Contents

Original Papers

Forecasting COVID-19 Hospital Census: A Multivariate Time-Series Model Based on Local Infection Incidence (e28195)
Hieu Nguyen, Philip Turk, Andrew McWilliams. ................................................................. 2

Census Tract Patterns and Contextual Social Determinants of Health Associated With COVID-19 in a Hispanic Population From South Texas: A Spatiotemporal Perspective (e29205)
Cici Bauer, Kehe Zhang, Miryoung Lee, Susan Fisher-Hoch, Esmeralda Guajardo, Joseph McCormick, Isela de la Cerda, Maria Fernandez, Belinda Reininger. ................................................................. 15

Viewpoint

With Great Hopes Come Great Expectations: Access and Adoption Issues Associated With COVID-19 Vaccines (e26111)
Zhaozhui Su, Dean McDonnell, Ali Cheshmehzangi, Xiaoshan Li, Daniel Maestro, Sabina Segalo, Junaid Ahmad, Xiaoning Hao. ......................... 24
Forecasting COVID-19 Hospital Census: A Multivariate Time-Series Model Based on Local Infection Incidence

Hieu M Nguyen1*, MSc; Philip J Turk1*, MSc, PhD; Andrew D McWilliams1, MPH, MD
Center for Outcomes Research and Evaluation, Atrium Health, Charlotte, NC, United States
* these authors contributed equally

Corresponding Author:
Hieu M Nguyen, MSc
Center for Outcomes Research and Evaluation
Atrium Health
1300 Scott Ave
Charlotte, NC, 28204
United States
Phone: 1 9706914892
Email: hieu.nguyen@atriumhealth.org

Abstract

Background: COVID-19 has been one of the most serious global health crises in world history. During the pandemic, health care systems require accurate forecasts for key resources to guide preparation for patient surges. Forecasting the COVID-19 hospital census is among the most important planning decisions to ensure adequate staffing, number of beds, intensive care units, and vital equipment.

Objective: The goal of this study was to explore the potential utility of local COVID-19 infection incidence data in developing a forecasting model for the COVID-19 hospital census.

Methods: The study data comprised aggregated daily COVID-19 hospital census data across 11 Atrium Health hospitals plus a virtual hospital in the greater Charlotte metropolitan area of North Carolina, as well as the total daily infection incidence across the same region during the May 15 to December 5, 2020, period. Cross-correlations between hospital census and local infection incidence lagging up to 21 days were computed. A multivariate time-series framework, called the vector error correction model (VECM), was used to simultaneously incorporate both time series and account for their possible long-run relationship. Hypothesis tests and model diagnostics were performed to test for the long-run relationship and examine model goodness of fit. The 7-days-ahead forecast performance was measured by mean absolute percentage error (MAPE), with time-series cross-validation. The forecast performance was also compared with an autoregressive integrated moving average (ARIMA) model in the same cross-validation time frame. Based on different scenarios of the pandemic, the fitted model was leveraged to produce 60-days-ahead forecasts.

Results: The cross-correlations were uniformly high, falling between 0.7 and 0.8. There was sufficient evidence that the two time series have a stable long-run relationship at the .01 significance level. The model had very good fit to the data. The out-of-sample MAPE had a median of 5.9% and a 95th percentile of 13.4%. In comparison, the MAPE of the ARIMA had a median of 6.6% and a 95th percentile of 14.3%. Scenario-based 60-days-ahead forecasts exhibited concave trajectories with peaks lagging 2 to 3 weeks later than the peak infection incidence. In the worst-case scenario, the COVID-19 hospital census can reach a peak over 3 times greater than the peak observed during the second wave.

Conclusions: When used in the VECM framework, the local COVID-19 infection incidence can be an effective leading indicator to predict the COVID-19 hospital census. The VECM model had a very good 7-days-ahead forecast performance and outperformed the traditional ARIMA model. Leveraging the relationship between the two time series, the model can produce realistic 60-days-ahead scenario-based projections, which can inform health care systems about the peak timing and volume of the hospital census for long-term planning purposes.

(JMIR Public Health Surveill 2021;7(8):e28195) doi:10.2196/28195

KEYWORDS

COVID-19; forecasting; time-series model; vector error correction model; hospital census; hospital resource utilization; infection incidence
Introduction

SARS-CoV-2 is a novel member of the coronavirus family, and infections in humans can result in the disease COVID-19. The virus is transmitted primarily through droplets from coughing and sneezing and is highly infectious. Its basic reproduction rate is estimated to be in the low to mid 2s based on different models [1], compared to 2 for severe acute respiratory syndrome (SARS) and 1.3 for the 2009 swine flu [2]. Moderate to severe disease typically manifests with acute hypoxemia, and can progress to acute respiratory distress syndrome, multiorgan dysfunction, and death. Furthermore, an estimated 25%-30% of patients admitted to hospitals require intensive care admission [2]. In December 2019, the first cases were recorded in Wuhan, China, with subsequent spread across the world. In early 2020, the World Health Organization declared COVID-19 to be a global health emergency [3]. At the end of December 2020, SARS-CoV-2 had resulted in over 82 million documented cases and nearly 2 million deaths [4].

Our work is motivated by the need of hospital leaders to have timely and accurate forecasts to guide planning for surges in hospital demands due to the pandemic. Adequate preparation can help prevent or mitigate strains on hospital resources that result when hospitals exceed their historical capacity. On the contrary, being caught off-guard under a pandemic can devastate the population and health care systems. For example, previous models in India suggested falsely that it had reached herd immunity, encouraging complacency and insufficient preparation; however, on May 4, 2021, there was still a reported rolling average of 378,000 cases a day, which overwhelmed hospitals and health workers and resulted in a national health crisis [5]. Thus, to a health care system, an essential tool is a model that provides short- and long-range forecasting of the number of COVID-19-positive patients who will be admitted. This COVID-19 hospital census plays a central role in planning decisions that frequently require considerable lead time, such as increasing staff, creating physical beds and rooms, and procuring vital equipment (eg, ventilators and personal protective equipment).

Prior research has demonstrated the utility of forecasting hospital demands (eg, hospital admissions, intensive care unit census, and hospital overall census) using univariate time-series models such as the autoregressive integrated moving average (ARIMA), the seasonal autoregressive integrated moving average (SARIMA), and exponential smoothing [6-8]. Another approach is to use ensemble-based modeling. For example, a hybrid of a SARIMA model and a nonlinear autoregression artificial neural network model has been used to forecast hospital admissions [9]. In another example, two separate models, a time-series model for hospital admission and a patient-level logistic regression model for hospital discharge, were combined to predict the hospital census [10]. While these examples demonstrate the powerful potential of univariate time-series and ensemble modeling, neither incorporate factors inherent to the behavior of the pandemic, which may serve as important leading indicators of hospital census, especially at times when infection rates become increasingly dynamic (eg, on the approach or descent of peak infection prevalence). To incorporate pandemic indicators into modeling requires recognition that such indicators are typically nonstationary. Consequently, while a stationary multivariate time-series model, called vector autoregression (VAR), has been successfully employed to forecast emergency department patient census by including other hospital resource indicators [11], it cannot be used in this situation. Rather, our problem will require nonstationary multivariate time-series models like the vector error correction model (VECM).

Recently, VECM has been used to forecast the demand for intensive care units during the COVID-19 pandemic by including hospital admission as a leading indicator [12]. Although hospital admission is a natural choice as a leading indicator, it has a short period of lead time (ie, hours to days) and thus, limited predictive power. A more powerful indicator for planning purposes would lead by days to weeks. We have previously used VECM to forecast COVID-19 hospital census using leading indicators from Google relative search volumes for COVID-19 testing–related terms combined with the number of people flagged as having possible COVID-19 when using an internet-based virtual health screening bot [13]. However, these COVID-19 indicators, which are based on symptoms, have limitations. For example, the symptoms of COVID-19 cannot be easily separated from other common conditions, such as the seasonal flu, and search patterns may change due to other external factors over time.

During the COVID-19 pandemic, many papers have been devoted to developing predictive models for the volume of new cases (ie, infection incidence) using various methods from time-series analyses [14-16] to advanced machine learning [17,18]. However, virtually no effort was focused on developing statistical models linking infection incidence to hospitalization. Because hospital admission typically follows the symptoms or exposure that may provoke a person to be tested by roughly 1 week, we hypothesize that at a local population level, infection incidence rates may have a stable relationship with and serve as a reliable leading indicator for the COVID-19 hospital census. In this paper, our main objective is to explore whether the local COVID-19 infection incidence and the COVID-19 hospital census can be successfully incorporated within a VECM to delivery satisfactory 7-days-ahead forecast performance and examine the application of this model to scenario-based long-term forecasting. From our experience, since there can be systematic changes due to the day of the week in a hospital time series, we will need to account for weekly seasonal effects and examine implications on short-term resource planning.

Methods

Time-Series Data

Atrium Health is a large, integrated health care system operating in North Carolina, South Carolina, and Georgia. In this paper, the COVID-19 hospital census (census) refers to the daily aggregate number of beds occupied by patients with COVID-19 at midnight across the subset of 11 Atrium Health hospitals in the greater Charlotte metropolitan area of North Carolina, plus a virtual hospital (Atrium Health Hospital at Home). The virtual hospital uses telemedicine to treat patients who require only a
minimal level of care. The local COVID-19 infection incidence (incidence) is the aggregate daily count of new COVID-19–positive cases from 11 local counties belonging to the Cities Readiness Initiative (CRI) region, as designated by the North Carolina Department of Health and Human Services. The CRI region roughly approximates the market catchment area of these hospitals.

Using STL (seasonal and trend decomposition using Loess) time-series decomposition [19], we observed that the two time series had multiplicative weekly seasonality. We transformed both time series to achieve additive seasonality and linearize their relationship. The usual log transformation was applied to incidence. For operational purposes, the health system had previously decided to place an upper bound of 1000 patients with COVID-19 on the hospital time-series range, so we applied the following constrained log transformation so that the back-transformed census forecasts would satisfy the constraint:

\[
\text{The forecast model described in the following sections was developed for these transformed time series. Figure 1 shows a plot of transformed census and incidence on a standardized scale for the period from May 15 to December 5, 2020. To affirm the association between the two transformed time series, we computed the Pearson cross-correlations between census and values of incidence at lags 0, −1, …, −21.}
\]

**Figure 1.** Scaled time series for COVID-19 hospital census and local COVID-19 infection incidence in the Cities Readiness Initiative region for the period from May 15 to December 5, 2020. Transformed census (blue) and incidence (red) are linearly standardized to the 0-100 scale.

**VECM**

A VECM is a vector autoregressive model used for nonstationary multivariate time series and accounts for stable long-run relationships, that is, cointegration, between the time series. A \( k \times 1 \) time-series vector \( y_t \) is said to be cointegrated if there is at least one nonzero \( k \times 1 \) vector \( \beta_\alpha \) such that the linear combination is trend-stationary. If \( r \) such linearly independent vectors \( \beta_i \ (i=1,\ldots,r) \) exist, we say \( y_t \) is cointegrated with cointegration rank \( r \) [20].

Following Pfaff [20], we first describe the VAR representation of order \( p \) of the VECM:

\[
\Delta y_t = \Pi_1 y_{t-1} + \cdots + \Pi_p y_{t-p} + \mu + D_t \Phi + \varepsilon_t
\]

for time \( t=1,\ldots, T \), where \( \Pi_i \) (for \( i=1,\ldots,p \)) are \( k \times k \) coefficient matrices of the lagged series at lag \( i \), \( \mu \) is a \( k \times 1 \) vector of constants, \( D_t \) is a \( 6 \times 1 \) vector of weekly seasonal indicators, \( \Phi \) is a \( k \times 6 \) coefficient matrix for seasonal indicators, and \( \varepsilon_t \) is a \( k \times 1 \) vector of random errors.

The VECM specification can be formulated as an algebraic rearrangement of the VAR representation as:

\[
\Delta y_t = \Pi_1 y_{t-1} + \cdots + \Pi_p y_{t-p} + \mu + D_t \Phi + \varepsilon_t
\]

where \( \Delta y_t \) is a \( k \times 1 \) vector of the differenced series and.

The model has the following assumptions:
The VECM was specified and fitted with the steps below.

First, to choose the order $p$ of the VAR representation, we fitted a VAR model to the data and made the decision based on the Akaike information criterion (AIC) [21].

Second, we determined the number of cointegration relationships ($r=0$ or $r=1$) using the Johansen trace test [22].

Third, we needed to decide where to place the constant $\mu$ in the model. One option was to leave $\mu$ as shown previously to account for linear trend in the data. Another option was to restrict $\mu=\alpha \rho$. The constant would be absorbed into the cointegration relationship as an intercept, and the data would not exhibit linear trend.

We made our decision about whether to restrict $\mu$ based on a likelihood ratio test for linear trend, as described elsewhere [23,24].

Fourth, we used maximum likelihood estimation to fit the model, reported parameter estimates, the corresponding $T$ tests, and the omnibus $F$ tests with a significance level of .05, following Johansen [23].

Finally, we computed the 7-days-ahead forecasts and the 80% forecast intervals. Once the forecasts of the transformed census were made with the VECM, they were back-transformed to the original scale of census. We created 80% forecast intervals for the transformed census using a bootstrap procedure [25]. Then, the lower and upper bound of the forecast intervals were also back-transformed.

The model was fitted to the data between May 15 and December 5, 2020. All the data analysis was done using R statistical software, version 4.0.3 (R Core Team). The implementation of the VECM was done with the tsDyn, vars, and urca R packages. Since there were no packages to make bootstrapped forecast intervals for the VECM, we coded our own implementation.

The data and code used in the data analysis are publicly available on GitHub [26].

**Model Diagnostics**

We examined the omnibus $F$ tests to look for signs of lack of fit and also performed the multivariate Portmanteau test for the existence of serial correlation in the errors. Autocorrelation function and cross-correlation function plots were also generated for visual inspection. We performed the univariate and multivariate Jarque-Bera normality test on the errors [27] and also checked whether the cointegration relationship was stable, that is, stationary, using the Augmented Dickey-Fuller (ADF) test [28] and the Kwiatkowski-Phillips-Schmidt-Shin (KPSS) test [29]. Finally, we checked the stability of the estimated VAR representation. To do so, we looked at the companion matrix of the VAR representation and checked whether the maximum eigenvalue modulus was strictly smaller than 1, which, if true, would imply the stability of the VAR representation [30]. We also generated a trace plot of the maximum eigenvalue modulus, where the model was repeatedly fitted on a daily rolling basis, to check for the consistency of this value over time.

**Forecast Performance**

We used mean absolute percentage error (MAPE) to evaluate the 7-days-ahead forecasts of census:

$$\text{MAPE} = \frac{1}{n} \sum_{i=1}^{n} \left| \frac{F_i - A_i}{A_i} \right|$$

where $F_i$ is the forecast value and $A_i$ is the actual value.

In order to approximate the sampling distribution of MAPE, we performed time-series cross-validation. From June 16 to November 28, 2020, for each day, we iteratively fitted the model, made 7-days-ahead forecasts, and computed the MAPE. Eventually, we obtained 166 values of MAPE, plotted the distribution, and computed the median as well as the 95th percentile. We will consider a median MAPE below 10% to be satisfactory, based on the practical effect of a peak surge on bed capacity at our health care system.

**Scenario-Based Long-Term Forecasting**

Leading up to and at the peak of infection prevalence, there can be high anxiety and uncertainty about how much more incidence and, in particular, census may increase. Furthermore, traditional univariate time-series models may give linear forecasts for census that do not accurately represent pandemic behavior. However, cointegration allows for census forecasts that leverage subtle, but critical, changes in incidence (eg, concavity). This suggests, if not necessitates, the forecasting of census under different pandemic scenarios. For resource planning, hospital leaders will want to understand the implications associated with a worst-case scenario.

For our health care system, besides routine 7-days-ahead census forecasts, we also deployed our model for 60-days-ahead census forecasts, considering 3 different scenarios of what could happen with incidence (ie, best case, base case, and worst case). On January 9, 2021, we expected the winter surge to reach peak infection prevalence around February 5, 2021, based on an extension of an epidemiological model called the susceptible-infected-removed model [31]. While peak infection
incidence typically leads peak infection prevalence, in the absence of definitively knowing either peak date, we took a conservative approach and linearly extrapolated incidence with a positive trend up to the expected pandemic peak. The severity of a scenario was controlled by a trend-dampening parameter \([32]\). After the peak, the descent path was initially symmetric to its ascent and then eventually became linear (Figure 2).

Using our model refitted on January 9, 2021, with an increased capacity of 1250 patients, we generated forecasts iteratively forward for 60 days using the past census forecasts together with projected incidence under each scenario. To account for uncertainty in future census and incidence, we also simulated 1000 conditional sample paths of the two time series under each scenario using the bootstrap procedure mentioned earlier and computed the 10th and 90th percentile at each horizon to obtain the 80% forecast intervals.

**Figure 2.** The 60-day projected local COVID-19 infection incidence in the Cities Readiness Initiative region on the log scale, as of January 9, 2021. Past values (black), worst-case scenario (red), base-case scenario (orange), best-case scenario (blue) are shown.

### Ethical Review

Our research protocol was submitted to the Atrium Health Institutional Review Board (IRB) prior to execution, and the study was deemed exempt from IRB oversight. In compliance with HIPAA (Health Insurance Portability and Accountability Act) regulations, individual patient information was not disclosed, and all data have been deidentified and reported as aggregates. The procedures set out in this protocol, pertaining to the conduct, evaluation, and documentation of this study, were designed to ensure that the investigators abide by Good Clinical Practice guidelines and under the guiding principles detailed in the Declaration of Helsinki.

### Results

#### Estimation and Inference

Our model was specified as a VECM with 7 lags in its VAR representation \((p=7)\), 1 cointegration relationship \((r=1)\), and a restricted constant parameter \(\mu\) so that the series would not have linear trend. The AIC scores of VAR models with a varying number of lags from 2 to 14 were inconclusive. However, we found that 7 lags were sufficient to account for all the correlation in the data, as evidenced by the autocorrelation function and cross-correlation function plots of the residuals (Figure 3). The Johansen trace test indicated that there was 1 cointegration relationship (significant at 1%, based on tabulated critical values). Finally, the likelihood ratio test for linear trend indicated that there was no linear trend in the data \((P=.32)\). Furthermore, the restricted model had a lower AIC score than the unrestricted model (the AIC scores were \(-1519\) and \(-1516\), respectively).

The output from the maximum likelihood estimation showed that the cointegration relationship, that is, the error correction term, had a significant negative effect on census change \((P<.001)\); no significant effect was observed for incidence change \((P=.26)\) (Table 1). The long-run cointegration relationship was estimated as:

\[
ect_{t-1} = \text{census}_{t-1} - 0.8013 \text{incidence}_{t-1} + 7.8266
\]
where $ect_{t-1}$ was the (lagged) error correction term. Table 1 also shows that past changes in census and incidence also had meaningful effects on current census change. Past census changes had significant effect at lag 2 ($P=0.002$). Past incidence changes had significant effects at lag 1 ($P=0.005$), lag 2 ($P=0.04$), lag 4 ($P=0.02$), lag 5 ($P=0.03$), and lag 6 ($P=0.02$).

From Table 2, there were some significant seasonal effects, that is, differences in both census and incidence changes among days of the week. Compared to Thursday, census change was higher on Monday and incidence change was lower on Sunday, with significant differences ($P=0.01$ and $P=0.002$, respectively).

**Figure 3.** Autocorrelation functions and cross-correlation functions of the residuals: (A) census residuals, (B) lagged census residuals and incidence residuals, (C) census residuals and lagged incidence residuals, and (D) incidence residuals.
Table 1. Parameter estimates and $T$ tests for nonseasonal effects.

<table>
<thead>
<tr>
<th>Predictor</th>
<th>$\Delta$Census$_t$</th>
<th>$\Delta$Incidence$_t$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Estimate</td>
<td>$T$ statistics</td>
</tr>
<tr>
<td>$ect_{t-1}$</td>
<td>-0.1265</td>
<td>-5.6993</td>
</tr>
<tr>
<td>$\Delta$Census$_{t-1}$</td>
<td>-0.0489</td>
<td>-0.7143</td>
</tr>
<tr>
<td>$\Delta$Incidence$_{t-1}$</td>
<td>-0.0665</td>
<td>-2.8222</td>
</tr>
<tr>
<td>$\Delta$Census$_{t-2}$</td>
<td>-0.2220</td>
<td>-3.2277</td>
</tr>
<tr>
<td>$\Delta$Incidence$_{t-2}$</td>
<td>-0.0532</td>
<td>-2.0881</td>
</tr>
<tr>
<td>$\Delta$Census$_{t-3}$</td>
<td>-0.0700</td>
<td>-0.9949</td>
</tr>
<tr>
<td>$\Delta$Incidence$_{t-3}$</td>
<td>-0.0472</td>
<td>-1.9094</td>
</tr>
<tr>
<td>$\Delta$Census$_{t-4}$</td>
<td>-0.0785</td>
<td>-1.1224</td>
</tr>
<tr>
<td>$\Delta$Incidence$_{t-4}$</td>
<td>-0.0567</td>
<td>-2.4165</td>
</tr>
<tr>
<td>$\Delta$Census$_{t-5}$</td>
<td>-0.0499</td>
<td>-0.7140</td>
</tr>
<tr>
<td>$\Delta$Incidence$_{t-5}$</td>
<td>-0.0465</td>
<td>-2.1907</td>
</tr>
<tr>
<td>$\Delta$Census$_{t-6}$</td>
<td>0.0077</td>
<td>0.1107</td>
</tr>
<tr>
<td>$\Delta$Incidence$_{t-6}$</td>
<td>-0.0373</td>
<td>-2.4015</td>
</tr>
</tbody>
</table>

Table 2. Parameter estimates and $T$ tests for day-of-the-week effects, in comparison with Thursday being the reference.

<table>
<thead>
<tr>
<th>Predictor</th>
<th>$\Delta$Census$_t$</th>
<th>$\Delta$Incidence$_t$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Estimate</td>
<td>$T$ statistics</td>
</tr>
<tr>
<td>Friday</td>
<td>-0.0213</td>
<td>-1.1120</td>
</tr>
<tr>
<td>Saturday</td>
<td>0.0083</td>
<td>0.3980</td>
</tr>
<tr>
<td>Sunday</td>
<td>0.0030</td>
<td>0.1330</td>
</tr>
<tr>
<td>Monday</td>
<td>0.0585</td>
<td>2.6205</td>
</tr>
<tr>
<td>Tuesday</td>
<td>0.0291</td>
<td>1.3896</td>
</tr>
<tr>
<td>Wednesday</td>
<td>-0.0037</td>
<td>-0.1895</td>
</tr>
</tbody>
</table>

Model Diagnostics
The omnibus $F$ tests were significant for both census ($P<.001$) and incidence ($P<.001$) components.

The Portmanteau test did not show sufficient evidence that the errors were autocorrelated ($P=.19$). From the residual autocorrelation function and cross-correlation function plots, the correlations were within the 95% confidence band (Figure 3). The Jarque-Bera normality tests failed to reject the normality null hypothesis for the census errors ($P=.71$) but did for incidence ($P<.001$). Specifically, the incidence residuals were moderately left-skewed. The Jarque-Bera multivariate test also rejected the multivariate normality null hypothesis ($P<.001$).

The Augmented Dickey-Fuller test for stationarity of the error correction term rejected the unit root null hypothesis at the 10% significance level but failed to reject the null hypothesis at the 5% significance level (based on tabulated critical values). The KPSS test failed to reject the stationarity null hypothesis ($P=.10$). Examination of the time plot of the predicted error correction term showed no obvious departure from stationarity.

The companion matrix of the VAR representation had a maximum eigenvalue modulus of 0.97, strictly less than 1. Although this value was close to 1, the trace plot showed that this value had been slowly declining and below 1 across time when the model was fitted repeatedly in a daily rolling basis from June 16 to November 28 (Figure 4).
Figure 4. Trace plot of the maximum eigenvalue modulus for the period from June 16 to November 28, 2020.

Forecast Performance

We obtained the approximate sampling distribution of the out-of-sample MAPE from the time-series cross-validation (Figure 5). The typical value (median) of MAPE was 5.9% and the 95th percentile of MAPE was 13.4%. For the sake of comparison, the corresponding values from an ARIMA model using the COVID-19 hospital census only were 6.6% and 14.3%. Additionally, after fitting the data from May 15 to December 5, we forecasted the census out to 7 days. Subsequently, the actual values were accurately forecasted with a MAPE of 1.9% and were all within the 80% bootstrapped forecast intervals (Figure 6).

Figure 5. Distribution of the 7-days-ahead mean absolute percentage error from the time-series cross-validation for the period from June 16 to November 28, 2020. Median (blue) and 95th percentile (red) are shown.
Figure 6. One-step-ahead in-sample and 7-days-ahead out-of-sample predictions for COVID-19 hospital census in the Cities Readiness Initiative region. True values (black), in-sample and out-of-sample predictions (red line), 95% prediction intervals (blue band), 80% forecast intervals (red band) are shown. The model is fitted on data from May 15 to December 5, 2020.

Scenario-Based Long-Term Forecasting

In all scenarios, due to cointegration, census followed corresponding concave trajectories with peaks occurring approximately 2 to 3 weeks later than incidence depending on the scenario. In the worst-case scenario, census was projected to peak on February 16, 2021 (11 days later than incidence), with approximately 850 patients at the 80% forecast interval upper bound (Figure 7).

Figure 7. Worst-case-scenario, 60-day forecasts for COVID-19 hospital census in the Cities Readiness Initiative region, as of January 9, 2021. Past values (black), forecasts (red line), and 80% forecast intervals (red band) are shown.
Discussion

Principal Results
Our VECM provides a very good fit to the data and outperforms models with no or other leading indicators. Significant omnibus F tests showed that the model fit was better than that of a reduced VECM representation with no predictors (ie, a bivariate random walk model). When we examined model diagnostics, there was no sign of any serious departure from model assumptions. From the Portmanteau test, the errors were not different from white noise (ie, the errors do not exhibit serial correlation). Although the normality assumption (for incidence) was not met, the asymptotic properties of our estimation and hypothesis tests in the VECM would not be affected [33]. To address the possible effect of this violation on the forecast intervals, we implemented a bootstrap procedure for the forecast intervals. Both the ADF test and KPSS test showed reasonable evidence that the long-run relationship was stable. With the maximum eigenvalue modulus of the VAR representation consistently below 1 across time, the model itself was quite stable. Examining the day-of-the-week effects, we observed a higher increase in census at the beginning of the week. This agrees with our observations of hospital operations and suggests higher resource allocation when starting the week, as is also reflected in the forecasts (Figure 7). In terms of forecast performance, the VECM yielded a smaller MAPE, in terms of the median and the 95th percentile, when compared to an ARIMA model using the COVID-19 hospital census only. Our VECM also performed better than another VECM that uses two internet-based leading indicators (median MAPE of 10.5%), albeit on time domains that were partially overlapping [13].

The long-run relationship plays a crucial role in the model. Our model results show how future census responds to perturbations in the long-run cointegration relationship in the direction that would preserve the stability of the relationship. For instance, if incidence increases significantly and drives the error correction term below 0, the next-day census will tend to increase so that the error correction term will move back toward 0. Compared to short-run relationships between census change and past changes in incidence and census, the long-run relationship effect is also strongly significant and is a major driver in the model.

We observed that local infection incidence led the hospital census by about 2 weeks. The cross-correlations between incidence and census were uniformly high, between 0.7 and 0.8 at different lags, but the highest correlation was at lag 14. Clinically, we know that after someone is diagnosed with SARS-CoV-2, it can take several days before they become sick enough to be hospitalized. During the summer 2020 wave of the pandemic, incidence peaked 18 days earlier, on July 10, than when census peaked, on July 28. In the model, we also saw that past incidence changes at multiple lags have statistically significant effects on census. While previous studies have focused on other types of leading indicators [12,13], our model results and our observations demonstrate that local infection incidence can be a very effective leading indicator for COVID-19 hospital census.

Applying the model to scenario-based forecasting in a health care system is an important method for long-term forecasting when approaching an infection prevalence peak and helps determine the potential for resource capacity to be exceeded under a worst-case scenario. There are several advantages to our approach. With a scenario-based and epidemiologically informed approach, the VECM produces realistic, nonlinear, long-range trajectories of census. In contrast, an ARIMA model can have an upward linear trajectory even as we approach and arrive at the infection prevalence peak because it is agnostic to incidence. Hence, the VECM fit with scenario-based incidence will provide better accuracy since it is more reflective of pandemic behavior. Additionally, when the concern is a specific scenario, our approach is particularly useful at minimizing long-range forecast uncertainty, since the bootstrapped sample paths are constrained to fluctuate around the marginalized scenario-based census projection. Without such a constraint, 60-day forecasts can typically have wide forecast intervals that are of no practical utility.

Our study has mathematically ascertained the stable long-run relationship, that is, cointegration, between the COVID-19 hospital census and the local infection incidence, and we have developed a statistical incidence-based model to forecast the COVID-19 hospital census. In comparison, prior COVID-19 hospital capacity planning models that make use of infection incidence data rely on simplified assumptions about the incidence-census relationship. For example, in the COVID-19 Hospital Impact Model for Epidemics (CHIME) at the University of Pennsylvania [34], the ratio between hospital admissions and infection incidence is a scenario parameter defined by the user and is not time varying.

Limitations
Although our model has been thoroughly developed, it is not free of limitations. First, it is possible that we may lose the stable long-run relationship at some point in the future, either because it has run its course or due to structural changes in the time series. For instance, in the latter case, inadequate community-based testing might suddenly underestimate the actual local infection incidence, and there may be a level shift in the relationship that would have to be accounted for by a modified VECM [35,36]. In other cases, more complex structural changes may arise and be challenging to model. Second, in the future, other regions may find that the ratio between asymptomatic and symptomatic cases fluctuates considerably over time. Because case severity affects the time to hospitalization, this situation may require model revision. A potential remedy is to include both the number of asymptomatic and symptomatic cases as two leading indicators with census in a VECM in the hopes that some cointegration exists among the three variables. Third, it is relatively more difficult to fit a VECM. For univariate models such as ARIMA and exponential smoothing, well-developed R packages exist for automated model specification and estimation. With the VECM, more deliberate modeling decisions and careful checking of assumptions need to be made to fit a reliable model. Finally, the inclusion of seasonal effects in our model requires that the seasonality is deterministic. However, another health care system may find that their time-series data have stochastic seasonality.

https://publichealth.jmir.org/2021/8/e28195
or multiple deterministic seasonality. If seasonality is not important, we potentially may resolve this by simply deseasonalizing the series. Otherwise, it may be possible to account for this with more advanced parameterization of the seasonal effects.

Conclusions
The construct presented here provides a framework in the context of a health care system for incorporating other leading indicators that may yield further increases in forecasting performance. For instance, the VECM that uses internet-based leading indicators [13] could potentially be improved by including incidence. It is also possible to incorporate other nested hospital-related time series, such as the number of intensive care units and the number of ventilators, into the VECM if there was a need to simultaneously forecast other resources. Additionally, a VECM could be a valuable candidate for a model-averaged ensemble. This can be particularly useful if the ensemble consists only of agnostic univariate time-series models.

We have shown that infection incidence can be successfully tethered with hospital census in a multivariate time-series model to achieve accurate forecasting of COVID-19 hospital census. When coupled with scenario-based forecasting, the model helped our leaders evaluate resource capacity against different possible peak resource demands. In hindsight, our analyses correctly assured our leaders of our capability to handle a worst-case scenario, alleviated uncertainty, and effectively guided long-term planning of adequate staffing, bed capacity, and equipment supplies through the pandemic.

Authors’ Contributions
HMN prepared the original draft. HMN and PJT were involved in study conceptualization, statistical analysis, and review and editing of the manuscript. ADM supervised the study and contributed to the review and editing of the manuscript.

Conflicts of Interest
ADM is an administrative member of iEnroll LLC.

References


Abbreviations

ADF: augmented Dickey-Fuller
AIC: Akaike information criterion
ARIMA: autoregressive integrated moving average
CRI: Cities Readiness Initiative
HIPAA: Health Insurance Portability and Accountability Act
IRB: Institutional Review Board
KPSS: Kwiatkowski-Phillips-Schmidt-Shin
MAPE: mean absolute percentage error
SARIMA: seasonal autoregressive integrated moving average

https://publichealth.jmir.org/2021/8/e28195

JMIR Public Health Surveill 2021 | vol. 7 | iss. 8 | e28195 | p.13
(page number not for citation purposes)
SARS: severe acute respiratory syndrome
STL: seasonal and trend decomposition using Loess
VAR: vector autoregressive
VECM: vector error correction model
Census Tract Patterns and Contextual Social Determinants of Health Associated With COVID-19 in a Hispanic Population From South Texas: A Spatiotemporal Perspective

Cici Bauer1, PhD; Kehe Zhang1, MS; Miryoung Lee2, PhD; Susan Fisher-Hoch2, MD; Esmeralda Guajardo3, MA; Joseph McCormick2, MD; Isela de la Cerda2, MS; Maria E Fernandez4, PhD; Belinda Reininger5, DrPH

1Department of Biostatistics and Data Science, School of Public Health, The University of Texas Health Science Center at Houston, Houston, TX, United States
2Department of Epidemiology, Human Genetics and Environmental Science, School of Public Health, The University of Texas Health Science Center at Houston, Brownsville, TX, United States
3Cameron County Public Health, San Benito, TX, United States
4Department of Health Promotion and Behavior Sciences, School of Public Health, The University of Texas Health Science Center at Houston, Houston, TX, United States
5Department of Health Promotion and Behavior Sciences, School of Public Health, The University of Texas Health Science Center at Houston, Brownsville, TX, United States

Corresponding Author:
Cici Bauer, PhD
Department of Biostatistics and Data Science
School of Public Health
The University of Texas Health Science Center at Houston
1200 Pressler Street
Houston, TX, 77030
United States
Phone: 1 713 500 9581
Email: cici.x.bauer@uth.tmc.edu

Abstract

Background: Previous studies have shown that various social determinants of health (SDOH) may have contributed to the disparities in COVID-19 incidence and mortality among minorities and underserved populations at the county or zip code level. Objective: This analysis was carried out at a granular spatial resolution of census tracts to explore the spatial patterns and contextual SDOH associated with COVID-19 incidence from a Hispanic population mostly consisting of a Mexican American population living in Cameron County, Texas on the border of the United States and Mexico. We performed age-stratified analysis to identify different contributing SDOH and quantify their effects by age groups. Methods: We included all reported COVID-19–positive cases confirmed by reverse transcription–polymerase chain reaction testing between March 18 (first case reported) and December 16, 2020, in Cameron County, Texas. Confirmed COVID-19 cases were aggregated to weekly counts by census tracts. We adopted a Bayesian spatiotemporal negative binomial model to investigate the COVID-19 incidence rate in relation to census tract demographics and SDOH obtained from the American Community Survey. Moreover, we investigated the impact of local mitigation policy on COVID-19 by creating the binary variable “shelter-in-place.” The analysis was performed on all COVID-19–confirmed cases and age-stratified subgroups. Results: Our analysis revealed that the relative incidence risk (RR) of COVID-19 was higher among census tracts with a higher percentage of single-parent households (RR=1.016, 95% posterior credible intervals [CIs] 1.005, 1.027) and a higher percentage of the population with limited English proficiency (RR=1.015, 95% CI 1.003, 1.028). Lower RR was associated with lower income (RR=0.972, 95% CI 0.953, 0.993) and the percentage of the population younger than 18 years (RR=0.976, 95% CI 0.959, 0.993). The most significant association was related to the “shelter-in-place” variable, where the incidence risk of COVID-19 was reduced by over 50%, comparing the time periods when the policy was present versus absent (RR=0.506, 95% CI 0.454, 0.563). Moreover, age-stratified analyses identified different significant contributing factors and a varying magnitude of the “shelter-in-place” effect.
Conclusions: In our study, SDOH including social environment and local emergency measures were identified in relation to COVID-19 incidence risk at the census tract level in a highly disadvantaged population with limited health care access and a high prevalence of chronic conditions. Results from our analysis provide key knowledge to design efficient testing strategies and assist local public health departments in COVID-19 control, mitigation, and implementation of vaccine strategies.

(JMIR Public Health Surveill 2021;7(8):e29205) doi:10.2196/29205

KEYWORDS
COVID-19; spatial pattern; social determinants of health; Bayesian; underserved population; health inequity

Introduction
COVID-19, which comes from SARS-CoV-2, has caused death, health care system stress, and global economic instability. In the United States, it also has disproportionately affected minority and underserved populations, where COVID-19 infection and fatality rates are significantly higher among African American and Hispanic populations [1-3]. Previous studies have shown various social determinants of health (SDOH) that may explain the disparity in COVID-19 incidence and mortality in ethnic and racial minorities [1,4,5].

The differential impact of COVID-19 on minorities and other groups facing health inequities has been described and underscores a critical need to target these underserved groups. However, the majority of these studies in the United States used aggregated county-level data from the COVID Tracking Project [6]. The geographical scale of the US county often lacks granularity to reveal the local spatial pattern and detect local hot spots (ie, areas with excessive infection rates). Moreover, the high variability of SDOH within a county population was not able to accurately examine the impact of SDOH on COVID-19 disparities in populations [5]. Studies that investigate the SDOH and COVID-19 incidence and mortality at a geographical scale smaller than the US county are limited [7,8]. The lack of studies on a granular spatial scale is largely due to insufficiently detailed COVID-19 surveillance data, particularly data that are publicly available.

In this study, we investigated the contextual SDOH and their potential association with COVID-19 incidence at the census tract level. The study population consists of a Hispanic population with mostly Mexican American people living in South Texas on the US-Mexico border. The Mexican American population are the largest and fastest-growing Hispanic subgroup in the United States and among those with low socioeconomic status compared to other ethnic groups in the nation [9]. The population in our study has high prevalence of obesity and diabetes [10]; both pre-existing conditions increase the risk of severe COVID-19 outcomes [11]. Our analysis provided a look at the SDOH at sufficient spatial granularity to detect local trends and hot spots for COVID-19 monitoring and control. Results from our study have informed the intervention strategies to increase COVID-19 testing uptake in underserved populations and the design of interventions and targeted vaccination programs.

Methods
Study Population
Our study population is from Cameron County, Texas with a current population of 423,163 and over 90% Hispanics [12], where the vast majority were Mexican-Hispanic [13]. Most Cameron County residents are uninsured (~29%) and live below the poverty line (~33%) [12]; additional research based on a well-documented cohort from this region estimated that around 52% of the population does not have any private or public health insurance coverage [10,13]. This population, similar to many others living in the South Texas region, also has a high prevalence of type 2 diabetes (over 27%) and obesity (over 50%) [10,13,14]. In our analysis, we included a total of 84 census tracts within Cameron County, as shown in Figure 1. The two largest cities in Cameron County are the City of Brownsville (population 183,677) on the US-Mexico border and the City of Harlingen (population 65,074) 20 miles north of Brownsville, together comprising 59% of the county population.

COVID-19 Reported Cases
The first confirmed COVID-19 case in Cameron County, Texas was reported on March 18, 2020. By December 16, a total of 28,111 cases had been reported. The cumulative case rate, calculated as the number of positive cases per 100 people, was 1.93% in May 2020 and increased to 6.64% by December 2020, when the cumulative case rate of the general US population in December 2020 was 5.16% [6]. The case-fatality rate in Cameron County was 4% compared to 1.98% in Texas by December.

To facilitate local COVID-19 control and mitigation, Cameron County Public Health Department, the City of Brownsville, and the University of Texas School of Public Health (UTHealth) formed a collaborative group soon after the first COVID-19 case was reported in March 2020. Cameron County Public Health Department maintains a local database of reported and confirmed COVID-19 cases, which were concurrently reported to the Texas Department of State Health Services through the National Electronics Disease Surveillance System. Researchers from UTHealth were given access to the local database and provided data management and analytical support to investigate the trends and risk factors associated with COVID-19 spread. This study was approved by the UTHealth Committee for the Protection of Human Subjects (HSC-SPH-20-1372) and the Data User Agreement between the UTHealth and Cameron County.
During the initial stage of the COVID-19 pandemic, individual-level information associated with each reported case included age, gender, ethnicity, race, residential address, and specimen collection date. Over time, additional variables were added to the database such as testing type, testing facility, case definition (ie, confirmed or probable), type of exposure, date of recovery, date of death, comorbidities, hospitalization, symptoms, and symptoms onset date. In this analysis, we included all reported COVID-19–positive cases confirmed by reverse transcription–polymerase chain reaction testing based on a sample collection date between March 18 and December 16, 2020, and with a reported residential address within Cameron County. We developed a geocoding algorithm that extracted residential address information and then obtained the corresponding census tract information using the Google application programming interface (API) and the Census Bureau API in R (R Foundation for Statistical Computing) [15,16]. Among the total of 28,111 cases, we were able to geocode 27,733 cases and obtained their census tract information. Of these, 27,731 cases had information on sex, with 14,903 (53.8%) females and 12,824 (46.2%) males. Of the 27,726 cases (missing 1.37%) with age information, 15% (n=4148) were younger than 18 years, 28% (n=7770) were between age 18 to 34 years, 42.7% (n=11,843) were between age 35 to 64 years, and 14.2% (n=3965) were 65 years and older. The age strata range was chosen based on the US Centers for Disease Control and Prevention (CDC) COVID-19 case reporting [6], with some age groups collapsed due to small case numbers. Figure 2 presented weekly confirmed cases stratified by these age groups during the study time.

Demographic and Social Determinants of Health
Census tract demographic and SDOH variables for Cameron County were obtained from 2013 to 2018 US Census Bureau American Community Survey (ACS) 5-year estimates. These variables included total population, unemployment (%), racial minority (%), poverty level (% living under poverty), education level (% with no high school diploma), income (per capita income in dollars), insurance (% of population uninsured), living conditions (% renters and % living in crowded housing), and transportation (% without vehicles). We also created a population density variable for the census tracts, calculated as the population size per kilometer squared (km$^2$), ranging from 17 to 1360 per km$^2$. We observed substantial spatial variation of these demographic and SDOH within the Cameron County (Multimedia Appendix 1).

Shelter-in-Place Indicator Variable
To evaluate the impact of local policy on COVID-19, we created a binary indicator variable with value 1 for time periods when a state or local stay-at-home order was in place, and value 0 otherwise. Mandatory policies of facial coverings, curfew, limitations on gatherings, or beach access closure were present during the shelter-in-place periods [17]. The time period between March 26 and May 1, 2020, corresponded to the presence of the state-level lockdown, at the end of which the phased business reopening began. The local stay-at-home order started from July 1, 2020, and became less restrictive after schools reopened in mid-August. The event timeline of the policy and holidays is shown in Figure 2 (panel A).

Statistical Analysis
Due to potential reporting lag, we aggregated the number of COVID-19–confirmed cases to weekly counts by census tract. We considered the following Bayesian spatiotemporal model [18,19]. Let $Y_{it}$ denote the number of confirmed cases from census tract $i$ and week $t$; we assumed a negative binomial distribution with incidence risk $\mu_{it}$ (ie, $Y_{it} \sim NB(\mu_{it})$), with $N_{it}$ the population size as the offset. The incidence risk was $\mu_{it}$ then modeled as follows:

$$\log (\mu_{it}) = \alpha + x_i' \beta + s_t \gamma + \phi_i + \delta_{it}$$

where $\alpha$ was the overall intercept, $x_i$ was the vector of census tract covariates (eg, unemployment and crowded housing) with the associated coefficient vector $\beta$. Covariate $s_t$ was the binary policy-in-place indicator previously described. To account for the tract-level spatial dependency, we included a spatial random effect $\phi_i$ using the intrinsic conditional autogressive model [20]. The spatiotemporal interaction term $\delta_{it}$ captured the unexplained residuals and was assumed an independent and identically distributed normal distribution with variance $\varphi$. We reported the relative risk (RR) associated with each covariate, which was calculated as the exponentiated coefficient, along with its 95% posterior credible intervals (CIs). We performed this model on the total COVID-19 cases and then on age subgroups of younger than 18 years, between ages 18 and 34 years, between ages 35 and 64 years, and older than 65 years. All analyses were performed in R [21] and R package INLA [22].

Results
Compared to the US general population, Cameron County has a higher proportion of people who are uninsured (29.1% vs 9.4%), living under poverty (29.6% vs 11.5%), less educated (36.2% with no high school diploma vs 13%), and with worse living conditions (11.8% with crowded housing vs 3.4%). Cameron County is also 90.6% Hispanic, in contrast to 38.3% nationally, and 75% of the population with Spanish as the primary language and 28% having limited English proficiency (Table 1).

Figure 2 presents the temporal patterns of COVID-19–confirmed cases, in total numbers and by proportion, between March and December 2020. We observed a clear increase in new cases starting in June, that gradually decreased through the end of August. At the beginning of the pandemic in March and April, most cases were from the older population; more cases emerged from the younger population as the pandemic progressed to the summer. Cases among those 18 years or younger substantially increased from June and peaked in September. Unlike the three waves seen in the US general population, we only observed one prominent wave during the summer, with a smaller second wave after the Thanksgiving holiday.

We fit the Bayesian spatiotemporal negative binomial model previously described to all COVID-19–confirmed cases and then to four age-stratified subgroups (age younger than 18 years,
19-35 years, 36-64 years, 65 years and older), and the results are presented in Figures 3 and 4. Of the various demographic and SDOH variables included, the RR of COVID-19 incidence was higher among census tracts with a higher percentage of single-parent households (RR=1.016, 95% CI 1.005, 1.027) and a higher percentage of the population with limited English proficiency (RR=1.015, 95% CI 1.003, 1.028). Lower income was associated with a reduced risk of COVID-19 (RR=0.972, 95% CI 0.953, 0.993) as was the percentage of the population younger than 18 years (RR=0.976, 95% CI 0.959, 0.993). The most striking association was the shelter-in-place variable, where the RR of COVID-19 incidence was 0.506 (95% CI 0.454, 0.563) when comparing policy present versus policy absent. This suggests the risk of COVID-19 was reduced by almost 50% when the shelter-in-place policy was present.

Age-stratified analyses identified different significant SDOH for each group, and results are presented in Figure 4. For the age group 19 to 34 years, the estimated RR associated with higher percentage of limited English proficiency was 1.025 (95% CI 1.010, 1.040), a higher risk compared to that of the overall population (RR=1.015, 95% CI 1.003, 1.028). Reduced COVID-19 risk was associated with census tracts with higher percentage of no high school education (RR=0.987, 95% CI 0.976, 0.998). For the age group 65 years and older, the percentages of renters and racial minority (ie, percentage of non-Hispanic White) were additional SDOH significantly associated with increased risk of COVID-19 (RR=1.014, 95% CI 1.008, 1.020 and RR=1.018, 95% CI 1.005, 1.032, respectively). The complete results are presented in Multimedia Appendix 2.

The COVID-19 incidence risk was consistently and substantially lower during the time when the “shelter-in-place” policy was present. The effect was the most remarkable for the age group 19 to 35 years, where the risk was reduced by almost 60% when the policy was in place (RR=0.378, 95% CI 0.335, 0.425). For the age group 35 to 65 years, the risk was reduced by almost 50% (RR=0.475, 95% CI 0.424, 0.532). COVID-19 risk reduction was attenuated for the age group 65 years and older (RR=0.690, 95% CI 0.599, 0.793) and the smallest for the age group 18 years or younger (RR=0.767, 95% CI 0.667, 0.881).
<table>
<thead>
<tr>
<th>Variable</th>
<th>Cameron (n=84)</th>
<th>US (n=73,056)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Younger than 18 years (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (CV&lt;sup&gt;a&lt;/sup&gt; %)</td>
<td>30.2 (18.9)</td>
<td>22.1 (30.1)</td>
</tr>
<tr>
<td>Median (Q1, Q3)</td>
<td>31.2 (27.5, 33.7)</td>
<td>22.2 (18.5, 26.0)</td>
</tr>
<tr>
<td><strong>Older than 65 years (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (CV %)</td>
<td>14.0 (38.3)</td>
<td>16.0 (50.2)</td>
</tr>
<tr>
<td>Median (Q1, Q3)</td>
<td>13.2 (10.4, 16.9)</td>
<td>15.2 (11.0, 19.6)</td>
</tr>
<tr>
<td><strong>Racial minority (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (CV %)</td>
<td>90.6 (12.1)</td>
<td>38.3 (78.3)</td>
</tr>
<tr>
<td>Median (Q1, Q3)</td>
<td>94.7 (86.8, 97.1)</td>
<td>29.7 (12.5, 60.8)</td>
</tr>
<tr>
<td><strong>Single-parent household (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (CV %)</td>
<td>14.6 (39.0)</td>
<td>9.3 (69.2)</td>
</tr>
<tr>
<td>Median (Q1, Q3)</td>
<td>14.1 (10.1, 18.8)</td>
<td>7.9 (4.8, 12.2)</td>
</tr>
<tr>
<td><strong>Disability (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (CV %)</td>
<td>13.5 (30.1)</td>
<td>13.4 (44.0)</td>
</tr>
<tr>
<td>Median (Q1, Q3)</td>
<td>13.7 (10.4, 16.2)</td>
<td>12.5 (9.2, 16.6)</td>
</tr>
<tr>
<td><strong>Limited English (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (CV %)</td>
<td>3.9 (51.5)</td>
<td>3.9 (68.1)</td>
</tr>
<tr>
<td>Median (Q1, Q3)</td>
<td>3.5 (2.4, 5.1)</td>
<td>3.3 (2.1, 4.9)</td>
</tr>
<tr>
<td><strong>No high school diploma (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (CV %)</td>
<td>36.2 (39.1)</td>
<td>13.0 (81.2)</td>
</tr>
<tr>
<td>Median (Q1, Q3)</td>
<td>35.7 (24.3, 48.6)</td>
<td>10.1 (5.4, 17.6)</td>
</tr>
<tr>
<td><strong>Per capita income (US $)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (CV %)</td>
<td>16,100 (42.5)</td>
<td>32,300 (52.1)</td>
</tr>
<tr>
<td>Median (Q1, Q3)</td>
<td>14,000 (11,300, 19,500)</td>
<td>28,600 (21,700, 38,200)</td>
</tr>
<tr>
<td><strong>Living poverty (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (CV %)</td>
<td>29.6 (38.6)</td>
<td>11.5 (93.1)</td>
</tr>
<tr>
<td>Median (Q1, Q3)</td>
<td>28.9 (21.0, 37.1)</td>
<td>8.2 (3.8, 15.9)</td>
</tr>
<tr>
<td><strong>Uninsured (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (CV %)</td>
<td>29.1 (29.1)</td>
<td>9.4 (75.7)</td>
</tr>
<tr>
<td>Median (Q1, Q3)</td>
<td>29.1 (23.3, 34.3)</td>
<td>7.6 (4.2, 12.6)</td>
</tr>
<tr>
<td><strong>Crowded housing (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (CV %)</td>
<td>11.8 (52.9)</td>
<td>3.6 (146.1)</td>
</tr>
<tr>
<td>Median (Q1, Q3)</td>
<td>11.2 (7.5, 15.0)</td>
<td>1.9 (0.6, 4.4)</td>
</tr>
<tr>
<td><strong>Renters (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (CV %)</td>
<td>36.9 (46.5)</td>
<td>36.8 (62.3)</td>
</tr>
<tr>
<td>Median (Q1, Q3)</td>
<td>34.5 (24.9, 44.9)</td>
<td>31.7 (18.6, 51.4)</td>
</tr>
<tr>
<td><strong>Rent burden (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (CV %)</td>
<td>55.8 (26.4)</td>
<td>48.2 (33.4)</td>
</tr>
</tbody>
</table>
Using reported and confirmed COVID-19 cases from the Cameron County Public Health Department, we identified SDOH that were associated with COVID-19 incidence risk at the census tract level for the overall population and age subgroups. Risk of COVID-19 incidence was statistically significantly higher among areas with higher percentages of single-parent households and limited English-speaking proficiency but lower among areas with younger populations and lower income. The protective effects of lower income (for all cases) and lower education (for the age group 19-34 years) were difficult to decipher. On one hand, people living in low employment areas during the pandemic may have reduced contact with those infected and hence less likely to get infected. On the other hand, people with essential jobs (eg, food services) also tend to live in low income and low education areas. They may not be able to shelter at home like those in other jobs and hence have a higher risk of getting infected. For example, a previous study from Orange County, California showed an increase in COVID-19 cases in Hispanic and Latinx populations who lived in low-income census tracts and had low education attainment [23]. We were not able to further investigate the association with the census tract unemployment rate due to the lack of employment data at the census tract level during the pandemic. Other SDOH variables and social vulnerability indices such as those provided by the CDC [24] were not included in this analysis since they are typically constructed using the ACS variables we included in this analysis or tend to be highly associated with those included. Our result on the shelter-in-place policy agreed with previous studies where stay-at-home orders were effective in decreasing the confirmed case growth rate [25], and cumulative COVID-19 cases fell by about 50% following 3 weeks of a shelter-in-place order [26], but the effects vary in magnitude by age subgroups.

Our study has some limitations. First, our analysis only included the reported and confirmed cases, and hence missed those that were unreported or undiagnosed. Second, we were not able to evaluate the individual contribution of each different mitigation plan on reducing COVID-19 incidence risk. Third, we could not include the pre-existing conditions such as diabetes and obesity prevalence in our analysis, which were shown to impact COVID-19 severity but were unclear on infection. Finally, and probably the most important one, is that we were not able to include the overall testing data due to the lack of complete and accurate testing data by census tract level in the study region. Accurately capturing the COVID-19 pandemic requires an enhanced surveillance database, where ideally testing and infection data can be linked at the individual level. We hope in our future endeavor to assist the county and city public health departments to construct a comprehensive surveillance database as such to provide real-time monitoring and early detection of future COVID-19 outbreaks.

The population we focus on in this analysis is one of the poorest in the United States, frequently uninsured, and with limited access to COVID-19 testing throughout the pandemic. Using a Bayesian spatiotemporal binomial model, we investigated the association of SDOH and COVID-19 shelter-in-place policies with confirmed COVID-19 cases. Though there has been a surge of studies investigating the association of SDOH and COVID-19–related health outcomes since the pandemic started, most of them focused on the county-level analysis [27-30]. This spatial unit may lack the granularity to detect local hotspots and, subsequently, is inadequate to inform the local public health officials for mitigation control and planning. To our knowledge, our study is the first conducted at a granular spatial scale of census tracts and on a highly disadvantaged Hispanic population with limited health care access and a high chronic health risk including diabetes and obesity. The analysis also provided key information in guiding the intervention strategies to increase the testing uptake in the underserved population. For example, we are currently using this methodology as part of the Rapid Access to Diagnostics for Underserved Populations program that aims to increase knowledge about and access to testing in high-risk communities. The information generated from this study and the application of this methodology is informing both the development of targeted intervention strategies and the deployment of services to these areas.

### Acknowledgments

We acknowledge the important contribution of data managers and staff in the extensive and tedious job of data entry and cleaning from Cameron County Public Health. These staff include Gabriela Saucedo, Raquel Castillo, Caludia Soto, and Saul Ruvalcaba. We also thank all the officials of the cities and counties for their tireless efforts in setting up and operating testing facilities, software for COVID-19 testing appointments, and all the other work necessary in epidemic control, in particular Art Rodriguez, Michelle Jones, and Alvaro Silva from the City of Brownsville.
This study was partially supported by National Institutes of Health funding 3UL1TR003167-02S1.

Authors’ Contributions
CB conceived and designed the analysis. EG and BR contributed to the acquisition of data. IC and KZ contributed to data processing and data curation. CB and KZ conducted the data analysis. CB, ML, and BR contributed to the interpretation of the results. CB, KZ, and ML drafted the initial manuscript. SFH and JM supervised the findings of the project. CB, KZ, SFH, JM, MEF, and BR contributed to critical revision of the article. MEF contributed to the acquisition of the financial support for the project leading to this publication.

Conflicts of Interest
None declared.

Multimedia Appendix 1
Maps of demographic and social determinants of health variables at census tract level in Cameron County, TX. Data were obtained from American Community Survey 2013-2018 5-year estimates. At the tract level, the average percentage of Hispanics is 89.4% (SD 13%), much higher compared to the national average of 16.4%.

Multimedia Appendix 2
Census tract level estimated relative risks associated with social determinants of health variables, with posterior 95% confidential intervals in parentheses. The relative risk (RR) estimates were obtained from fitting a Bayesian negative binomial regression model, with spatial and spatiotemporal random effects. RR with statistically significant results are shown in bold. COVID-19 case data between March 19, 2020, and December 16, 2020, from Cameron County, TX was used in reporting the results.

References
11. QuickFacts Cameron County, Texas; Texas; United States. United States Census Bureau. URL: https://www.census.gov/quickfacts/table/cameroncountytexas/TX/PST045219 [accessed 2021-01-04]


16. Welcome to geocoder. United States Census Bureau. URL: https://geocoding.geo.census.gov/ [accessed 2020-08-03]

17. Cameron County Public Health. URL: https://www.cameroncounty.us/covid-19/ [accessed 2021-02-02]


Abbreviations

ACS: American Community Survey
API: application programming interface
CDC: Centers for Disease Control and Prevention
CI: credible interval
RR: relative risk
SDOH: social determinants of health
UTHealth: University of Texas School of Public Health

Edited by T Sanchez; submitted 29.03.21; peer-reviewed by V Verma, A Sheon; comments to author 18.05.21; revised version received 26.05.21; accepted 02.06.21; published 05.08.21.

Please cite as:
JMIR Public Health Surveill 2021;7(8):e29205
URL: https://publichealth.jmir.org/2021/8/e29205
doi: 10.2196/29205
PMID: 34081608
With Great Hopes Come Great Expectations: Access and Adoption Issues Associated With COVID-19 Vaccines

Zhaohui Su, MA, PhD; Dean McDonnell, PhD; Ali Cheshmehzangi, PhD; Xiaoshan Li, PhD; Daniel Maestro, PhD; Sabina Segalo, PhD; Junaid Ahmad, PhD; Xiaoning Hao, PhD

Corresponding Author:
Xiaoning Hao, PhD
Division of Health Security Research, China National Health Development Research Center, National Health Commission, P.R. China, Beijing, China

Abstract

Although COVID-19 vaccines are becoming increasingly available, their ability to effectively control and contain the spread of the COVID-19 pandemic is highly contingent on an array of factors. This paper discusses how limitations to vaccine accessibility, issues associated with vaccine side effects, concerns regarding vaccine efficacy, along with the persistent prevalence of vaccine hesitancy among the public, including health care professionals, might impact the potential of COVID-19 vaccines to curb the pandemic. We draw insights from the literature to identify practical solutions that could boost people’s adoption of COVID-19 vaccines and their accessibility. We conclude with a discussion on health experts’ and government officials’ moral and ethical responsibilities to the public, even in light of the urgency to adopt and endorse “the greatest amount of good for the greatest number” utilitarian philosophy in controlling and managing the spread of COVID-19.

(JMIR Public Health Surveill 2021;7(8):e26111) doi:10.2196/26111

KEYWORDS

COVID-19; coronavirus; COVID-19 vaccine; made in China; vaccine efficacy; vaccine safety; vaccine; China; expectation; safety; efficacy; infectious disease; public health; consequence; public health; standard
(eg, the Economist) [2,3]. Although the pandemic has upended the lives and livelihoods of thousands of millions of families and has dragged the world economy into unknown terrain [4], COVID-19 vaccines offer rays of hope that continue to draw people closer to the end of the tunnel [5].

Determined to build some “normalcy,” a global race to develop vaccines that can halt the pandemic has elevated on decades of experience and knowledge on immunization, the most advanced establishment of infrastructure, and an unwavering talent and motivation united to curb the spread of the virus [6,7]. Starting from December 2020, nine months after the WHO first labeled COVID-19 a global pandemic [8], the United Kingdom became the first nation to roll out mass vaccination [9]. Owing to its success in administering shots at the arms, as of May 2021, after months of strict social distancing mandates and within the confines of certain rules, UK residents have once again been able to enjoy shots at pubs indoors [10], with the company of strangers, friends, or one’s inner peace. COVID-19 vaccines, essentially, are the shots of hope people have been anxiously waiting for; when human contact is no longer as contagious as it used to be, hugs, handshakes, and heart-shaped selfies will become possible again across the world. Not to mention the happiness experienced when reuniting with families through nursing home visits, rekindling friendships with face-to-face lectures, and the bittersweet dash to a closing gate for business and leisure travel.

However, it is important to note that COVID-19 vaccines are not equally distributed silver bullets. How well COVID-19 vaccines can help curb the pandemic is contingent upon factors ranging from vaccine accessibility and vaccine efficacy to vaccine hesitancy, particularly in light of uncertainties associated with COVID-19 mutations [11-15]. Not much is discussed about critical issues associated with COVID-19 vaccine access and adoption while sharing positive news on COVID-19 vaccines and during talks about recovery and normalcy. Therefore, in this paper, we examine key factors that shape people’s access to and adoption of COVID-19 vaccines. Furthermore, we draw insights from the literature and aim to identify strategies that could boost people’s adoption of and the availability of COVID-19 vaccines, and ethical considerations associated with these strategies.

Issues Associated With Vaccine Inequity and Accessibility

It is important to note that vaccine availability does not equate to vaccine accessibility [11]. As a result of limitations in vaccine production, although more COVID-19 vaccines will become available in the coming months, not all people will have the same level of access. In the United Kingdom, for instance, older adults and frontline workers (eg, health care professionals) will be vaccinated first [16]. Simultaneously, in the United States, vaccine distribution policy will be heavily influenced by federal and state policies [17]. In addition to the prioritized distribution of vaccines, trial data availability also affects COVID-19 vaccine accessibility to individual end-users. For example, although expectant mothers are susceptible to COVID-19 [18], most vaccines were not tested on pregnant or lactating women; these individuals will not have access to COVID-19 vaccines until data become available [19]. In other words, although COVID-19 vaccines are available to use, they are not available to use for everyone [19]. This revelation speaks volumes—even though women have been historically ignored and underrepresented in clinical trials [20], it is difficult to contemplate that the same gender inequality could occur amid a pandemic of COVID-19’s scale.

Equally disturbing, evidence further suggests that 90% of people living in 70 poor-income countries across the world will not have access to COVID-19 mass immunization campaigns until 2022 or 2023 [21,22], with the worst estimate pointing to 2024 [23]. On the other hand, high-income countries are hoarding vaccines; by early December 2020, Canada, for instance, had ordered enough doses of COVID-19 vaccines to inoculate each Canadian five times [24]. Overall, as of May 21, 2021, wealthy countries such as the United States, the United Kingdom, Australia, and other nations within the European Union (EU), have collectively ordered approximately 7.8 billion doses of COVID-19 vaccines, whereas only 270,200,000 vaccines are available for low-income countries [23].

COVID-19 vaccines often require advanced infrastructure for storage and delivery (see Table 1) [25]. For instance, to safeguard their potency, Pfizer-BioNTech vaccines are required to be stored and transported between −112°F and 76°F (−80°C to −60°C) [26]; this condition can only be achieved with advanced cold chain systems that are difficult to build and navigate [27,28]. In the United States, due to a failure in storage, a company responsible for vials of the Moderna vaccine, which must be kept cold, spoiled 890 doses destined for older adults in eight nursing home residents in Ohio [29]. At least in the United States, even though several states are not sharing their data, available evidence already shows that vaccine waste is prevalent across states [15]. Considering how higher-income countries face logistical issues using state-of-the-art and high-capacity cold chain systems [28], it is difficult to imagine how low- and middle-income countries will gain access to these vaccines, and how will they deliver these vials to their citizens. Furthermore, pressing issues such as accessibility of glass vials, syringes, and needles may further worsen the COVID-19 accessibility conundrum [28,30].
Table 1. Details of leading COVID-19 vaccines with known efficacy (as of June 2, 2021).

<table>
<thead>
<tr>
<th>Name</th>
<th>Developer</th>
<th>Country</th>
<th>Type</th>
<th>Efficacy (Dose)</th>
<th>Status</th>
<th>Storage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Convidecia (or Ad5-nCoV)</td>
<td>CanSino</td>
<td>China</td>
<td>Adenovirus</td>
<td>65.28% (single dose)</td>
<td>Approved in China, emergency use in Chile, Hungary, Pakistan, etc</td>
<td>Stable in regular refrigerator for at least 6 months</td>
</tr>
<tr>
<td>BBIBP-CorV</td>
<td>Sinopharm</td>
<td>China</td>
<td>Inactivated</td>
<td>86% (2 doses, 3 weeks apart)</td>
<td>Approved in UAE and Bahrain; emergency use in Egypt and Jordan</td>
<td>Stable in regular refrigerator for at least 6 months</td>
</tr>
<tr>
<td>CoronaVac (formerly PiCoVacc)</td>
<td>Sinopharm-Wuhan</td>
<td>China</td>
<td>Inactivated</td>
<td>72.8%</td>
<td>Limited use in China and UAE</td>
<td>Stable in regular refrigerator for at least 6 months</td>
</tr>
<tr>
<td>Covaxin (or BBV152 A, B, C)</td>
<td>Bharat Biotech</td>
<td>India</td>
<td>Inactivated</td>
<td>78% (2 doses, 4 weeks apart)</td>
<td>Emergency use in India, Philippines, Zimbabwe, etc</td>
<td>At least a week at room temperature</td>
</tr>
<tr>
<td>Sputnik V</td>
<td>Gamaleya</td>
<td>Russia</td>
<td>Adenovirus</td>
<td>91.4% (2 doses, 3 weeks apart)</td>
<td>Early use in Russia</td>
<td>Freezer storage</td>
</tr>
<tr>
<td>EpiVacCorona</td>
<td>Vector Institute</td>
<td>Russia</td>
<td>Protein</td>
<td>— (2 doses, 3 weeks apart)</td>
<td>Limited use in Russia and Turkmenistan</td>
<td>Stable in refrigerator for up to 2 years</td>
</tr>
<tr>
<td>Vaxzevria (or AZD1222/Covishield)</td>
<td>Oxford-AstraZeneca</td>
<td>UK and Sweden</td>
<td>Inactivated</td>
<td>60%-90% (2 doses, 4 weeks apart)</td>
<td>Stopped use in Denmark and Norway; emergency use in UK, Lebanon, Canada, etc</td>
<td>Stable in regular refrigerator for at least 6 months</td>
</tr>
<tr>
<td>Ad26.COV2.S</td>
<td>Johnson &amp; Johnson</td>
<td>US</td>
<td>Adenovirus</td>
<td>57%-72% (1 dose)</td>
<td>Stopped use in Denmark and Finland; emergency use in US, the European Union, etc</td>
<td>Up to 2 years at –4°F (~−20°C) or up to 3 months at 36-46°F (2-8°C)</td>
</tr>
<tr>
<td>mRNA-1273</td>
<td>Moderna</td>
<td>US</td>
<td>mRNA</td>
<td>94.5% (2 doses, 4 weeks apart)</td>
<td>Approved in Canada; emergency use in US, UK, etc</td>
<td>Stable in refrigerator for up to 30 days</td>
</tr>
<tr>
<td>NVX-CoV2373</td>
<td>Novavax</td>
<td>US</td>
<td>Protein</td>
<td>49.4%-89.3% (2 doses, 3 weeks apart)</td>
<td>—</td>
<td>Stable in regular refrigerator for at least 6 months</td>
</tr>
<tr>
<td>Tozinameran or Comirnaty or BNT162b2</td>
<td>Pfizer-BioNTech</td>
<td>US and Germany</td>
<td>mRNA</td>
<td>95% (2 doses, 3 weeks apart)</td>
<td>Approved in Canada, Saudi Arabia, UAE, Bahrain, and Kuwait; emergency use in UK, US, etc</td>
<td>Freezer storage only at −94°F (~−70°C)</td>
</tr>
</tbody>
</table>

aUAE: United Arab Emirates.
bNot available.
cUS: United States.
dUK: United Kingdom.

Issues Associated With COVID-19 Vaccine Safety and Vaccine Hesitancy

Assuming everything goes as planned, COVID-19 vaccine efficacy will still be contingent upon the abilities of individual health facilities to administer their doses. Emerging concerns point to the fact that these institutions often vary in terms of safety protocols, equipment maintenance, and staff training—critical competency criteria that could impact the vaccine administration process, and in turn, vaccine efficacy [17,31]. Competency of vaccine distribution centers also impacts end-user safety. For instance, in the state of West Virginia, 42 people who were scheduled to receive COVID-19 vaccines were mistakenly injected with an experimental monoclonal antibody treatment that should be administered via an intravenous infusion [32]. In reality, hospitals and medical centers across the world are overstretched and are at a breaking point in addressing the skyrocketing COVID-19 cases [33-36]; many further compound the moral (eg, who should receive COVID-19 vaccines?) and logistical (eg, how to administer these vaccines effectively and safely?) issues associated with vaccine administration.

After severe allergic reaction cases were first reported in the United Kingdom, regulators warned that Pfizer-BioNTech vaccine administration should not be carried out on people with a history of serious allergies [37]. It is worth noting that these
reports occurred prior to the incidents of blood clots reported across the globe, especially in the EU nations [38]. The ever-emerging reports on COVID-19 vaccine side effects are alarming [39-41], as some individuals may not be aware of their allergies or underlying conditions that could expose them to severe vaccine side effects [11]. When they do, vaccine distribution facilities will have to face medical emergencies that they may or may not be capable of tackling. For the Pfizer-BioNTech vaccine trial alone, four volunteers developed Bell palsy or partial facial paralysis during the trial period [42]. For most established vaccines, such as seasonal influenza vaccines, allergic reactions often occur at a low rate estimated at one in a million people [43]; this number is substantially lower number compared to the current known allergic cases associated with COVID-19 vaccines, which is 11.1 per million people for the Pfizer-BioNTech COVID-19 vaccine [44].

In Norway, 23 older adults died shortly after COVID-19 vaccination [45]. Although the investigation is still underway, reports on vaccine side effects, especially if taken out of context, be it by legacy media outlets or conspiracy theory influencers, may further deepen the public’s fear, uncertainty, and distrust over COVID-19 vaccines [46]. Not to mention the tsunami of fact-based reports or how fake news may further exacerbate the public’s pandemic fatigue, along with potential mental health issues [47-49]. Inevitably, concerns associated with vaccine safety and reports on vaccine side effects may further hinder COVID-19 vaccine adoption [50-53], especially among those who spread unfounded vaccine rumors (eg, vaccine conspirators) or those who are already hesitant about COVID-19 vaccine uptake (eg, vaccine hesitants) [12]. Emerging reports on the impacts of COVID-19 mutations on vaccine efficacy may further compound the situation. Trial data on the Johnson & Johnson vaccines, for instance, show that although the vaccine efficacy is 72% in the United States, it dropped significantly in places where COVID-19 mutations are more prevalent—66% in Latin America and 57% in South Africa [54].

**Strategies to Promote COVID-19 Vaccine Accessibility and Adoption**

**“Reimagining” COVID-19 Vaccine Doses to Improve Vaccine Accessibility**

One way to increase vaccine accessibility that many governments are considering is by giving as many people as possible one dose instead of the original and approved two-dose vaccination regimen for fewer people [55]. Britain, for instance, along with other European countries [56], has already delayed administering the scheduled second doses of COVID-19 vaccines on the ground that “vaccinating a greater number of people with a single dose will prevent more deaths and hospitalizations than vaccinating a smaller number with two doses” [55]. In addition to delaying the administration of the second vaccine dose and capitalizing on vaccine overfill (ie, some Pfizer-BioNTech vaccine vials were found to contain a greater amount of the vaccine dose than expected), a surprise that many health care professionals are happy to unveil [57], epidemiologists are also weighing in the option of cutting COVID-19 vaccine doses in half (ie, from 100 mg to 50 mg), hoping to double the available Moderna vaccine supply in a timely fashion [58].

**“Extra” Doses or “Expected” Doses?**

Although all the abovementioned measures could help health experts and government officials to capitalize on available vaccine doses, they each come with their own sets of caveats. Among all three measures, the least problematic approach is probably leveraging the vaccine overfill issue. However, even this approach has issues. The first problem lies in the knowledge and experience needed to extract extra doses from the vaccine vials. COVID-19 vaccines are fancy magic delicately packaged in tiny glass vials—they are exceedingly expensive in the way they are designed, developed, delivered, and deployed with care, or lack thereof [11]. The vaccine extraction procedures require medical expertise and special equipment to succeed, which could be an issue considering that hospitals in worst-hit places are often stretched thin. The particular syringe needed for the procedure is in short supply [59]. The second issue is rooted in Pfizer-BioNTech’s very business-minded calculations. Not wishing to break its Big Pharma stereotypes, Pfizer will deliver fewer numbers of vaccine vials to account for the difficult-to-extract “extra” doses—Pfizer’s contractual agreement with the US government counts doses, rather than vials [60].

In other words, health care professionals in the United States may soon have to extract the “expected” doses from each Pfizer-BioNTech vaccine vial. It is important to incentivize businesses, especially powerful Big Pharmas, amid COVID-19 to contribute to social goods. However, particularly in light of mechanisms such as the Defense Production Act of 1950 [61], it is questionable whether financial incentives are the only approaches governments can use. When all members of the public have to follow the COVID-19 safety measures, such as the United Kingdom’s waves of lockdowns, or get fined or jailed, for the greater good, then why are Big Pharma companies such as Pfizer-BioNTech not expected to do the same? Perhaps rather than arguing with governments about wording, dosing, and business bottom lines, Big Pharma companies like Pfizer-BioNTech should focus on producing more COVID-19 vaccines. Overall, it is not a sustainable approach to allow Big Pharma to see lucrative financial benefits in pandemics; societies at large have too many of these already for them to secure their astronomical bonus payments, ranging from the obesity epidemic, HIV epidemic, cancer epidemic, to communicable disease epidemics such as the annual seasonal influenza epidemics.

**Utilitarianism Without Consequentialism?**

For the approaches that disregard the originally and only clinically tested and approved sets of dosing guidelines, both the problems and solutions may be substantially more challenging to obtain. Essentially, the splitting doses (ie, getting more people to receive one dose of COVID-19 vaccine) and halving doses (ie, getting more people to receive at least some dose of COVID-19 vaccine) methods are a manifestation of “the greatest amount of good for the greatest number” utilitarian philosophy developed by famed scholars such as John Stuart Mill [62]. These approaches have the potential to allow more
people to have access to COVID-19 vaccines without actually improving COVID-19 production rates; however, an important caveat is that there is a lack of data on what might be the health consequences of administering one or halved dose of COVID-19 vaccines, rather than the clinically validated dosing regimen. Data on Pfizer-BioNTech vaccines already shows that the high threshold efficacy for single dose of COVID-19 vaccine is 52%. It could only reach the much-lauded 95% efficacy after the second dose is administered successfully within the prescribed time frame [63]. Available evidence from real-world mass vaccination in Israel further suggests that the actual efficacy of a single dose Pfizer-BioNTech vaccine may have a more disappointing number [64].

It is important to note that the statistics above only address the vaccine efficacy issue rather than other looming issues such as side effects and the interaction between coronavirus and vaccination. Some epidemiologists have already aired their concerns about the potential impacts of inoculating a large portion of the society with the same vaccine in a short time. Collectively, we have yet to figure out how coronavirus might evolve in light of these triggers; will a more potent and powerful variant of SARS-CoV-2 develop that is even more worrisome than the B.1.1.7 mutation first identified in the United Kingdom? It is important to note that some governments have already voiced their concerns over splitting and halving dosing COVID-19 vaccines. Even before data from Israel become available, making it the first country that has managed to vaccinate over 20% of its population and en route to inoculate the entire nation [65], the US Food and Drug Administration, for instance, warned public health officials of the danger associated with tempering with vaccine doses, citing that the idea is not supported by scientific evidence and “may ultimately be counterproductive to public health” [66].

A group of international advisers to the WHO, on the other hand, have recommended public health officials to follow the Pfizer-BioNTech vaccine schedule (ie, two doses given 3-4 weeks apart) rigorously when possible, but they have also suggested that countries with limited supplies of vaccines can consider delaying the second dose for up to 6 weeks [67]. It is important to note that initial evidence on dose splitting and extending intervals between shots is available from the AstraZeneca-Oxford trial [68]. Researchers found comparable efficacies between the two different time frames but disparate efficacies between dosages. Although these insights cannot be directly applied to mRNA vaccines developed by Pfizer-BioNTech and Moderna, they provide preliminary data on the interaction between dosing the vaccine efficacy, which should be further validated or updated by the mentioned effort undertaken by Moderna. Moreover, the Strategic Advisory Group of Experts on Immunization (SAGE), the committee that is tasked to advise WHO when it comes to immunization research and development (eg, COVID-19 vaccine guidelines) [69,70], recommended WHO and all health officials to follow Pfizer-BioNTech dosing and timeframe scheme as the group was reporting the results of their discussion on the approval of the WHO’s emergency use listing of Pfizer-BioNTech vaccines [71]. In extrapolation, then, it can be argued that it is recommended for officials to follow evidence-based schedules of the corresponding vaccines.

Moral and Ethical Obligations in Public Health Policy-Making

Overall, considering the tsunami of information—fact-based or not—on COVID-19 vaccines, data are urgently needed to shed light on the safety and practicality of changing previously agreed-upon vaccine dosing regimens. Promisingly, a group of scientists in the United States is currently collecting and analyzing data on Moderna vaccines to evaluate the possibility of halving COVID-19 vaccine doses to increase vaccine accessibility [72]. It is essential to digest the fact that devising a different dosing schedule is different from squeezing an additional dose from COVID-19 vaccine vials due to overfilling; the former changes the clinically tested and validated guidelines, whereas the latter simply capitalizes on the fact that some glass vials contain more amount of vaccine.

Although the exact impact of changing the COVID-19 vaccine dosing schedule on personal and public health amid the pandemic is still unclear, what is clear is that governments need to make sure they base their decisions on scientific evidence rather than hopeful assumptions [73]. Yet, baseless assumptions, let alone politics, influencing any decision about COVID-19 vaccines could potentially impact thousands of millions of people’s lives and livelihoods. What is also clear is that, for people who have already received their first dose of COVID-19 vaccines, denying their access to the second dose is a blatant violation of informed consent, the very foundation of medical ethics, a baseline that should not be violated even in a time like the COVID-19 pandemic, particularly in light of dark events ranging from the Nazi’s medical experiments [74], Unit 731 atrocities [75], and the Tuskegee scandal [76]. Obtaining informed consent from potential vaccine receivers has been a tricky task [11], and the violation of informed consent—a contractual trust between individuals and health organizations and governments—may further exacerbate vaccination hurdles for all other immunization efforts.

Conclusions

In this paper, we identified vaccine accessibility and adoption issues that can be collaboratively addressed by both private and public health sectors. Overall, more research is needed to shed light on these tasks, especially factoring in the ever-evolving nature of COVID-19 (eg, mutations) and phenomena such as “pandemic fatigue.” Great hopes have been invested in COVID-19 vaccines. However, it is important to understand that, for COVID-19 vaccines to effectively protect people from the pandemic, issues such as vaccine accessibility, vaccine efficacy, and vaccine hesitancy need to be solved first. In the context of COVID-19, great hopes will almost always mean great expectations—health experts and government officials have a fiduciary and an unwavering duty to the public to make sure they promise what can be delivered and they deliver what is promised. Although even rays of hope can light up the tunnel,
in an environment where distrust is rampant, hope could be easily lost and difficult to rebuild.

Acknowledgments
The authors wish to express their gratitude to the editor and reviewers for their constructive input and insightful feedback along with the kindness they showed to the team throughout the process. This work was supported by the Asia-Pacific Economic Cooperation (APEC) Funded Projects: Building the New Leadership of Infectious Disease Prevention and Control among APEC Economies and the United Nations Development Program (UNDP) South-South Cooperation: Learning from China's Experience to improve the Ability of Response to COVID-19 in Asia and the Pacific Region.

Authors' Contributions
ZS developed the research idea and drafted the manuscript. DMD, AC, XL, DM, SS, JA, and XH reviewed and revised the manuscript. All authors have read and approve the final manuscript.

Conflicts of Interest
None declared.

References
3. There have been 7m-13m excess deaths worldwide during the pandemic. The Economist. 2021 May 15. URL: https://www.economist.com/briefing/2021/05/15/there-have-been-7m-13m-excess-deaths-worldwide-during-the-pandemic [accessed 2021-05-24]


63. Mahase E. Covid-19: Pfizer vaccine efficacy was 52% after first dose and 95% after second dose, paper shows. BMJ 2020 Dec 11;371:m4826. [doi: 10.1136/bmj.m4826] [Medline: 33310706]
64. Mahase E. Covid-19: Reports from Israel suggest one dose of Pfizer vaccine could be less effective than expected. BMJ 2021 Jan 22;372:n217. [doi: 10.1136/bmj.n217] [Medline: 33483332]


66. FDA statement on following the authorized dosing schedules for covid-19 vaccines. U.S. Food and Drug Administration. 2021 Jan 4. URL: https://tinyurl.com/3cz3sx7x [accessed 2021-01-06]


