

Abstract

Introduction

Throughout the past two decades of civilizations, from Severe acute respiratory syndrome (SARS) in 2003, to Middle East Respiratory Syndrome (MERS) first identified in 2012, to the novel coronavirus (COVID-19) outbreak in 2020, humans are threatened by respiratory infectious disease almost every 8 years. Except for an active search for vaccine, centered around all scientific efforts is the estimation of the disease spread.

Accompanied by this outbreak, studies related to the spread of COVID-19 mounted: Scientists and scholars around the globe are actively gathering COVID-19 data from all countries, predicting the peak time, and evaluating the effective of different public health policies. Among these publications, there are numerous estimations for serial interval [1],[2] using data from China, studies showing positive association between environmental factors and mortality rate of COVID-19 [3] , and post-pandemic seasonality forecast [4]. However, since COVID-19 outbreak happened in China and other European countries two months earlier than it happened in the US, most of the publications up to today focused on disease spread outside of America, and publications focused on the US are mostly descriptive and state-level. In this paper, we shift perspective to US territory, and more specifically, we aim to predict county-level disease spread in the US, taking into account three public health policies (Social-Distancing, Mask Policy and testing) and six demographic characteristics (population density, proportion of older population, education level, poverty percentage, ethnicity, and relative humidity).

Data Source

County-level daily cases were extracted from Johns Hopkins University GitHub repository https://raw.githubusercontent.com/CSSEGISandData/COVID-19/master/csse_covid_19_data/csse_covid_19_daily_reports/. State-level public health policies and effective dates were extracted from <https://www.kaggle.com/lin0li/>. State-level testing data was extracted from <https://covidtracking.com/data>, which is the most credible source before CDC released the number. Various county-level demographic characteristics were extracted from <https://www.census.gov/>, county-level environmental data was extracted from <https://www.ncei.noaa.gov/news/noaa-offers-climate-data-counties>

Method

In epidemiology, the basic reproductive number R_0 is often computed to quantify the intensity of an outbreak. R_0 could be intuitively thought of the the expected number of infectees directly generated by one infector in a population where all individuals are susceptible to be infected. However, in the context of COVID-19, we don't assume that everyone is susceptible due to cross-immunity [4], thus a daily effective reproductive number is computed for every county in the US [5].

$$R(t) = \sum_{s=t}^{t+stop} \frac{b(s)g(s-t)}{\sum_{a=0}^{stop} b(s-a)g(a)} \quad (1)$$

where $b(s)$ is the incidence number on day s , $g(a)$ is the value of serial interval distribution at day a , and $stop$ is maximum serial interval as first day that captures $> 99\%$ of the density.

The daily effective reproductive number $R(t)_i$ on day t of i^{th} county can be expressed as a county-specific constant modified by the proportion of susceptible individuals at the beginning of day t and further modified by external fixed and time-varying covariates [6]

$$R(t)_i = constant_i \times S_i(t)^{z_i} \times \prod_{k=1}^6 x_{ik}^{\beta_k} \times \prod_{j=1}^3 c_{ij}(d)^{\alpha_j(d)} \quad (2)$$

where x_{ik} is the k^{th} fixed variables for i^{th} county, and $c_{ij}(d)$ is the j^{th} time-varying variables for i^{th} county at day d . To account for the fact the policies are usually not immediately effective in terms of adherence, time-varying effects $\alpha_j(d)$ for all three policy measures are incorporated to account for the delayed response. $S_i(t)$ stands for the proportion of susceptible individuals up to today adjusting for cumulative infections, fixed variables are population per squared-mile, proportion of population over 60 years old, proportion of population with more than high school degree, poverty percentage, proportion of African American, and relative humidity. Time-varying variables are the social-distancing order, mask-wearing order and the number of tests per 1000 people. Taking the log on both side,

$$\begin{aligned} \log(R(t)_i) &= \log(R_{0i}) + z_i \log S_i(t) + \sum_{k=1}^6 \beta_k \log(d_{ik}) + \underbrace{\sum_{j=1}^3 \alpha_j(t - b_j) \log(c_{ij}(t - b_j))}_{(3)} \\ &= \log(R_{0i}) + z_i \log S_i(t) + \sum_{k=1}^6 \beta_k \log(d_{ik}) + \sum_{j=1}^3 \left\{ \sum_{d=t-b_j}^t \alpha_j(d) \log(c_{ij}(d)) \right\} \end{aligned}$$

- Time-varying effects estimation

Results

- findings

Discussion

- whether policies are effective

Reference

- [1] Du, Zhanwei, et al. “The Serial Interval of COVID-19 from Publicly Reported Confirmed Cases.” 2020, doi:10.1101/2020.02.19.20025452.
- [2] Nishiura, Hiroshi, et al. “Serial Interval of Novel Coronavirus (2019-NCoV) Infections.” 2020, doi:10.1101/2020.02.03.20019497.
- [3] Wu, Xiao, et al. “Exposure to Air Pollution and COVID-19 Mortality in the United States.” July 2020, doi:10.1101/2020.04.05.20054502.
- [4] Kissler, Stephen M, et al. “Projecting the Transmission Dynamics of SARS-CoV-2 through the Post-Pandemic Period.” June 2020, doi:10.1101/2020.03.04.20031112.
- [5] Wallinga, J, and M Lipsitch. “How Generation Intervals Shape the Relationship between Growth Rates and Reproductive Numbers.” *Proceedings of the Royal Society B: Biological Sciences*, vol. 274, no. 1609, 2006, pp. 599–604., doi:10.1098/rspb.2006.3754.
- [6] Beest, Dennis E. Te, et al. “Driving Factors of Influenza Transmission in the Netherlands.” *American Journal of Epidemiology*, vol. 178, no. 9, Dec. 2013, pp. 1469–1477., doi:10.1093/aje/kwt132.
- [7] Wang, Molin, et al. “Quantifying Risk over the Life Course - Latency, Age-Related Susceptibility, and Other Time-Varying Exposure Metrics.” *Statistics in Medicine*, vol. 35, no. 13, Oct. 2016, pp. 2283–2295., doi:10.1002/sim.6864.

Supplementary

Model for the i^{th} county at time point t :

$$R(t)_i = R_{0i} \times S_i(t)^{z_i} \times \prod_{k=1}^6 d_{ik}^{\beta_k} \times \prod_{j=1}^3 c_{ij}(d_j)^{\alpha_j(t-d_j)} \quad (4)$$

Annotations:

- $R(t)_i$: effective reproductive number at time t for the i^{th} county
- R_{0i} : basic reproductive number at the beginning for the i^{th} county
- $S_i(t)$: proportion of susceptible at time t in the county i: $\frac{S_i(0)-h(t)_i}{S(0)_i}$
- $S_i(0)$: susceptible at the beginning in the county i (assuming all population)
- $h(t)_i$: number of cases up to time t-1
- $d_{i1}...d_{i6}$: 6 fixed variable/effects for the i^{th} county: % of essential workers, humidity, poverty, population density, education, and % over 60 years old
- $c_{i1}...c_{i3}$: 3 time-varying variables/effects for i^{th} county: # of tests per 1000 people, social distancing policy, and mask policy

Taking the log on both side

$$\begin{aligned}
 \log(R(t)_i) &= \log(R_{0i}) + z_i \log S_i(t) + \sum_{k=1}^6 \beta_k \log(d_{ik}) + \underbrace{\sum_{j=1}^3 \alpha_j(t - b_j) \log(c_{ij}(t - b_j))}_{(5)} \\
 &= \log(R_{0i}) + z_i \log S_i(t) + \sum_{k=1}^6 \beta_k \log(d_{ik}) + \sum_{j=1}^3 \left\{ \sum_{d=t-b_j}^t \alpha_j(d) \log(c_{ij}(d)) \right\}
 \end{aligned}$$

Interpretation:

- $\log(R_{0i})$: county specific intercept
- b_j : # of days we will look back for variable c_j , this will define the time window when the variable could affect $R(t)_i$
- z_i : how quickly susceptibles deplete
- $c_{ij}(t)$: the exposure value for covariate j for county i at time t

We will estimate each $\alpha_j(0), \alpha_j(1) \dots \alpha_j(d_j)$, $j = 1, 2$, and 3 with a restricted cubic spline approach with $q=5$ knots (approximately 3 months, each 2 weeks will be an interval)

$$\sum_{d=t-b_j}^t \alpha_j(d) \log(c_{ij}(d)) = \sum_{d=t-b_j}^t \{ [\phi_1 B_{-1}(d) + \dots + \phi_Q B_{Q-2}(d)] \log(c_{ij}(d)) \}$$

Where Q is the number of knots (Q=5)

Step 1: Estimate R_0 for each county in the US

”J. Wallinga, M. Lipsitch, How generation intervals shape the relationship between growth

rates and reproductive numbers. Proc. R. Soc. B Biol. Sci. 274, 599–604 (2007).”

$$R(t) = R(today) = \sum_{s=today}^{today+stop} \frac{b(s)g(s - today)}{\sum_{a=0}^{stop} b(s - a)g(a)} \quad (6)$$

Annotation:

- ”The reproductive number to the time t at could be find by summing over all possible times t”
- $\sum_{s=t}^{t+stop}$: look ahead starting today through t+stop day
- $R(t)$: the effective reproductive number today (t)
- $b(t)$: incidence number at time t
- $g(t)$: value for general interval distribution at time t (the generation interval distribution is the probability distribution function for the time from infection of an individual to the infection of a secondary case by that individual)
- stop: max generation interval as first day that captures > 99% of the density

Step 2: Estimate time-varying effect by ML using restricted cubic spline

”Wang, Molin, et al. “Quantifying Risk over the Life Course - Latency, Age-Related Susceptibility, and Other Time-Varying Exposure Metrics.” Statistics in Medicine, vol. 35, no. 13, Oct. 2016, pp. 2283–2295., doi:10.1002/sim.6864.”

This is a function of d_1

$$\alpha_\phi(t - d_1) = \phi_1 B_{-1}(t - d_1) + \phi_2 B_0(t - d_1) + \phi_3 B_1(t - d_1) + \phi_4 B_2(t - d_1) + \phi_5 B_3(t - d_1)$$

This is a function of d_2

$$\alpha_\pi(t - d_2) = \pi_1 B_{-1}(t - d_2) + \pi_2 B_0(t - d_2) + \pi_3 B_1(t - d_2) + \pi_4 B_2(t - d_2) + \pi_5 B_3(t - d_2)$$

This is a function of d_3

$$\alpha_\psi(t - d_3) = \psi_1 B_{-1}(t - d_3) + \psi_2 B_0(t - d_3) + \psi_3 B_1(t - d_3) + \psi_4 B_2(t - d_3) + \psi_5 B_3(t - d_3)$$

Step 3: Estimate fixed effect by OLS

Step 4: Estimate random intercept by BLUP