A Novel Machine Learning Approach to Identify COVID-19 Deaths Among Excess Deaths Reported to Non-COVID-19 Causes

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ABSTRACT

The total number of deaths caused by the SARS-CoV-2 virus in the United States has been heavily debated since the start of the COVID-19 pandemic. Researchers have previously developed excess mortality models to estimate the number of deaths that would have occurred in the absence of the pandemic and the number of COVID-19 deaths that were not reported to COVID-19. However, estimates of excess deaths represent an upper-bound of total COVID-19 deaths as some of these deaths were likely related to health care interruptions and others to the pandemic's social and economic effects. We use a machine learning approach to leverage information from death certificate data, county characteristics related to population, health systems, and the death investigation system, and county-month trends in excess deaths and reported COVID-19 deaths to produce refined estimates of the total number of COVID-19 deaths throughout the United States from 2020 through 2022.

PROPOSAL

Background:

Since the beginning of the COVID-19 pandemic, it has been widely recognized that official COVID-19 death counts which include death certificates on which COVID-19 is listed as a cause or contributor to deaths are likely to be an incomplete account of the total mortality impacts of the pandemic in the United States.[1–5] There remains however a significant scholarly and public discussion about several related points. First, were "uncounted deaths" (deaths related to the pandemic that did not list COVID-19 on the certificate) mostly a feature of the early pandemic when health systems were unprepared to recognize COVID-19 deaths?[6,7] Second, have over-counts of COVID-19 deaths occurred in any substantial manner during the pandemic?[7,8] Third, do "uncounted deaths" primarily reflect deaths caused by the SARS-CoV-2 virus or deaths caused by pandemic-related health care interruptions, the pandemic's social and economic effects, and/or public health policies related to the pandemic such as lockdowns and physical distancing?[9–14] Lastly and relatedly, what was the total number of deaths caused by the SARS-CoV-2 virus, adding both deaths recognized in official counts and "uncounted deaths"?[15]

Excess mortality models are one approach that has been utilized throughout the public health literature to better understand the accuracy of official COVID-19 mortality statistics.[16] Excess mortality refers to the difference between the observed number of deaths that occurred during a given period and the number of deaths that would be expected based on earlier mortality trends.[17] Recent estimates have found that an estimated 1,179,024 excess deaths occurred during the first 2 years of the pandemic, with 634,830 excess deaths occurring in the first year and 544,194 in the second year.[7] Most prior studies have found that the number of excess deaths in the United States has substantially exceeded the number of COVID-19 deaths.[1,2,4,5,9] Prior comparisons of excess deaths to COVID-19 deaths have suggested that there have been approximately 10% to 35% more excess deaths than COVID-19 deaths, but estimates have varied across modeling specifications and time periods studied.[1,2,4,5,7,15,18]

Another important complexity that has contributed to differences between models (especially across analyses that use data from different health systems, states, or regions) is how excess deaths, COVID-19 deaths, and "uncounted deaths" differ in important ways demographically, geographically, and temporally.[5,7,10,12,19–29] Structural racism has caused substantial racial and ethnic inequities in COVID-19 and excess mortality during the pandemic, which have varied regionally and across the rural-urban continuum and temporally as the pandemic has progressed.[19,20,30–33] Relatedly, prior research has shown that the proportion of excess deaths not reported to COVID-19 deaths has varied demographically. For example, predominately Black communities have experienced more "uncounted deaths", which suggests that the true racial and ethnic inequities in COVID-19 mortality may be even larger than revealed in official death counts.[4,34] Geographic analyses have also revealed that excess deaths were less likely to be reported as COVID-19 deaths in the Mountain division, in the South, and in nonmetropolitan counties.[15] Temporally, there was a very significant spike in "uncounted deaths" early in the pandemic when death investigators were unfamiliar with the manifestations of COVID-19.[15,35,36] After this initial spike, it is possible that reporting may have gradually improved as guidelines were developed and refinements were made to the national vital statistics system.[15,37–39]

A factor that could serve as one mechanism explaining geographic and temporal differences in "uncounted deaths" is how the death investigation system operates and is funded.[40] In particular, cause-of-death assignment often varies significantly between in-hospital and out-of-hospital settings.[10,41–43] While inaccuracies do exist with in-hospital assignment practices, physicians have significantly more information available to them about decedents and often have far more training than other death investigators.[44–46] The United States death investigation system is a patchwork system with distinct offices across counties and states.[42] While many counties (typically more urban counties) have forensic pathologists working as medical examiners, other counties (typically more rural counties) have coroners, sheriff-coroners, and justices of the peace who are generally elected officials with limited medical training.[40,47] Another factor is that there is significant variability in the amount of funding that death investigation offices have available in each county, meaning counties had differential resources available to investigate COVID-19 deaths through interviews and post-mortem testing.[48] In line with this discussion, prior research during the pandemic has shown that most "uncounted deaths" occurred in out-of-hospital settings and were more common in areas without medical examiners.[10,41]

While estimating the precise number of COVID-19 deaths that have occurred during the pandemic given these challenges may appear as a largely technical project, accurate estimates of the burden of infectious diseases such as COVID-19 have critical importance for informing ongoing pandemic-related health policy and for future public health emergency preparedness. We offer three examples here to illustrate this point.[40,49] First, differential under-counting of COVID-19 deaths could disguise demographic groups and geographic areas that had significant COVID-19 mortality burdens that either went unnoticed or were underrecognized in official death counts.[34] This suggests that improving the accuracy of death counts may be important for ongoing investigation of the long-term impacts of the pandemic on marginalized groups. Second, many social and health policies were designed using official COVID-19 death data. One striking example is the FEMA funeral assistance program, which is an important social program to reduce the financial impact of pandemic-related losses on families.[6] This program, however, requires individuals to submit a death certificate that lists

COVID-19, meaning that “uncounted deaths” are not eligible and that inequities in reporting would extend to this social benefit. Third, COVID-19 deaths are just one issue related to cause-of-death assignment in the death investigation system. Prior research has shown that other causes of death such as drug overdose, Alzhemier’s disease and related dementias, and deaths in police custody are also under-counted in the United States.[46,50–52] We believe new approaches for identifying COVID-19 uncounted deaths could potentially be adapted to these other causes of death, and methods developed using retrospective data could ultimately be leveraged for improved surveillance.

Research Objectives:

In this analysis, we use a novel machine learning approach to leverage individual-level demographic information from multiple cause of death data, county-level characteristics related to demographics, population, health systems, and the death investigation system, and county-month trends in excess deaths and reported COVID-19 deaths by place of death to produce refined estimates of the total number of COVID-19 deaths throughout the United States from 2020 through 2022. In addition to highlighting the performance and utility of our approach, we will also produce updated estimates of COVID-19 mortality for counties and states and identify geographic areas and demographic groups (e.g. by age, sex, race, ethnicity, gender, and education) who had large numbers of uncounted COVID-19 deaths. By sharing a new approach for improving estimates of COVID-19 deaths to account for inaccuracies and inequities, we will generate discussion about new approaches for monitoring multiple types of deaths in the United States to account for the possibility of inconsistent cause-of-death assignment, death investigator bias, and differential under-funding of death investigation systems to mislead public health researchers and policy-makers about the burden of disease.

Data:

We used restricted-access multiple cause of death files from the National Center for Health Statistics (NCHS) for March 2020 through December 2021. These data contain all 6.35 million deaths that occurred in the US during this time period and contain information such as underlying cause of death and up to 20 contributory causes of death (coded in ICD-10) as well as decedent information such as age (in years), month and year of death, county of residence and death, educational attainment, marital status, sex, smoking status, and race and ethnicity. Importantly, the death certificates also contain information about the place of death (e.g., in hospital, at home, long-term care facility, etc.). Based on previous work, we created derived variables using contributing cause of death codes including the presence of diabetes, pneumonia, kidney failure, essential hypertension, and hyperlipidemia, ICD-10 codes.

We combined these individual-level data with both time-invariant and time-varying contextual data. Our time-invariant contextual data includes the rural-urban continuum code of the county of residence, the proportion of the population that is non-Hispanic White, the proportion of the population that is Hispanic, the proportion of the population that is non-Hispanic Black, the proportion of the population that is over 65 years of age, median household income, the proportion of the population that owns a home, county-level income inequality, the proportion of the county with diabetes, county-level obesity and smoking rates, and the proportion of the county that reports poor or fair health. For all time-invariant covariates, we used data from before 2020 to prevent data leakage. In addition, we included two time-varying covariates at the county-month level: the CDC community transmission level categorization and the percent

of the population that received a vaccine. In sensitivity analyses, we also included county of residence and each of the NCHS 113 cause of death codes as fixed effects.

Research Methods:

Analytic Approach

Because COVID-19 deaths among those under 25 years of age is uncommon, we removed them from the data for a final data set of 6.2 million deaths. We further split these data into a gold standard analytic data set and a prediction data set. The gold standard analytic data set consisted of all deaths that occurred in the hospital among those receiving in-patient care (N=1.98 million), reflecting our belief that in-hospital, in-patient deaths during this time period were more likely to be accurately classified as COVID-19 deaths. These gold standard data were used for model tuning, model selection, and building a final classification model. The remaining, out-of-hospital (or in-hospital emergency room or dead on arrival) deaths (N=4.24 million) are used during the prediction phase.

Creating a Classification Model

We divided the gold standard analytic data set into 60-20-20 train-validate-test splits. During hyperparameter tuning, models were trained on 60% of the data and validated against 20% of the data until an optimal set of hyperparameters was found. The model was then refit with the finalized hyperparameters on 80% of the data and evaluated against the 20% test set, which was only used for model evaluation (i.e., never used for model training). Using true holdout data for our test split ensures that our model performance metrics accurately reflect the expected out-of-sample performance.

We fit five types of models: logistic regression with ElasticNet regularization, logistic regression with LASSO regularization, random forests, LightGBM, and XGBoost. We used Bayesian optimization, which is a sequential tuning optimization that explores the hyperparameter space using an acquisition function to continually find a set of hyperparameters that improves upon a pre-specified metric. We used the area under the receiver operating characteristics curve (AUC ROC) as our primary model performance metric. We allowed the Bayesian optimization to continue for up to 125 iterations with two tweaks. First, tuning stopped early if there was no model performance improvement for 25 iterations. Second, if there was no model performance improvement for 7 iterations, the model would select a high variance area of the hyperparameter space to explore.

For each of the five model types, we fit our primary covariate set and three additional sensitivity sets. Our primary covariate set consisted of all information available on the death certificate and both time-invariant and time-varying contextual variables based on the decedent's county of residence. The three sensitivity covariate sets included adding county fixed effects to county for unobserved factors that may vary across areas (but not time), contributing cause of death fixed effects, and both county and contributing cause of death fixed effects.

For the regularized logistic regressions, we preprocessed the data by creating binary indicator variables for all categorical predictors, creating a third-degree polynomial of age, and performing a mean-centered, unit-standard deviation normalization on all numeric predictors.

For the remaining tree-based models, we preprocessed the data by using one-hot coding for all categorical covariates. For all models, we used mean imputation for time-invariant county-level contextual variables with missing data and downsampled observations to address the slight imbalance in COVID-19 classifications.

Model Selection

After tuning and refitting all models, we selected the best model with the highest AUC ROC value. This model was then refit to all (i.e., 100%) of the gold-standard data and was used to create our final classification model to classify COVID-19 deaths in the prediction (i.e., out of hospital) data set.

Predicting COVID-19 Deaths

To quantify potential over- or under-reporting of official COVID-19 deaths, we used the final classification model to identify COVID-19 deaths on the prediction (i.e., out of hospital) data set across a variety of individual- and county-level strata. We estimated the adjusted reporting ratio (ARR) for each stratum as

$$ARR_i = \frac{{D_i}^H + \widetilde{D_\iota}}{{D_i}^T}$$

where i is our strata of interest, ${D_i}^H$ is the number of official in-hospital COVID-19 deaths, $\widetilde{D_\iota}$ is the number of predicted out-of-hospital COVID-19 deaths, and ${D_i}^T$ is the total number of official COVID-19 deaths. We estimated 95% uncertainty intervals (95% UI) by using 5,000 bootstrapped samples of the out-of-hospital predictions and reporting the 2.5th and 97.5th quantiles.

Preliminary Results:

Across all models, the XGBoost models had the highest ROC AUC of 0.902, while maintaining high accuracy, sensitivity, and specificity (Figure 1). In fact, our preferred model, the XGBoost with no county and no contributing cause data had the highest performance in 8 of the 13 measures used and was within less than 1% of the best performing model for the remaining 5 measures (Table S1) and exhibited excellent performance across all standard evaluations (Figures S1-S4).

The adjusted reporting ratio (ratio of predicted COVID-19 deaths over observed COVID-19 deaths) was 1.28 for the total population. The ratio differed across individual and community-level factors, including such factors as age, educational attainment, race and ethnicity, and urban-rural status (Figures 1-2). There was also substantial spatial temporal variation in the adjusted reporting ratio by state and over pandemic months (Figure 3).

Next Steps:

Having identified significant differences in the adjusted reporting ratio across social and demographic characteristics, states, and pandemic months, we will expand our research by further refining the spatial resolution of the analysis. We will also perform regression

modeling to examine the association of the reporting ratio with public health and health care factors as well as features of the death investigation system.

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Figure 1. Ratio of the predicted total number of COVID-19 deaths to the number of COVID-19 deaths recorded on death certificates across individual-level decedent characteristics

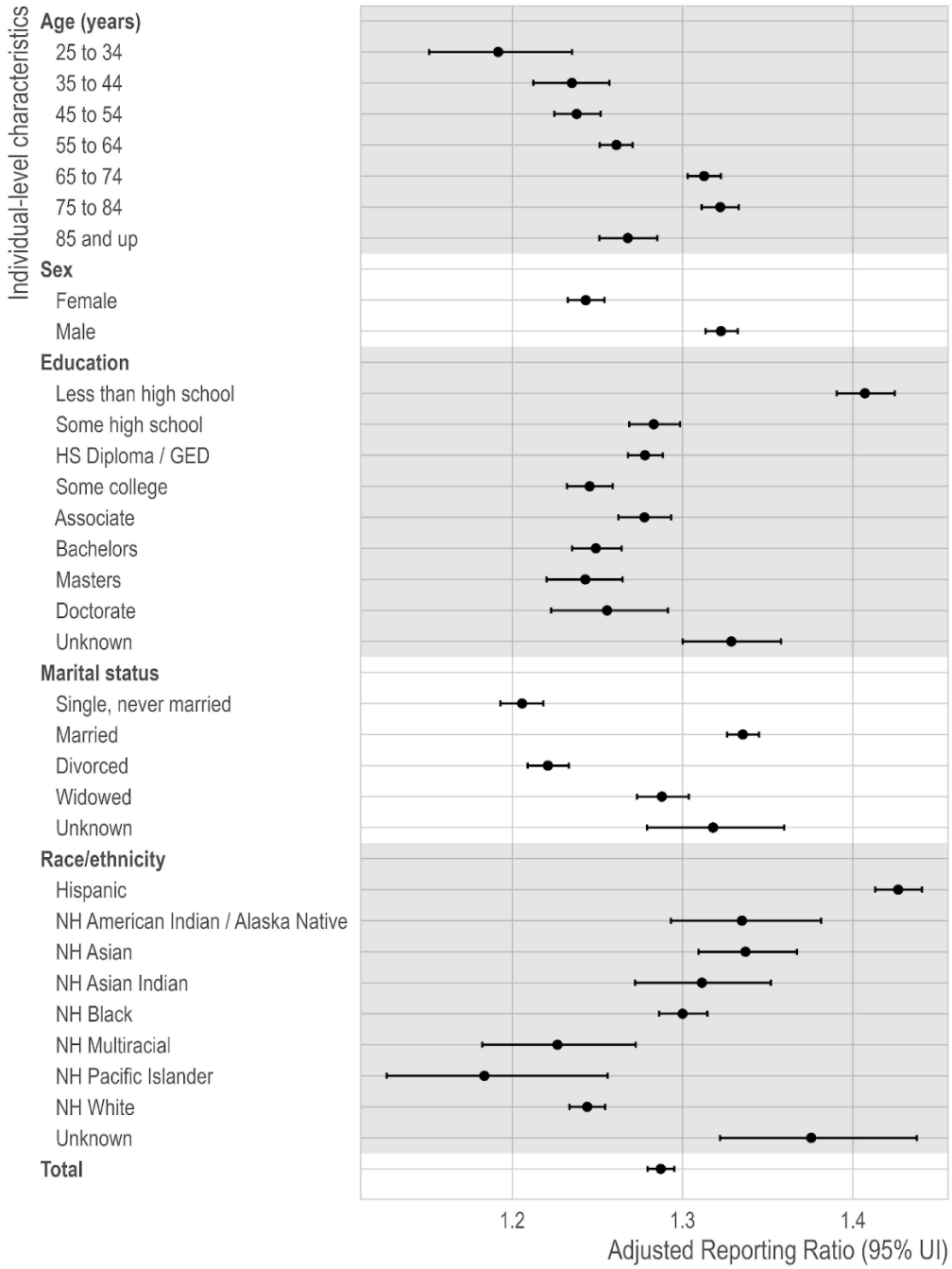


Figure 2. Ratio of the predicted total number of COVID-19 deaths to the number of COVID-19 deaths recorded on death certificates across county-level characteristics

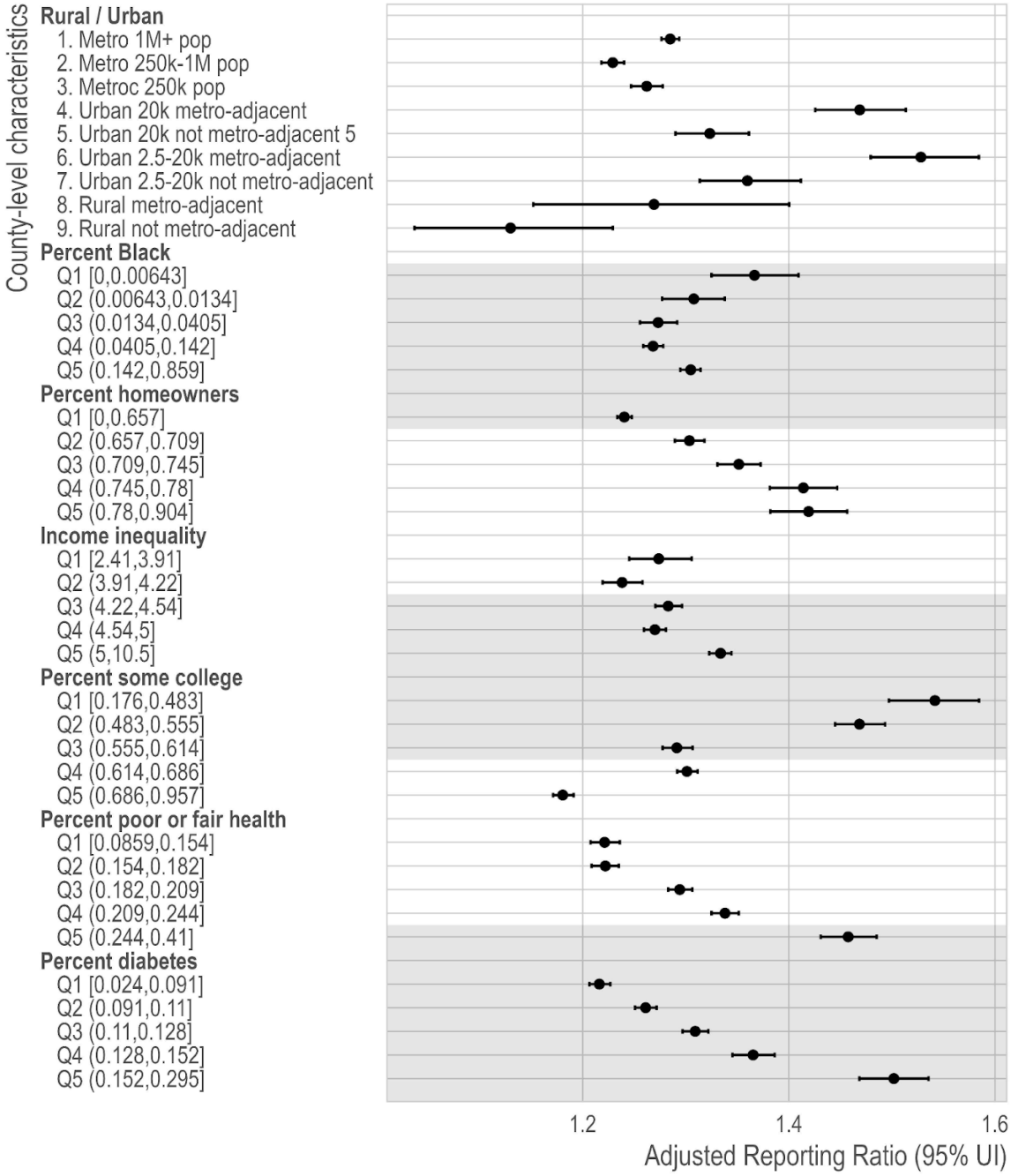
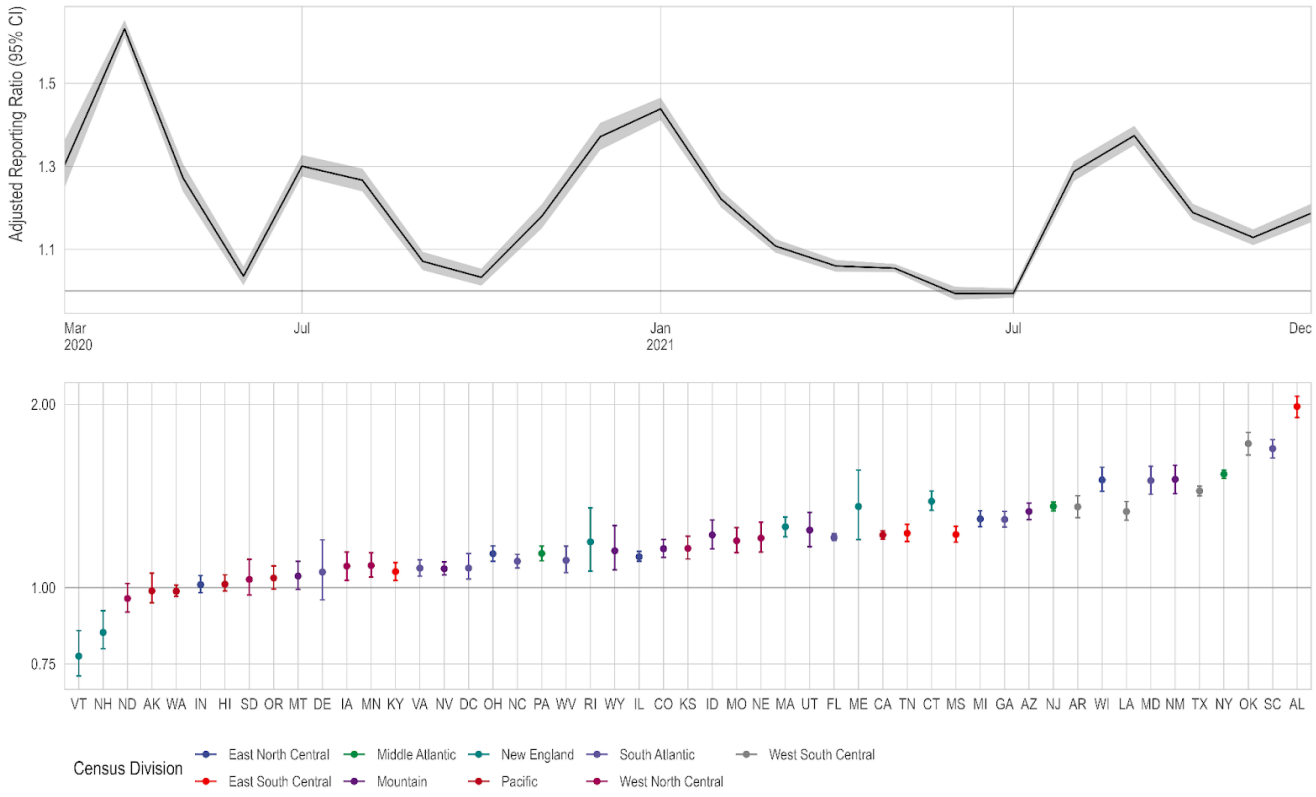


Figure 3. Monthly and state-level ratios of the predicted total number of COVID-19 deaths to the number of COVID-19 deaths recorded on death certificates



Appendix

Table S1. Performance metrics across all models

Model	Preprocessing	AUC ROC	Sens.	Spec.	Accu.	NPV	PPV	F1	J	MCC	Kappa	Bal. Accu.	Accu. ratio	AUC PR
XGBoost	No county, no contributing cause	**0.902**	0.799	0.849	**0.835**	0.916	0.671	**0.729**	**0.648**	**0.617**	**0.612**	**0.824**	**0.804**	**0.806**
XGBoost	No county	**0.902**	**0.801**	0.846	0.834	**0.917**	0.668	**0.729**	0.647	0.615	0.610	**0.824**	**0.804**	**0.806**
XGBoost	No contributing causes	0.901	0.797	0.849	**0.835**	0.915	0.671	**0.729**	0.646	0.615	0.611	0.823	0.802	0.805
XGBoost	All covariates	0.901	0.798	0.847	0.834	0.916	0.669	0.728	0.645	0.614	0.609	0.823	0.802	0.805
LightGBM	No county, no contributing cause	0.899	0.793	0.849	0.834	0.914	0.670	0.727	0.643	0.613	0.608	0.821	0.798	0.801
LightGBM	No county	0.899	0.795	0.847	0.832	0.914	0.667	0.725	0.641	0.611	0.606	0.821	0.797	0.801
LightGBM	No contributing causes	0.897	0.790	0.848	0.832	0.913	0.668	0.724	0.638	0.608	0.604	0.819	0.794	0.798
LightGBM	All covariates	0.896	0.789	0.848	0.832	0.912	0.667	0.723	0.637	0.608	0.603	0.819	0.792	0.796
Random Forest	No county, no contributing cause	0.895	0.786	0.852	0.833	0.912	0.672	0.725	0.638	0.610	0.606	0.819	0.790	0.794
Random Forest	No county	0.895	0.783	**0.854**	0.834	0.911	0.675	0.725	0.637	0.611	0.607	0.819	0.790	0.794
Random Forest	No contributing causes	0.895	0.785	0.853	0.834	0.911	0.674	0.725	0.638	0.611	0.607	0.819	0.791	0.795
Random Forest	All covariates	0.895	0.784	0.854	0.834	0.911	**0.675**	0.725	0.638	0.611	0.608	0.819	0.790	0.794
BART	No county, no contributing cause	0.894	0.786	0.846	0.829	0.911	0.663	0.720	0.632	0.602	0.598	0.816	0.788	0.793
BART	No county	0.894	0.787	0.846	0.829	0.911	0.663	0.720	0.633	0.603	0.598	0.816	0.789	0.794
Logistic (ElasticNet)	No county, no contributing cause	0.864	0.727	0.850	0.815	0.889	0.651	0.687	0.576	0.558	0.556	0.788	0.729	0.741
Logistic (ElasticNet)	No county	0.864	0.727	0.849	0.815	0.889	0.650	0.687	0.576	0.558	0.556	0.788	0.729	0.741
Logistic (ElasticNet)	No contributing causes	0.869	0.737	0.848	0.817	0.893	0.652	0.692	0.585	0.564	0.562	0.792	0.737	0.744
Logistic (ElasticNet)	All covariates	0.868	0.734	0.850	0.817	0.892	0.654	0.692	0.584	0.565	0.563	0.792	0.737	0.744
Logistic (LASSO)	No county, no contributing cause	0.864	0.726	0.850	0.815	0.889	0.651	0.687	0.576	0.558	0.556	0.788	0.729	0.741
Logistic (LASSO)	No county	0.864	0.727	0.849	0.815	0.889	0.651	0.687	0.576	0.558	0.556	0.788	0.729	0.741

Figure S1. Receiver operating characteristic curve of the primary model (black) and all other models (grey). The white circle represents the model performance at the standard threshold (Pr>.5).

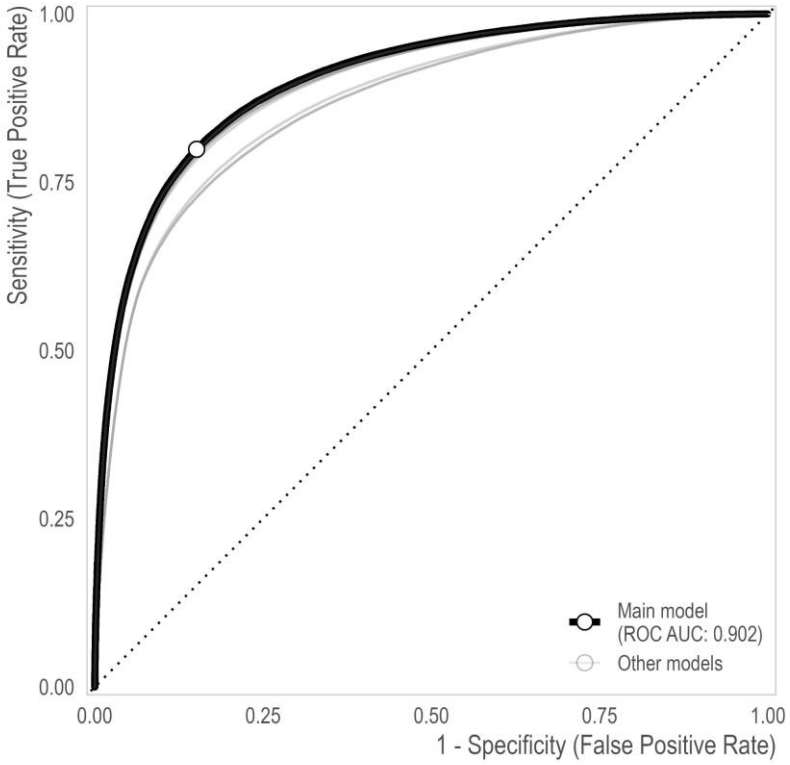


Figure S2. Precision-recall curve of the primary model (black) and all other models (grey). The white circle represents the model performance at the standard threshold (Pr>.5).

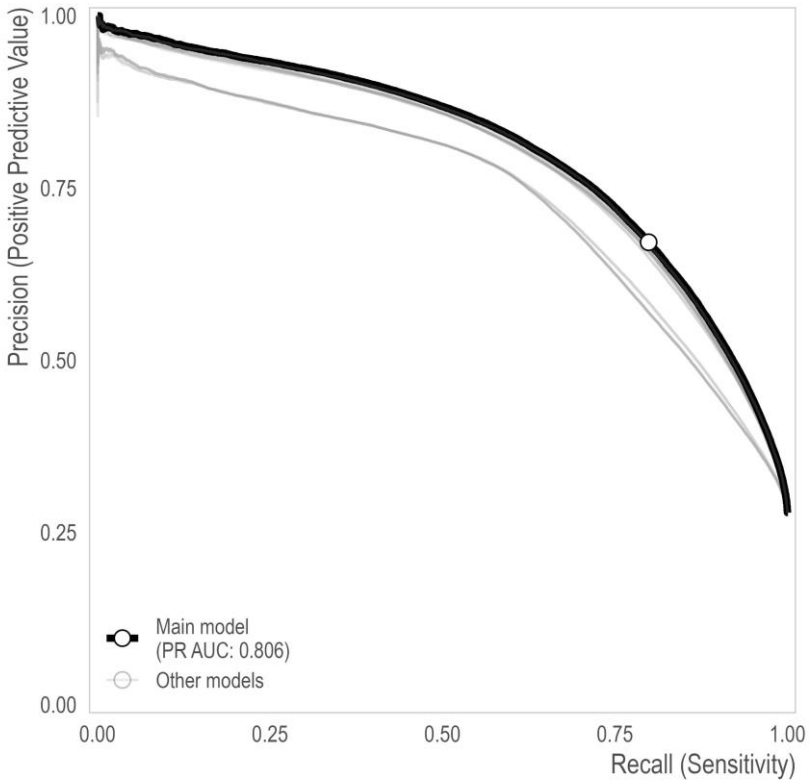


Figure S3. Cumulative gain of the primary model (black) and all other models (grey) compared to a perfect classifier (red) and random chance (blue).

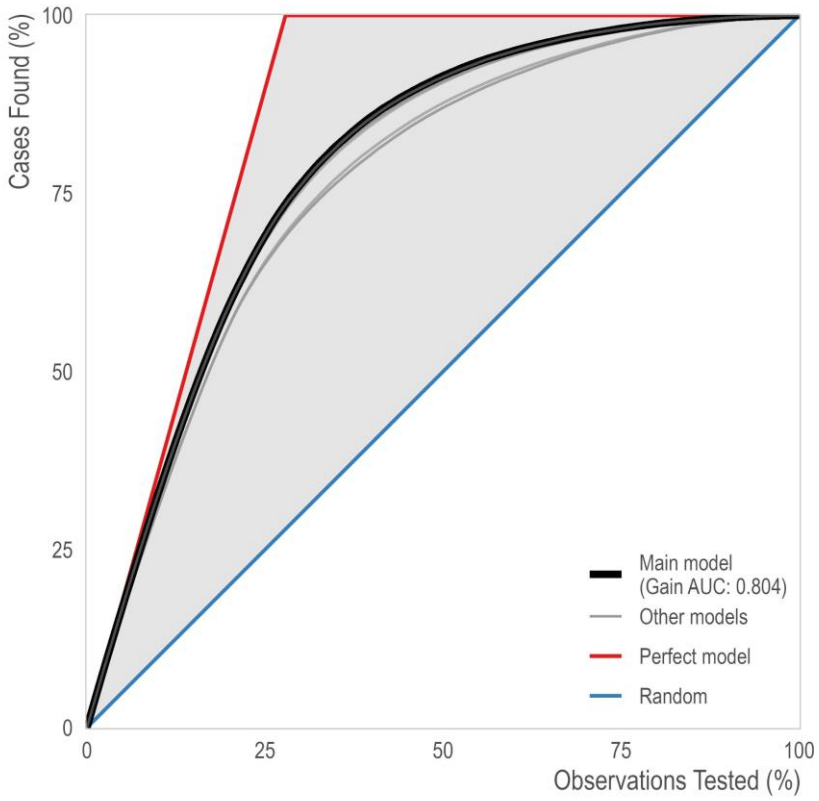


Figure S4. Lift curve of the primary model (black) and all other models (grey).