Covid-19 Social Distancing Interventions by State Mandate and Their Correlation to Mortality

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Abstract

Purpose Evaluate the correlation between state mandated social interventions and Covid-19 mortality Design Prospective design and retrospective analysis of Institute for Health Metrics and Evaluation (IHME) state data. Methods Twelve European Union countries were selected on April 12, 2020 from IHME data which had clearly defined and dated establishment of statewide mandates for social distancing measures to include: School closures, stay at home orders, severe travel restrictions, and closure of non-essential businesses. The state Covid-19 mortality prevalence was defined as total normalized deaths to the peak daily mortality rate. The state mortality prevalence was correlated to the total number of mandates-days from their date of establishment to the peak daily mortality date. The slope of the maximum daily mortality rate was also correlated to mandate-days. Results The slope of standardized mortality per country did have a slight negative correlation to the total mandate days ($R2 = 0.083$, $p= 0.36$), though the negative correlation was not statistically significant. The standardized mortality prevalence to the peak mortality rate per country exhibited no discernable statistical correlation to the total mandate days ($R2 = 0.004$,$p=0.85$). Discussion The analysis appears to suggest a mandate effective reduction in the slope of the mortality rate, but no effective reduction in Covid-19 mortality to its defined initial peak when interpreting the mean-effect of the mandates as present in the data. The study is presented as a potential methodology to evaluate the effectiveness of state mandated social distancing policy.

Introduction

Socially mandated distancing policy has been theorized to be effective in reducing the rate of transmission of contagious diseases.[1,2,3] State-wide policy mandating social distancing has been instituted to varying degrees during the Covid-19 pandemic recognized globally in 2020. The theory of reducing the rate of contagion transmission by decreasing social interactions has been extended to possibly reduce the overall mortality by allowing for social/medical mobilization and proper allocation of resources.[3] Little data exists to verify the theoretical model, except analyses demonstrating marginal social distancing effectiveness in delaying the peak infection[5]. Due to the pervasive global incidence of the Covid-19 pandemic and extensive real-time record keeping, it presents an opportunity to evaluate the social distancing theory over a large population with considerably different social distancing measures instituted.

Methods

The study was conducted using the Institute for Health Metrics and Evaluation (IHME) openly published data on Covid-19 infections by sovereign country, to include daily infections/deaths as well as onset and discontinuation dates of state mandated social interaction interventions. As this was the primary source of information used for predictive modeling and setting public policy, it was chosen for its accuracy and regular updates.[6]

The primary goal was to quantify the decrease in the infection/mortality or decrease in the maximum infection/mortality rate as a result of defined state mandated social distancing measures. Mortality was chosen to define endpoint peaks and rates of change over registered infections within a state. Covid-19 registered infections are beset by inaccuracies due to: Inaccurate testing, asymptomatic patients, test availability, and regional variations in testing criterial. In most developed countries, the cause and time of death is typically consistently and accurately recorded.

IHME data accessed on April 12, 2020 at 1900 EST was used to preliminarily select more than 10 sovereign states which fit into a geographic area of similar genomic constituency and indicated by WHO to have developed healthcare standards.[7] Each of the selected countries was an independent state which nationally instituted preventive social interaction law on a given date to include one of the four (4) possible mandates:

1. Public School Closures
2. Closure of non-essential businesses
3. Severe travel restrictions
4. Stay at home order

Countries which did not meet all of these criteria in the IHME data set were excluded from the analysis. Also, countries which did not maintain their state-wide mandated social distancing through the end of the examination period (May 1, 2020) were excluded. Twelve western European countries were included as listed in Table 1. These countries were in close geographically proximity, have a similar genomic alleles, have established and recognized healthcare systems, and have similar social behaviors.[8,9,10] All states mandated social distancing universally across their respective country of the 4 variations listed above on a specific date provided by the IHME data set accessed on April 12, 2020 and maintained them through their peak infection rate.

Defined endpoints for the analysis included the date of the initial peak mortality in deaths per day. A state's peak mortality was defined as the highest recorded daily deaths over a seven day moving average which was followed by a seven or more day decline in mortality with no other discernable peaks using these criteria. The dates of maximum mortality for all 12 countries were identifiable by the design criteria on the IHME data set accessed on May 1, 2020 at 2030 EST. (Table 1).[7] The IHME data set was re-examined on May 15, 2020 to insure no secondary mortality rate peaks were noted and the rate was in a continued decline.[7] The maximum daily mortality rate or peak infection rate was used an easily defined and universal endpoint in any infectious disease progression to examine the total viral mortality up to the maximum mortality rate.

Additionally, the maximum slope of the Covid-19 mortality was determined by evaluating the maximum of the derivative of the infection curve. Specifically, this slope was defined as the total recorded mortality five days after the maximum daily mortality rate minus the total recorded mortality five days before the maximum daily mortality rate divided by the 10 day interval. Both the total mortality and maximum mortality rate were normalized by dividing by the population of the selected state.

Equation 1 – Formula on how the estimate for the maximum mortality rate was calculated from the Covid-19 mortality data from IHME.

$$Estimate\ for\ Maximum\ Mortality\ Rate = \frac{(Mortality\ 5\ Days\ After\ Peak) - (Mortality\ 5\ Days\ Before\ Peak)}{10\ Days}$$

All data was analyzed with Matlab[14] and Microsoft Excel software to determine correlation coefficients and probabilities. General linear mixed effects (GLME) was used to examine combined effects of the multiple variables.

The study was conducted within the ethical principles contained in Declaration of Helsinki, Code of Federal Regulations (CRF), Obligations of Clinical Investigators (21 CFR 812). All data was public and anonymous so no IRB was needed.

We conducted two high-level bivariate studies of this data: the first being the *peak daily death rate* (same as maximum mortality rate) against the *total mandate days*, and the second being the *mortality on the peak date* against the *total mandate days*. Each mandate, if implemented, was implemented some number of days before the peak. The *total mandate days* is the simple summation of these number of days from all four social mandate categories. For example, Belgium implemented stay-at-home orders 25 days prior to it peaks, school-closures 29 days prior to its peak, non-essential business closures 25 days prior to its peak, and did not implement travel restrictions, resulting in 79 total mandate days.

Equation 2 – Formula on how the *Total Mandate Days* are calculated from individual mandates and the number of days prior to the peak daily death rate that the mandates were implemented.

$$Total\ Mandate\ Days = Days_{PriorToPeak}^{StayAtHome} + Days_{PriorToPeak}^{SchoolClosure} + Days_{PriorToPeak}^{NonEssentBus} + Days_{PriorToPeak}^{TravelRestrict}$$

Then, we conducted two multi-variate studies of this data. The multivariate studies use the same response variables as in the univariate data: *peak mortality rate* and *mortality at peak*. The multivariate studies will then consider the effects of each mandate independently as well as incorporate genomic variation and median age in each country's population.

Equation 3 – Peak mortality rate model studied in the multivariate analysis.

$$
\begin{aligned}
Peak\ Mortality\ Rate = {} & \mu_{PMR} && \text{Overall mean peak mortality rate} \\
& +\alpha_{StayAtHome} \cdot Days_{PriorToPeak}^{StayAtHome} && \text{Fixed-effect from stay-at-home orders} \\
& +\alpha_{SchoolClosure} \cdot Days_{PriorToPeak}^{SchoolClosure} && \text{Fixed-effect from school closure} \\
& +\alpha_{NonEssentBus} \cdot Days_{PriorToPeak}^{NonEssentBus} && \text{Fixed-effect from non-essential business closure} \\
& +\alpha_{TravelRestrict} \cdot Days_{PriorToPeak}^{TravelRestrict} && \text{Fixed-effect from travel restrictions} \\
& +\alpha_{GeneVar} \cdot GenomeVar && \text{Fixed-effect from genome variation} \\
& +\alpha_{MedAge} \cdot MedianAge && \text{Fixed-effect from median age} \\
& +\varepsilon_{PMR} && \text{Random Gaussian error}
\end{aligned}
$$

Equation 4 – Mortality at peak model studied in the multivariate analysis.

$$
\begin{aligned}
Mortality\ At\ Peak = {} & \mu_{MAP} && \text{Overall mean mortality at peak} \\
& +\beta_{StayAtHome} \cdot Days_{PriorToPeak}^{StayAtHome} && \text{Fixed-effect from stay-at-home orders} \\
& +\beta_{SchoolClosure} \cdot Days_{PriorToPeak}^{SchoolClosure} && \text{Fixed-effect from school closure} \\
& +\beta_{NonEssentBus} \cdot Days_{PriorToPeak}^{NonEssentBus} && \text{Fixed-effect from non-essential business closure} \\
& +\beta_{TravelRestrict} \cdot Days_{PriorToPeak}^{TravelRestrict} && \text{Fixed-effect from travel restrictions} \\
& +\alpha_{GeneVar} \cdot GenomeVar && \text{Fixed-effect from genome variation} \\
& +\alpha_{MedAge} \cdot MedianAge && \text{Fixed-effect from median age} \\
& +\varepsilon_{MAP} && \text{Random Gaussian error}
\end{aligned}
$$

These models were then regressed onto the IHME data.

Results

Results From Bivariate Analysis

Twelve similar western European sovereign states were pre-selected April 12, 2020 to examine their collective correlation between standardized mortality and total mandate-days of state directed social distancing directives. All states maintained social distancing directives through the study endpoint on May 1, 2020.[7] States were found to have a significant diversity in total mandated intervention over time (mean = 58 total-mandate-days, std-dev = 30.6 total-mandate-days). The total population studied was 298 million. All states had statistically similar age distributions (mean = 41.8 years-old, std-dev = 1.23 years-old).

The slope standardized mortality per country did have a slight negative correlation to the total mandate days (R^2 = 0.083, p=0.36), though the negative correlation was not statistically significant at the 5% level. The bivariate data as well as regression results are shown in Figure 1 in the form of a scatter-plot and table.

The standardized mortality to the peak per country exhibited no statistical correlation to the total mandate days (R^2 = 0.004, p=0.85). The bivariate data as well as regression results are shown in Figure 2 in the form of a scatter-plot and table.

Results From Multivariate Analysis

In the multivariate analysis, a regression analysis on the data from Table 1 was fitted onto models presented in Equation 3 and Equation 4. The results are presented as MATLAB console outputs in Figure 3 and Figure 4 for each of the two response variables, respectively. The key outputs are in the "*Fixed effects coefficients (95% Cis):*" section of the console output. The rows in this section correspond to each fixed-effect factor in the model. The "*Estimate*" column lists the nominal estimate for the coefficient corresponding to the fixed-effect. For example, the estimate for the '*StayHome_DaysBeforePeak*' factor in the peak mortality rate model (Equation 3, Figure 3) reports a value of *-0.000443* in units of deaths per 1 million population per day per day of mandated stay-at-home orders. This is an estimate for the coefficient . This corresponds to about a reduction in the peak daily death rate by 444 deaths per 1 trillion population per day for each additional day of stay-at-home mandates. The "*pValue*" column lists each of the calculated p-values associated with each coefficient estimation under the null-hypothesis that the true coefficient value is zero. From Figure 3, we find the '*StayHome_DaysBeforePeak*' coefficient has a corresponding p-value of 0.43748. Meaning, there is not enough evidence from the data as analyzed to claim additional stay-at-home mandate days have a statistically significant effect on a state's peak covid-19 daily mortality rate at a significance level any lower than 43.748% (typical significance levels being 5%).

Table 2 collects the coefficient estimates and associated p-values from both GLME regressions.

In Table 2 there is no coefficient with a p-value that is smaller than 0.09. This would mean that at a typical 5% significance level, none of these values would be statistically significantly different from zero. This indicates that implementation date of social-distancing mandates (along with population genome variation and median age) do not sufficiently explain the country-to-country variation in covid-19 mortality and mortality rates. However, in spite of the large p-values, some interesting trends can be drawn from the comparison in the mean trends between peak mortality rate and total mortality on date of peak death rate versus the days of implementing social-distancing mandates prior to the peak.

Discussion

The analysis appears to show no statistically significant reduction in neither the slope of the Covid-19 mortality rate (p-val = 0.8452) nor in Covid-19 mortality (p-val = 0.3631) to its defined initial infection peak. However, the mean-effect of social-distancing mandates on the slope of the mortality rate was larger than the mean-effect on the mortality of Covid-19 in these twelve European countries. Interpreting this mean-effects alone could hypothesize that early social-distancing mandates may have a modesteffect in reducing the maximum increase in rate of infection or 'flattening' the rate of infection but does not demonstrate an effect on the Covid-19 mortality itself.

Several factors influence the effectiveness of social distancing interventions. These include the basic reproduction number (R_0) of the virus, the mortality rate, and the individual isolation effectiveness of the mandated interventions.[11,12] The 'flattening' or reduction of the slope of the maximum infection rate with no change in total viral mortality is consistent with mathematical theory of viral infections.[13] The theory can be summarized as: "Assuming a fixed population without novel medical interventions, flatten the rate of infection is possible delaying the infection the peak infection". Theorized reductions in total mortality due to a reduced burden on a healthcare system or advancements in medical care did not materialize in this analysis. However, the time from the probable first infection to the peak of the infection rate was likely only around 3 months. It is possible that if the viral mortality estimated at 0.6% to 1.2% or the viral reproduction R_0, estimated between 2.8 and 3.3, were significantly higher, there may have been some correlation present.[11,12] Also, if the interventions had been significantly more isolating then the mortality may have been reduced. Theoretically, the viral infection ceases once the hosts are identified and completely isolated.

The analysis is presented as a potential methodology to evaluate the effectiveness of state mandated social distancing policy. Western European countries were selected for this study due to their cultural and healthcare similarities. A possible future study would be to conduct a similar analysis on other clusters of countries with cultural similarities and variations in strictness of intervention. These methodologies could be applied to individual states within the United States once the peak infections have been identified.

Abbreviations

FDA- Food and Drug Administration

CFR- Code of Federal Regulations

IHME- Institute of Health Metrics and Evaluation

Declarations

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None

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Authorization for use of data:

Authors' contributions:

S.A.- Drafting, analysis, and interpretation

M. – Design, drafting, analysis, and interpretation

Ethics:

This clinical study was conducted in accordance with the ethical principles contained within Declaration of Helsinki, Protection of Human Volunteers (21 CFR 50), Institutional Review Boards (21 CFR 56), and Obligations of Clinical Investigators (21 CFR 812).

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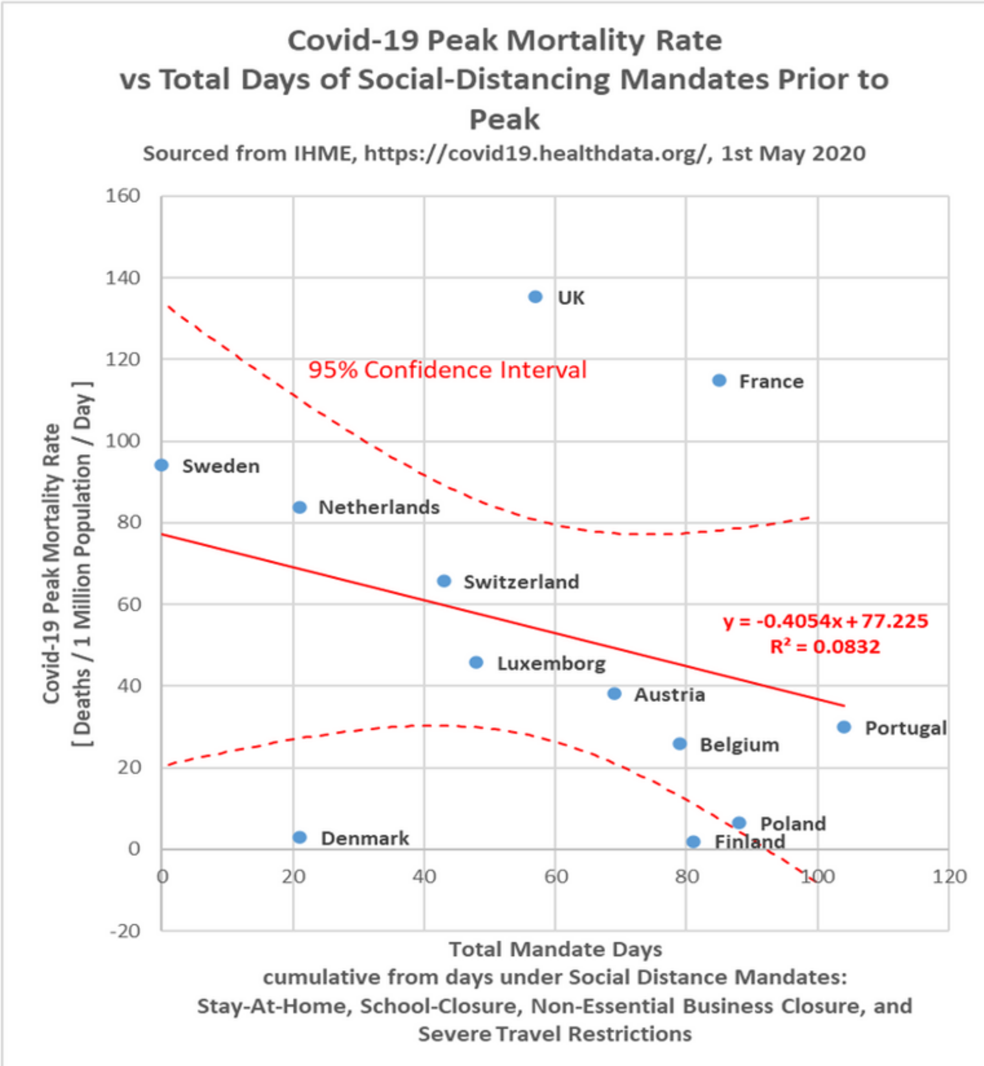
Tables

Due to technical limitations, the tables are only available as a download in the supplemental files section.

Figures



Regression/ANOVA Summary on Peak Mortality Rate vs Total Mandate Days

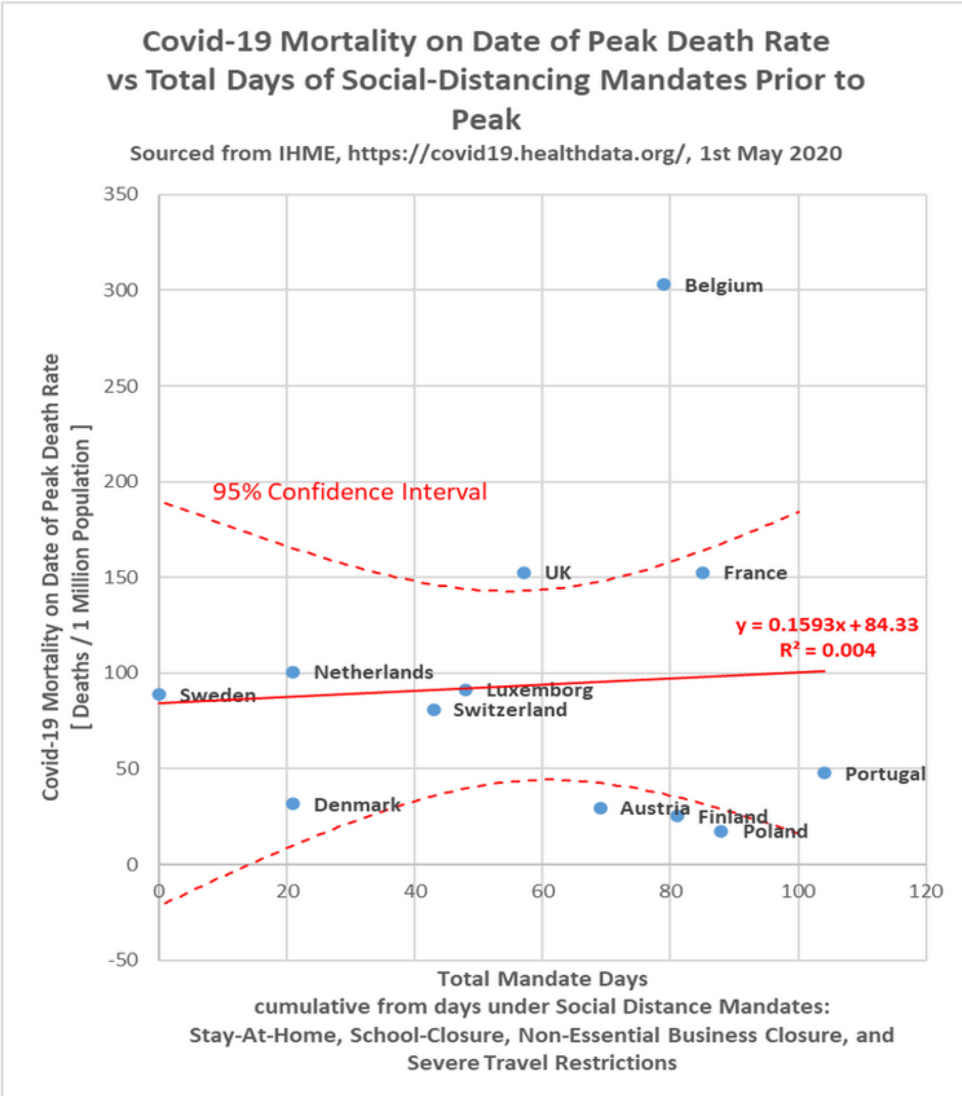
Regression Statistics	
Multiple R	0.28852
R Square	0.08324
Adjusted R Square	-0.00843
Standard Error	45.15364
Observations	12

ANOVA	*df*	*SS*	*MS*	*F*	*Significance F*
Regression	1	1851.31359	1851.31359	0.90802	0.36311
Residual	10	20388.51178	2038.85118		
Total	11	22239.82537			

	Coefficients	*Standard Error*	*t Stat*	*P-value*	*Lower 95%*	*Upper 95%*	*Lower 95.0%*	*Upper 95.0%*
Intercept	77.22540424	27.90714	2.76723	0.01988	15.04443	139.40638	15.04443	139.40638
Total Mandate Days	-0.405409268	0.42545	-0.95290	0.36311	-1.35337	0.54255	-1.35337	0.54255

Figure 1

1A- Maximum slope of the standardized Covid-19 state mortality (peak mortality rate) correlated to days under state-mandated social distancing directives prior to the peak. 1B- Regression ANOVA



Regression/ANOVA Summary on Mortality At Peak vs Total Mandate Days

Regression Statistics	
Multiple R	0.06322
R Square	0.00400
Adjusted R Square	-0.09560
Standard Error	84.37317
Observations	12

ANOVA	*df*	*SS*	*MS*	*F*	*Significance F*
Regression	1	285.66392	285.66392	0.04013	0.84525
Residual	10	71188.32274	7118.83227		
Total	11	71473.98667			

	Coefficients	*Standard Error*	*t Stat*	*P-value*	*Lower 95%*	*Upper 95%*	*Lower 95.0%*	*Upper 95.0%*
Intercept	84.33012547	52.14671	1.61717	0.13691	-31.85998	200.52024	-31.85998	200.52024
Total Mandate Days	0.15925071	0.79498	0.20032	0.84525	-1.61208	1.93058	-1.61208	1.93058

Figure 2

2A- Standardized Covid-19 state mortality on the day of peak mortality rate correlated to days under state-mandated social distancing directives prior to the peak. 2B- Regression ANOVA

```
Generalized linear mixed-effects model fit by ML

Model information:
    Number of observations             12
    Fixed effects coefficients          7
    Random effects coefficients         0
    Covariance parameters               1
    Distribution                    Gaussian
    Link                            Identity
    FitMethod                       Laplace

Formula:
    Linear Mixed Formula with 6 predictors.

Model fit statistics:
    AIC       BIC       LogLikelihood    Deviance
    136.06    139.94    -60.032          120.06

Fixed effects coefficients (95% CIs):
    Name                                Estimate       SE            tStat       DF    pValue     Lower         Upper
    '(Intercept)'                           671.44        403.52       1.6639    5     0.15701       -365.85        1708.7
    'StayHome_DaysBeforePeak'          -0.00044395    0.00052637      -0.8434    5     0.43748     -0.001797    0.00090914
    'CloseSchool_DaysBeforePeak'         0.0011464     0.0010914       1.0504    5     0.34161    -0.0016591     0.0039519
    'NonEssent_DaysBeforePeak'         -0.00016855    0.00079223     -0.21275    5     0.83992     -0.002205     0.0018679
    'TrvlRestr_DaysBeforePeak'          -0.0002521    0.00070522     -0.35748    5     0.73533    -0.0020649     0.0015607
    'GenomeVariation'                      -9715.3         16473     -0.58977    5     0.58098        -52060         32630
    'MedianAge'                            -13.339        8.9171      -1.4959    5     0.19492       -36.262        9.5828

Random effects covariance parameters:
Group: Error
    Name                      Estimate
    'sqrt(Dispersion)'        36.007
```

Figure 3

GLME regression results from multivariate analysis on peak mortality rate, the model described by Equation 3.

```
Generalized linear mixed-effects model fit by ML

Model information:
    Number of observations             12
    Fixed effects coefficients          7
    Random effects coefficients         0
    Covariance parameters               1
    Distribution                    Gaussian
    Link                            Identity
    FitMethod                       Laplace

Formula:
    Linear Mixed Formula with 6 predictors.

Model fit statistics:
    AIC       BIC       LogLikelihood    Deviance
    148.66    152.54    -66.332          132.66

Fixed effects coefficients (95% CIs):
    Name                              Estimate      SE            tStat       DF    pValue      Lower          Upper
    '(Intercept)'                           1429        682.17      2.0948    5     0.090352       -324.59       3182.6
    'StayHome_DaysBeforePeak'         -0.0011465    0.00088985     -1.2884    5      0.25401    -0.0034339     0.001141
    'CloseSchool_DaysBeforePeak'        0.000444      0.001845     0.24065    5      0.81938    -0.0042988    0.0051868
    'NonEssent_DaysBeforePeak'         -0.000702     0.0013393    -0.52416    5      0.62257    -0.0041448    0.0027408
    'TrvlRestr_DaysBeforePeak'        0.00019839     0.0011922     0.16641    5      0.87436    -0.0028663     0.003263
    'GenomeVariation'                     -16890         27848    -0.60652    5      0.57065        -88476        54695
    'MedianAge'                          -29.527        15.075     -1.9587    5      0.10746       -68.278       9.2237

Random effects covariance parameters:
Group: Error
    Name                        Estimate
    'sqrt(Dispersion)'          60.871
```

Figure 4

GLME regression results from multivariate analysis on mortality on date of peak death rate, the model described by Equation 4.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Table1.PNG
- Table2.PNG