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Stay-at-home policy: is it a case of exception fallacy? An internet-based ecological study — Source link [2]

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1	Title page
2 3	Title: "Stay-at-home policy: is it a case of exception fallacy? An internet-based ecological study".
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17	

18 Abstract:

- 19 Background: Countries with strict lockdown had a spike on the number of deaths. A recent
- 20 mathematical model has suggested that staying at home did not play a dominant role in reducing
- 21 COVID-19 transmission. Comparison between number of deaths and social mobility is difficult
- 22 due to the non-stationary nature of the COVID-19 data.
- 23 **Objective**: To propose a novel approach to assess the association between staying at home
- 24 values and the reduction/increase in the number of deaths due to COVID-19 in several regions
- around the world.
- 26 **Methods**: In this ecological study, data from www.google.com/covid19/mobility/,
- 27 ourworldindata.org and covid.saude.gov.br were combined. Countries with >100 deaths and with
- a Healthcare Access and Quality Index of ≥ 67 were included. Data were preprocessed and
- analyzed using the difference between number of deaths/million between 2 regions and the
- 30 difference between the percentage of staying at home. Analysis was performed using linear
- 31 regression and residual analysis
- 32 **Results**: After preprocessing the data, 87 regions around the world were included, yielding 3,741
- 33 pairwise comparisons for linear regression analysis. Only 63 (1.6%) comparisons were
- 34 significant.
- **Discussion**: With our results, we were not able to explain if COVID-19 mortality is reduced by
- 36 staying as home in ~98% of the comparisons after epidemiological weeks 9 to 34.
- 37

38 Introduction

39 By late September, 2020, approximately one million people worldwide had died from the new 40 coronavirus (COVID-19) (Coronavirus Update (Live): 13,578,330 Cases and 583,696 Deaths 41 from COVID-19 Virus Pandemic - Worldometer). Wearing masks, taking personal precautions, 42 testing for COVID-19 and social distancing have been advocated for controlling the pandemic 43 (Huang and Chen 2020; Lin et al. 2020; Wu and Qi 2020). To achieve source control and stop 44 transmission, social distancing has been interpreted by many as staying at home. Such policies 45 across multiple jurisdictions were suggested by some experts (Guest et al. 2020). These measures 46 were supported by the World Health Organization (WHO Director-General's opening remarks at 47 the media briefing on COVID-19 - 13 April 2020), local authorities (Ministry of Housing, 48 Communities and Local Government 2020; Mucientes and Carrasco 2020; Governor Cuomo 49 Signs the "New York State on PAUSE" Executive Order 2020), and encouraged on social media 50 platforms (Criativo; A Movement to Stop the COVID-19 Pandemic | #StayTheFuckHome, 51 #[stayathome] (Brazilian twitter)).

52 Some mathematical models and meta-analyses have shown a marked reduction in COVID-19 53 cases (Ambikapathy and Krishnamurthy 2020; Espinoza et al. 2020; Ibarra-Vega 2020; Liu et al. 54 2020; Nussbaumer-Streit et al. 2020; Sjödin et al. 2020) and deaths (Ferguson et al. 2020; 55 Semenova et al. 2020) associated with lockdown policies. Brazilian researchers have published 56 mathematical models of spreading patterns (Peixoto et al. 2020) and suggested implementing 57 social distancing measures and protection policies to control virus transmission (Aquino et al. 58 2020). By May 5th, 2020, an early report, using number of curfew days in 49 countries, found 59 evidence that lockdown could be used to suppress the spread of COVID-19 (Atalan 2020). 60 Measures to address the COVID-19 pandemic with Non-Pharmacological Interventions (NPIs) 61 were adopted after Brazil enacted Law No. 13979 (Imprensa Nacional), and this was followed by 62 many states such as Rio de Janeiro (Decreto 46970 27/03/2020), the Federal District of Brasília (Decree No. 40520, dated March 14th, 2020) (Decreto 40520 de 14/03/2020), the city of São 63 Paulo (Decree No. 59.283, dated March 16th, 2020) (Decreto 59283 2020 de São Paulo SP), and 64 the State of Rio Grande do Sul (Decree No. 55240/2020, dated May 10th, 2020) (Decreto 55240) 65 66 de 10/05/2020). It was expected that, with these actions, the number of deaths by COVID-19 67 would be reduced. Of note, the country's most populous state, São Paulo, adopted rigorous quarantine measures and put them into effect on March 24th, 2020 (Decreto 59283 2020 de São 68 69 Paulo SP). Internationally, Peru adopted the world's strictest lockdown (Tegel 2020).

70 Recently, Google LLC published datasets indicating changes in mobility (compared to an 71 average baseline before the COVID-19 pandemic). These reports were created with aggregated, 72 anonymized sets of daily and dynamic data at country and sub-regional levels drawn from users 73 who had enabled the Location History setting on their cell phones. These data reflect real-world 74 changes in social behavior and provide information on mobility trends for places like grocery 75 stores, pharmacies, parks, public transit stations, retail and recreation locations, residences, and 76 workplaces, when compared to the baseline period prior to the pandemic (Google LLC). 77 Mobility in places of residence provides information about the "time spent in residences", which 78 we will hereafter call "staying at home" and use as a surrogate for measuring adherence to stay-79 at-home policies.

Studies using Google COVID-19 Community Mobility Reports and the daily number of new
COVID-19 cases have shown that over 7 weeks a strong correlation between staying at home
and the reduction of COVID-19 cases in 20 counties in the United States (Badr et al. 2020);
COVID-19 cases decreased by 49% after 2 weeks of staying at home (Banerjee and Nayak)

84 2020); the incidence of new cases/100,000 people was also reduced (Wang et al. 2020); social 85 distancing policies were associated with reduction in COVID-19 spread in the US (Gao et al. 2020); as well as in 49 countries around the world (Atalan 2020). A recent report using Brazilian 86 and European data has shown a correlation between NPI stringency and the spread of COVID-19 87 88 (Candido et al. 2020; Islam et al. 2020); these analyses are debatable, however, due to their short 89 time span and the type of time series behavior (Bernal et al. 2017), or for their use of Pearson's 90 correlation in the context of non-stationary time series (Gao et al. 2020). For instance, applying 91 the same statistical analysis to stationary and non-stationary time series is not sufficient for 92 statistical analysis (Nason 2006), and the latter is the case with this COVID-19 data. A 2020 93 Cochrane systematic review of this topic reported that they were not completely certain about 94 this evidence for several reasons. The COVID-19 studies based their models on limited data and 95 made different assumptions about the virus (Nussbaumer-Streit et al. 2020); the stay-at-home 96 variable was analyzed as a binary indicator (Sen et al. 2020); and the number of new cases could 97 have been substantially undocumented (Li et al. 2020); all which may have biased the results. A 98 sophisticated mathematical model based on a high-dimensional system of partial differential 99 equations to represent disease spread has been proposed (Zamir et al. 2020). According to this 100 model, staying at home did not play a dominant role in disease transmission, but the combination 101 of these, together with the use of face masks, hand washing, early-case detection (PCR test), and 102 the use of hand sanitizers for at least 50 days could have reduced the number of new cases. 103 Finally, after 2 months, the simulations that drove the world to lockdown have been questioned 104 (Boretti 2020).

After more than 25 epidemiological weeks of this pandemic, verifying if staying at home had an impact on mortality rates is of particular interest. A PUBMED search with the terms "COVID-19" AND (Mobility) (search made on September 8th, 2020) yielded 246 articles; of these, 35 were relevant to mobility measures and COVID-19, but none compared mobility reduction to mortality rates.

We are looking for the association between two variables: deaths/million and the percentage of 110 111 people who remained in their residences. Comparison, however, is difficult due to the non-112 stationary nature of the data. To overcome this problem, we proposed a novel approach to assess the association between staying at home values and the reduction/increase in the number of 113 114 deaths due to COVID-19 in several regions around the world. If the variation in the difference 115 between the number of deaths/million in two countries, say A and B, and the variation in the 116 difference of the staying at home values between A and B present similar patterns, this is due to 117 an association between the two variables. In contrast, if these patterns are very different, this is 118 evidence that staying at home values and the number of deaths/million are not related (unless, of 119 course, other unaccounted for factors are at play).

120 Material and methods

121

122 Study design

- 123 This is an ecological study using data available on the Internet.
- 124

125 Setting - Data collection on mobility

126 Google COVID-19 Community Mobility Reports provided data on mobility from 138 countries 127 and regions (Coronavirus Source Data 2020, Coronavírus Brasil) between February 15th and

128 August 21^{st} , 2020.(Google LLC) Data regarding the average times spent at home was generated

- 129 in comparison to the baseline. Baseline was considered to be the median value from between
- 130 January 3rd and February 6th, 2020. Data obtained between February 15th and August 21th 2020
- 131 was divided into epidemiological weeks (epi-weeks) and the mean percentage of time spent
- 132 staying at home per week was obtained.

Data collection on mortality

Numbers of daily deaths from selected regions were obtained from open databases (Coronavirus
 Source Data 2020, Coronavírus Brasil) on August 27st, 2020.

136 Inclusion criteria for analysis

137 Only regions with mobility data and with more than 100 deaths, by August 26th, 2020, were 138 included in this study. For data quality, only countries with Healthcare Access and Quality 139 Index (HAQI) of ≥ 67 were included.(Barber et al. 2017) By choosing a HAQI of ≥ 67 , we 140 assumed that data from these countries were reliable and healthcare was of high quality. For 141 Brazilian regions, a HAQI was substituted for the Human Development Index (HDI), and those 142 with <0.549 (low) were excluded.

Three major cities with >100 deaths and well-established results (Tokyo, Japan; Berlin,
Germany, and New York, USA) were selected as controlled areas.

145 Dataset of COVID-19 cases and associated data

146 After inclusion of the countries/regions, further data were obtained to reduce comparison bias,

147 including population density (population/km²), percentage of the urban population, HDI, and the

- 148 total area of the region in square kilometers. All data were obtained from open databases.(2019
- 149 Human Development Index Ranking, [Cities and States Statistics], Population by Country (2020)
- 150 Worldometer)

151 **Classification of areas with COVID-19**

Regions were classified as controlled for cases of COVID-19 if they present at least two out of the three following conditions: **a**) type of transmission classified as "clusters of cases", **b**) a downward curve of newly reported deaths in the last seven days, and **c**) a flat curve in the cumulative total number of deaths in the last seven days (variation of 5%) according to the World Health Organization.(WHO Coronavirus Disease (COVID-19) Dashboard) An example is shown in Figure S3 (supplement).

- Data from the cities (Tokyo, Berlin, New York, Fortaleza, Belo Horizonte, Manaus, Rio de
 Janeiro, São Paulo, and Porto Alegre) were obtained from official government sites.(Population
- 160 of Tokyo Tokyo Metropolitan Government, Berlin, COVID-19:Data, Planning-Population-
- 161 Census 2010-DCP) Tokyo, Berlin and New York were chosen for having controlled the COVID-
- 162 19 dissemination, for representing three different continents, and for similarity to major Brazilian
- 163 cities (Fortaleza, Belo Horizonte, Manaus, Rio de Janeiro, São Paulo, and Porto Alegre).

164 Merged database

- 165 Different databases from the sites mentioned above were merged using Microsoft Excel Power
- 166 Query (Microsoft Office 2010 for Windows Version 14.0.7232.5000) and manually inspected for
- 167 consistency.

168 **Processing the data - cleaning**

- 169 Data collected from multiple regions were processed using Python 3.7.3 in the Jupyter Notebook
- 170 environment through the use of the Python Data Analysis Library in Google Colab Research.

- 171 Details of preprocessing are described in Python script (Supplemental material). Briefly, after
- taking the sum of deaths/million per epi-week, and the average of the variable "staying at home"
- 173 per epi-week, non-stationary patterns were mitigated by subtracting week_t by week_{t-1}.

174 **Time series data setup and variables**

- 175 Details regarding the pre-processing and methodological details were presented on the *approach*
- 176 for analyzing the time series data. Our variables were the difference in the variation of deaths
- 177 between locations A and B (dependent variable outcome), and the difference in the variation of
- 178 staying at home values between the same location (independent variable).

179 **Comparison between areas**

Direct comparison, between regions with and without controlled COVID-19 cases, was
considered in two scenarios: 1) Restrictive if, at least three out of four of the following
conditions were similar: a) population density, b) percentage of the urban population, c) HDI and
d) total area of the region. Similarity was considered adequate when a variation in conditions a),
b), and c) was within 30%, while, for condition d), a variation of 50% was considered adequate.
2) Global: all regions and countries were compared to each other.

186 Statistical analysis

187 Rationale

188 Time series on COVID-19 mortality (deaths/millions) display a non-stationary pattern. The daily 189 data present a very distinct seasonal behavior on the weekends, with valleys on Saturdays and 190 Sundays followed by peaks on Mondays (Figure S1)

191 To make it stationary, one may introduce dummy variables for Saturdays, Sundays, and 192 Mondays, regress the number of deaths in these dummy variables, and then analyze the residuals. 193 However, in most cases, the residuals are still non-stationary time series, and special treatment 194 would be required in each case. Although this approach may be feasible for a few series, we are 195 interested in analyzing hundreds of time series from different countries and regions. Hence, we 196 need a more efficient way to deal with this amount of data. The covariates present another issue 197 in regressing the daily time series of deaths/staying at home. The covariates are typically 198 correlated with error terms due to public policies adopted by regions/countries. Mechanisms 199 controlling social isolation are intrinsically related to the number of deaths/cases in each 200 location. An increase in the death rate may cause more stringent policies to be adopted, which 201 increases the percentage of people staying at home. This change causes an imbalance between 202 the observed number of deaths and staying at home levels. In a regression model, this 203 discrepancy is accounted for in the error term. Hence, the error term will change in accordance 204 with staying at home levels.

205 Approach for analyzing the time series data

Data aggregation by epidemiological week is a plausible alternative (Figure S2). In this way, artificial seasonality, imposed by work scheduled during weekends and the effect of governmental control over social interaction, in a regression framework, are mitigated. The drawback is that the sample size is significantly reduced from 187 days (Figure S1) to 26 epidemiological weeks (Figure S2).

Aggregation by epidemiological week, however, still yields non-stationary time series in most

- 212 cases. To overcome this problem, we differentiated each time series. Recall that if Z_t denotes the
- 213 number of deaths in the *t*-th epidemiological week, we define the first difference of Z_t as

$$\Delta Z_t = Z_t - Z_{t-1}.$$

Intuitively, ΔZ_t denotes the variation of deaths between weeks t and t-1, also known as the flux 215 216 of deaths. The same is valid for the staying at home time series. This simple operation yielded, in 217 most cases, stationary time series, and verified with the so-called Phillips-Perron stationarity test 218 (Perron 1988). In the few cases where the resulting time series did not reject the null hypothesis 219 of non-stationarity (technically, the existence of a unitary root, in the time series characteristic), 220 this was due to the presence of one or two outliers combined with the small sample size. These 221 outliers were usually related to the very low incidence of COVID-19 deaths by the 9th 222 epidemiological week when paired with countries with a significant number of deaths in that 223 same week, thus resulting in an outlier which cannot be accounted for by linear 224 regression.(Perron 1988)

To investigate pairwise behavior, we propose a method to assess the relationship between deaths and staying at home data between various countries and regions. For two countries/regions, say A and B, let Y_t^A and Y_t^B denote the number of deaths per million at epidemiological week t for country A and B respectively, while X_t^A and X_t^B denote the staying at home at epidemiological week t for A and B, respectively. The idea is to regress the difference $\Delta Y_t^A - \Delta Y_t^B = \Delta (Y_t^A - 230 Y_t^B)$ on $\Delta X_t^A - \Delta X_t^B = \Delta (X_t^A - X_t^B)$. Formally, we perform the regression

$$\Delta(Y_t^A - Y_t^B) = \beta_0 + \beta_1 \Delta(X_t^A - X_t^B) + \varepsilon_t,$$

where β_0 and β_1 are unknown coefficients and ε_t denotes an error term. Estimation of β_0 and β_1 is carried out through ordinary least squares. The interpretation of the model is important. We are regressing the difference in the variation of deaths between locations A and B into the difference in the variation of staying at home values between the same location.

235 If the number of deaths in locations A and B have a similar functional behavior over time, then $Y_t^A - Y_t^B$ tends to be near-constant, and $\Delta(Y_t^A - Y_t^B)$ tends to oscillate around zero. If the same 236 applies to $\Delta(X_t^A - X_t^B)$, then we expect $\beta_1 \neq 0$; consequently, we conclude that the behavior, 237 between A and B, is similar and the number of deaths and the percentage of staying at home are 238 239 associated in these regions. The other non-spurious situation implying $\beta_1 \neq 0$ occurs when the 240 variation in the number of deaths in locations A and B increases/decreases over time following a 241 certain pattern, while the variation in the percentage of "staying at home" values also 242 increases/decreases following the same pattern (apart from the direction). In this situation, we 243 found different epidemiological patterns as in the variation in the number of deaths, and in the 244 staying at home values, in locations A and B were on opposite trends. However, if these patterns 245 were similar (proportional), this would be captured in the difference and, as a consequence, in 246 the regression. This means that the different trends were near proportional and, hence, the 247 variation in staying at home is associated with the variation in deaths.

The proposed approach presents a way to evaluate staying at home and the number of deaths between two countries/regions. In the section below "Definition of areas with and without controlled cases of COVID-19", each country/region was classified into a binary class: either controlled or not controlled areas for COVID-19. The proposed method allows for insights regarding the association of the number of deaths and staying at home levels between countries/regions with similar/different degrees of COVID-19 control.

Estimation of β_0 and β_1 is carried out through ordinary least squares. Assumptions related to consistency, efficiency, and asymptotic normality of the ordinary least squares, in the context of time series regression, can be found in Greene, 2012 (Greene 2012). Since we are comparing many time series, to avoid any problem with spurious regression, we performed a cointegration

test between the response and covariates. In this context, this is equivalent to testing the stationarity of ε_t , which was done by performing the Phillips-Perron test. Residual analysis is of utmost importance in linear regression, especially in the context of small samples. The steps and tests performed in the residual analysis are described in the statistical analysis section.

After data preprocessing, the association between the number of deaths and staying at home was verified using a linear regression approach. Data were analyzed using the Python model statsmodels.api v0.12.0 (statsmodels.regression.linear_model.OLS; statsmodels.org), and double-checked using R version 3.6.1. False Discovery Rate proposed by Benjamini-Hochberg (FDR-BH) was used for multiple testing.

We checked the residuals for heteroskedasticity using White's test; for the presence of autocorrelation using the Lagrange Multiplier test; for normality using the Shapiro-Wilk's normality test; and for functional specification using the Ramsey's RESET test. All tests were performed with a 0.05 significance level and the analysis was performed with R version 3.6.1.

Data from 30 restrictive comparisons were manually inspected and checked a third time using
Microsoft Excel (Microsoft). A heat map was designed using GraphPad Prism version 8.4.3 for
Mac (GraphPad Software, San Diego, California, USA). Graphs plotting the number of
deaths/million and staying at home over epidemiological weeks were obtained from Google
Sheets.

276 **Results**

A flowchart of the data manipulation is depicted in Figure 1. Briefly, Google COVID-19 Community Mobility Report data between February 16th and August 21st, 2020, yielded 138 separate countries and their regions. The website Our World in Data provided data on 212 countries (between December 31st, 2019, and August 26th, 2020), and the Brazilian Health Ministry website provided data on all states (n=27) and cities (n=5,570) in Brazil (February 25th to August 26th, 2020).

After data compilation, a total of 87 regions and countries were selected: 51 countries, 27 States in Brazil, six major Brazilian State capitals [Manaus, Amazonas (AM), Fortaleza, Ceará (CE), Belo Horizonte, Minas Gerais (MG), Rio de Janeiro, Rio de Janeiro (RJ), São Paulo, São Paulo (SP) and Porto Alegre, Rio Grande do Sul (RS)], and three major cities throughout the world (Tokyo, Berlin and New York) (Figure 1).

Characteristics of these 87 regions are presented in Table 1 (further details are in <u>Supplemental</u>
 <u>Material - Characteristics of Regions</u>).

290

291 Comparisons

The restrictive analysis between controlled and not controlled areas yielded 33 appropriate comparisons, as shown in Table 2. Only one comparison out of 33 (3%) - state of Roraima (Brazil) versus state of Rondonia (Brazil) - was significant (p-value = 0.04). After correction for residual analysis, it did not pass the autocorrelation test (Lagrange Multiplier test=0.04). (Further details are in <u>Supplemental Material - Restrictive Analysis</u>).

The global comparison yielded 3,741 combinations; from these, 184 (4.9%) had a p-value < 0.05, after correcting for False Discovery Rate (Table S3). After performing the residual analysis, by testing for cointegration between response and covariate, normality of the residuals, presence of residual autocorrelation, homoscedasticity, and functional specification, only 63 (1.6%) of models passed all tests (Table S4). Closer inspection of several cases where the model

did not pass all the tests revealed a common factor: the presence of outliers, mostly due to differences in the epidemiological week in which deaths started to be reported. A heat map showing the comparison between the 87 regions is presented in Figure 2.

305 Discussion

306 We were not able to explain the variation of deaths/million in different regions in the world by 307 social isolation, herein analyzed as differences in staying at home, compared to baseline. In the 308 restrictive and global comparisons, only 3% and 1.6% of the comparisons were significantly 309 different, respectively. These findings are in accordance with those found by Klein et al. (Klein 310 et al.). These authors explain why lockdown was the least probable cause for Sweden's high death rate from COVID-19 (Klein et al.). Likewise, Chaudry et al. made a country-level 311 312 exploratory analysis, using a variety of socioeconomic and health-related characteristics, similar 313 to what we have done here, and reported that full lockdowns and wide-spread testing were not 314 associated with COVID-19 mortality per million people (Chaudhry et al. 2020). Different from 9th 315 Chaudry et al., in our dataset, after 25 epidemiological weeks, (counting from the 316 epidemiological week onwards in 2020) we included regions and countries with a "plateau" and 317 a downslope phase in their epidemiological curves. Our findings are in accordance with the 318 dataset of daily confirmed COVID-19 deaths/million in the UK. Pubs, restaurants, and barbershops were open in Ireland on June 29th and masks were not mandatory (Therese 2020); 319 320 after more than 2 months, no spike was observed; indeed, death rates kept falling (Daily 321 confirmed COVID-19 deaths per million, rolling 7-day average). Peru has been considered to be 322 the most strict lockdown country in the world (Tegel 2020), nevertheless, by September 20th, it 323 had the highest number of deaths/million (Coronavirus Update (Live): 31,036,957 Cases and 324 962.339 Deaths from COVID-19 Virus Pandemic - Worldometer). Of note, differences were 325 also observed between regions that were considered to be COVID-19 controlled, e.g., Sweden 326 versus Macedonia. Possible explanations for these significant differences may be related to the 327 magnitude of deaths in these countries.

328 Our results are different from those published by Flaxman et al. These authors calculated that 329 NPIs would prevent 3.1 million deaths across 11 European countries (Flaxman et al. 2020). The 330 discrepant results can be explained by different approaches to the data. While Flaxman et al. 331 assumed a constant reproduction number (Rt) to calculate the total number of deaths, which 332 eventually did not occur, we calculated the difference between the actual number of deaths 333 between 2 countries/regions. The same explanation for the discrepancy can be applied to other 334 publications where mathematical models were created to predict outcomes (Ambikapathy and 335 Krishnamurthy 2020; Ibarra-Vega 2020; Liu et al. 2020; Nussbaumer-Streit et al. 2020; Sjödin et 336 al. 2020). Most of these studies dealt with COVID-19 cases (Banerjee and Nayak 2020; Wang et 337 al. 2020) and not observed deaths. Despite its limitations, reported deaths are likely to be more 338 reliable than new case data. Further explanations for different results in the literature, besides 339 methodological aspects, could be explained by the complexity of the virus dynamic and its 340 interaction with the environment. It is unwise to try to explain a complex and multifactorial 341 condition, with the inherent constant changes, using a single variable. An initial approach would 342 employ a linear regression to verify the influence of one factor over an outcome. Herein we were 343 not able to identify this association.

This study has limitations. Different from the established paradigm of randomized clinical trial, this is an ecological study. An ecological study observes findings at the population level and generates hypotheses (Pearce 2000). Population-level studies play an essential part in defining the most important public health problems to be tackled (Pearce 2000), which is the case here.

348 Another limitation was the use of Google Community Mobility Reports as a surrogate marker for 349 staying at home. This may underestimate the real value: for instance, if a user's cell phone is 350 switched off while at home, the observation will be absent from the database. Furthermore, the 351 sample does not represent 100% of the population. This tool, nevertheless, has been used by 352 other authors to demonstrate the efficacy in reducing the number of new cases after NPI (Delen 353 et al. 2020; Vokó and Pitter 2020). Using different methodologies for measuring mobility may 354 introduce bias and would prevent comparisons between different countries. The number of 355 deaths may be another issue. Death figures may be underestimated, however, reported deaths 356 may be more relevant than new case data. The arbitrary criteria used for including countries and 357 regions, the restrictive comparisons, and our definition of an area as COVID-19 controlled are 358 open for criticism. Nonetheless, these arbitrary criteria were created a priori to the selection of 359 the countries. With these criteria, we expected to obtain representative regions of the world, 360 compare similar regions, and obtain accurate data. By using a HAQI of \geq 67, we assumed that 361 data from these countries would be accurate, reliable, and health conditions were generally good. 362 Nevertheless, the global analysis of the regions (n = 3741 comparisons) overcame any issue of 363 the restrictive comparison. Indeed, the global comparison confirmed the results found in the restrictive one; only 1.6% of the death rates could be explained by staying at home. Also, our 364 365 effective sample size in all studies is only 25 epidemiological weeks, which is a very small 366 sample size for a time series regression. The small sample size and the non-stationary nature of 367 COVID-19 data are challenges for statistical models, but our analysis, with 25 epidemiological 368 weeks, is relatively larger than previous publications which used only 7 weeks (Ghosal et al. 369 2020). The effects of small samples in this case are related to possible large type II errors and 370 also affect the consistency of the ordinary least square estimates. Nevertheless, given the 371 importance of social isolation promoted by world authorities (COVID-19 advice - Physical 372 distancing), we expected a higher incidence of significant comparisons, even though it could be 373 an ecological fallacy. The low number of significant associations between regions for mortality 374 rate and the percentage of staying at home may be a case of exception fallacy, which is a 375 generalization of individual characteristics applied at the group-level characteristics (Miller and 376 Brewer 2003).

377 There are strengths to highlight. Inclusion criteria and the Healthcare Access and Quality Index 378 were incorporated. We obtained representative regions throughout the world, including major 379 cities from 4 different continents. Special attention was given to compiling and analyzing the 380 dataset. We also devised a tailored approach to deal with challenges presented by the data. To 381 our knowledge, our modeling approach is unique in pooling information from multiple countries 382 all at once using up-to-date data. Some criteria, such as population density, percentage of urban 383 population, HDI, and HAQI, were established to compare similar regions. Finally, we gave 384 special attention to the residual analysis in the linear regression, an absolutely essential aspect of 385 studies using small samples.

In conclusion, using this methodology and current data, in ~98% of the comparisons using 87 different regions of the world we found no evidence that the number of deaths/million is reduced by staying at home. Regional differences in treatment methods and the natural course of the virus may also be major factors in this pandemic, and further studies are necessary to better understand it.

Supplemental Material:

- 392 The Python and R scripts are available at
- 393 https://gist.github.com/rsavaris66/eccfc6caf4c9578d676c134fac74d3fe

394

- 395 More supplemental material, including raw data, is available at this
- 396 https://drive.google.com/drive/folders/1239llmxz9YenWweWXA1wgdf07WFYDrYG
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Development maex (the	inglier, the be				
Region/Country	Density people/km ²	Urban Pop (%)	HDI	Population	Land area (km ²)
Controlled areas					
Austria	109	57	0.914	9,014,380	82,40
Bahrain	2,239	89	0.838	1,709,919	76
Belgium	383	98	0.919	11,597,489	30,28
Berlin	4,118	100	0.950	3,669,491	89
Canada	4	81	0.922	37,793,085	9,093,51
Czech Republic	139	74	0.891	10,712,102	78,86
Denmark	137	88	0.930	5,795,391	42,43
Finland	18	86	0.925	5,542,073	303,89
city of Fortaleza, Ceará, Brazil	7,786	100	0.754	2,686,612	31
France	119	82	0.891	65,296,176	547,55
Germany	240	76	0.939	83,825,861	348,56
Greece	81	85	0.870	10,414,904	128,90
Hungary	107	72	0.845	9,656,450	90,53
Ireland	72	63	0.942	4,946,213	68,89
Italy	206	69	0.883	60,447,728	294,14
Japan	347	92	0.915	126,414,795	364,55
Kuwait	240	100	0.808	4,280,111	17,82
Macedonia	83	59	0.759	2,083,360	25,22
city of Manaus, Amazonas, Brazil	158	100	0.737	2,219,580	11,40
Netherlands	508	92	0.934	17,140,821	33,72
New York City	10,194	100	0.941	8,336,817	78
Norway	15	83	0.954	5,427,784	365,26
Portugal	111	66	0.850	10,191,976	91,59
city of Rio de Janeiro, RJ, Brazil	5,266	100	0.799	6,747,815	1,20
Russia	9	74	0.824	145,944,331	16,376,87
Slovenia	103	55	0.902	2.078.983	20.14

579Table 1. Characteristics of the 87 regions and countries used for comparison in the study. HDI = Human580Development Index (the higher, the better).

South Korea	527	82	0.906	51,276,136	97,230
Spain	94	80	0.893	46,757,635	498,800
State of Acre	4	73	0.663	894,470	164,124
State of Amazonas	2	79	0.674	4,207,714	1,559,169
State of Pará	6	68	0.646	8,602,865	1,245,871
State of Roraima	2	76	0.707	631,181	223,645
Sweden	25	88	0.937	10,109,031	410,340
Switzerland	219	74	0.946	8,664,406	39,516
Tokyo, Japan	6,158	100	0.941	13,491,000	2,191
United Kingdom	279	83	0.920	67,886,011	241,930
Not Controlled areas					
Argentina	17	93	0.83	45,259,525	2,736,690
Australia	3	86	0.938	25,545,026	7,682,300
Belarus	47	79	0.817	9,448,832	202,910
city of Belo Horizonte, MG, Brazil	7167	100	0.81	2,521,564	331
Bosnia and Herzegovina	64	52	0.769	3,277,541	51,000
Bulgaria	64	76	0.861	6,940,012	108,560
	26	95	0.047	10 1 41 470	742 522
	20	83	0.847	19,141,470	/43,532
Colombia	46	80	0.761	50,965,881	1,109,500
Costa Rica	100	80	0.794	5,101,269	51,060
Croatia	73	58	0.837	4,101,200	55,960
Brasília, FD Brazil	444.66	96.62	0.824	3,055,149	5,761
Israel	400	93	0.906	9,197,590	21,640
Lebanon	667	78	0.73	6,820,558	10,230
Libya	4	78	0.708	6,885,460	1,759,540
Luxembourg	242	88	0.909	627,509	2,590
Moldova	105	43	0.711	4,032,473	32,850
Oman	16	87	0.834	5,125,566	309,500
Peru	26	79	0.759	33,041,424	1,280,000
Poland	124	60	0.872	37,840,045	306,230
city of Porto Alegre, RS, Brazil	2837.53	100	0.805	1,488,252	495

Qatar	248	96	0.848	2,807,805	11,610
Romania	84	55	0.816	19,217,049	230,170
city of São Paulo, SP, Brazil	7398.26	100	0.805	12,325,232	1,521
Saudi Arabia	16	84	0.857	34,895,566	2,149,690
Serbia	100	56	0.799	8,731,751	87,460
state of Alagoas	112.23	73.64	0.631	3,351,543	27,843
state of Amapá	4.69	89.81	0.708	861,773	142,471
state of Bahia	24.82	72.07	0.66	14,930,634	564,760
state of Ceará	56.76	75.09	0.682	9,187,103	148,894
state of Espírito Santo	76.25	85.29	0.74	4,064,052	46,074
state of Goiás	17.65	90.29	0.735	7,113,540	340,203
state of Maranhão	19.81	63.07	0.639	7,114,598	329,642
state of Mato Grosso	3.36	81.9	0.725	3,526,220	903,207
state of Mato Grosso do Sul	6.86	85.64	0.729	2,809,394	357,146
state of Minas Gerais	33.41	83.38	0.731	21,292,666	586,521
state of Paraíba	66.7	75.37	0.658	4,039,277	56,467
state of Paraná	52.4	85.31	0.749	11,516,840	199,299
state of Pernambuco	89.63	80.15	0.673	9,616,621	98,068
state of Piauí	12.4	65.77	0.646	3,281,480	251,757
state of Rio de Janeiro	365.23	96.71	0.761	17,264,943	43,750
state of Rio Grande do Norte	59.99	77.82	0.684	3,534,165	52,810
state of Rio Grande do Sul	37.96	85.1	0.746	11,422,973	281,707
state of Rondônia	6.58	73.22	0.69	1,796,460	237,765
state of Santa Catarina	65.27	83.99	0.774	7,252,502	95,731
state of São Paulo	166.23	95.88	0.783	46,289,333	248,219
state of Sergipe	94.35	73.51	0.665	2,318,822	21,925
state of Tocantins	4.98	78.81	0.699	1,590,248	277,467
Turkey	110	76	0.807	84,477,895	769,630
Ukraine	75	69	0.75	43,691,576	579,320
United Arab Emirates	118	86	0.866	9,908,607	83,600
United States of America	36	82	0.92	331,303,997	9,834,000

Table 2. Comparisons using the 4-point criteria. Comparability was considered if at least 3 out of 4 of the following conditions were similar: a) population density, b) percentage of the urban population, c) Human Development Index and d) total area of the region. Similarity was considered adequate when a variation in conditions a), b) and c) was within 30%, while, for condition d), a variation of 50% was considered adequate (Further details are in <u>Data sharing - 4</u> point criteria).

Region/Country (controlled)	Region/Country (not controlled)	Comparability ^a	p-value ^b
Austria	Serbia	4	0.055
Bahrain	city of Porto Alegre, RS, Brazil	4	0.911
Belgium	Israel	4	0.114
Canada	Australia	4	0.965
Czech Republic	State of Alagoas	3	0.3501
Denmark	Turkey	3	0.911
Finland	State of Goiás	4	0.268
city of Fortaleza, CE, Brazil	city of Belo Horizonte, MG, Brazil	4	0.301
France	Ukraine	3	0.623
Germany	Qatar	3	0.892
Greece	Bulgaria	4	0.275
Ireland	Croatia	4	0.711
Italy	State of São Paulo	3	0.928
Japan	Israel	3	0.102
Kuwait	Luxembourg	3	0.060
city of Manaus, AM, Brazil	Qatar	3	0.524
Macedonia	Romania	3	0.6169
Netherlands	city of Brasília, Brazil	3	0.459
New York City	city of São Paulo, SP, Brazil	3	0.645
Norway	Saudi Arabia	3	0.379
Portugal	United Arab Emirates	3	0.248
Russia	United States of America	3	0.557
Slovenia	Poland	4	0.875
South Korea	Lebanon	3	0.645
Spain	State of Minas Gerais	3	0.853

State of Acre	State of Amapá	4	0.803
State of Amazonas	Colombia	3	0.638
State of Pará	Libya	3	0.681
State of Roraima	State of Rondônia	3	0.042
Sweden	State of Bahia	4	0.131
Switzerland	State of Espírito Santo	3	0.745
Tokyo, Japan	city of São Paulo, SP, Brazil	4	0.731
United Kingdom	State of Rio Grande do Sul	3	0.084

^a From four-point criteria, how many criteria were present ^b Linear regression 588

590 Figure caption

- 592 Figure 1. Flow chart of the data setup (Further details are in <u>Supplemental Material Flow</u>
- 593 <u>chart</u>).
- 594
- 595 Figure 2. Heat map comparing different regions with COVID-19. The bar below represents p-
- 596 values for the linear regression.
- 597

598 Figure 1.





604 SUPPLEMENTAL MATERIAL

605

Approach for analyzing the time series data 606

- Time series on COVID-19 mortality (deaths/millions) display a non-stationary pattern. The daily 607
- 608 data present a very distinct seasonal behavior on the weekends, with valleys on Saturdays and Sundays followed by peaks on Mondays (Figure S1).
- 609



- 612 Figure S1. Characteristics of the time series data on new daily deaths/million in the city of São
- 613 Paulo over 187 days. Note the non-stationary time series pattern.



Figure S2. Data aggregation of the number of deaths/million in the city of São Paulo and in Argentina over several epidemiological weeks, compared to the percentage of staying at home. Data aggregation by epidemiological week is a plausible alternative. In this way, artificial seasonality, imposed by work scheduled during weekends and the effect of governmental control over social interaction, in a regression framework, are mitigated. The drawback is that the sample size is significantly reduced from 187 days (Figure S1) to 26 epidemiological weeks.

651

652 Definition of areas with and without controlled cases of COVID-19

Regions were classified as controlled for cases of COVID-19 if they present at least 2 out of the 3 following conditions: a) type of transmission classified as "clusters of cases", b) a downward curve of newly reported deaths in the last 7 days, and c) a flat curve in the cumulative total number of deaths in the last 7 days (variation of 5%) according to the World Health Organization (WHO Coronavirus Disease (COVID-19) Dashboard). An example is shown in Figure S3.



659

660 Figure S3. Example of areas with and without control of COVID-19

661

Table S3). Comparison between 184 countries and regions displaying a significant association 662 663 between the variation of number of deaths/million and the variation of the percentage of staying at home, after False Discovery Rate (FDR B-H) analysis. Intercept and coef isolation are $\beta 0$ and 664 β 1 from the linear regression formula; Shapiro is the test for normality; White is the test for 665 666 heteroskedasticity; LM is the Lagrange Multiplier test for autocorrelation, Reset is the Ramsey's 667 RESET test for functional specification (all should have a p-value ≥ 0.05 for a valid comparison), 668 Coint= the p-value of the Phillips-Perron test applied to the residual of the regression (for a valid 669 comparison, p-value<0.05)

670 **Table S4)** Comparison between 63 countries and regions displaying a significant association 671 between the variation of number of deaths/million and the variation of the percentage of staying 672 at home, after False Discovery Rate analysis and after residual analysis. Intercept and 673 coef isolation are $\beta 0$ and $\beta 1$ from the linear regression formula; Shapiro is the test for 674 normality; White is the test for heteroskedasticity; LM is the Lagrange Multiplier test for 675 autocorrelation, Reset is the Ramsey's RESET test for functional specification (all should have a p-value ≥ 0.05 for a valid comparison), Coint= the p-value of the Phillips-Perron test applied to 676 677 the residual of the regression (for a valid comparison, p-value<0.05).