Region, B) Central Denmark, C) North Denmark, D) Southern Denmark, E) Zealand.