Exponential phase of COVID-19 expansion is driven by airport connections

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The pandemic state of COVID-19 caused by the SARS CoV-2 put the world in quarantine, led to hundreds of thousands of deaths and is causing an unprecedented economic crisis. However, COVID-19 is spreading in different rates at different countries. Here, we tested the effect of three classes of predictors, i.e., socioeconomic, climatic and transport, on the rate of daily increase of COVID-19. We found that global connections, represented by countries' importance in the global air transportation network, is the main explanation for the growth rate of COVID-19 in different countries. Climate, geographic distance and socioeconomics had a milder effect in this big picture analysis. Geographic distance and climate were significant barriers in the past but were surpassed by the human engine that allowed us to colonize most of our planet land surface. Our results indicate that the current claims that the growth rate of COVID-19 may be lower in warmer and humid tropical countries should be taken very carefully, at risk to disturb well-established and effective policy of social isolation that may help to avoid higher mortality rates due to the collapse of national health systems.

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24 Abstract

The pandemic state of COVID-19 caused by the SARS CoV-2 put the world in 25 quarantine, led to hundreds of thousands of deaths and is causing an unprecedented economic 26 crisis. However, COVID-19 is spreading in different rates at different countries. Here, we tested 27 28 the effect of three classes of predictors, i.e., socioeconomic, climatic and transport, on the rate of daily increase of COVID-19. We found that global connections, represented by countries' 29 importance in the global air transportation network, is the main explanation for the growth rate of 30 31 COVID-19 in different countries. Climate, geographic distance and socioeconomics had a milder effect in this big picture analysis. Geographic distance and climate were significant barriers in 32 the past but were surpassed by the human engine that allowed us to colonize most of our planet 33 land surface. Our results indicate that the current claims that the growth rate of COVID-19 may 34 be lower in warmer and humid tropical countries should be taken very carefully, at risk to disturb 35 well-established and effective policy of social isolation that may help to avoid higher mortality 36 rates due to the collapse of national health systems. 37

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40 Introduction

With the worldwide spread of the novel Coronavirus Disease 2019 (COVID-19), caused 41 by the SARS-CoV-2 virus, we are experiencing a declared pandemic. One of the largest 42 preoccupations about this new virus regards, its notable ability to spread given the absence of any 43 effective treatment, vaccine and immunity in human populations. Epidemiologists quantify the 44 ability of infectious agents to spread by estimating the basic reproduction number ($R\theta$) statistic 45 (Delamater et al., 2019), which measures the average number of people each contagious person 46 infects. According to the World Health Organization (2020), the new coronavirus is transmitting 47 at an R0 around 1.4-2.5, which is greater than seasonal influenza viruses that spread every year 48 around the planet (median R0 of 1.28, Biggerstaff et al., 2014). To anticipate the timing and 49 50 magnitude of public interventions and mitigate the adverse consequences on public health and economy, understanding the factors associated with the survival and transmission of SARS-CoV-51 2 is urgent. 52

53 Because previous experimental (Lowen et al., 2007), epidemiological (Shaman et al., 2010, Barreca & Shimshack 2012) and modeling (Zuk et al., 2009) studies show the critical role 54 of temperature and humidity on the survival and transmission of viruses, recent studies are 55 testing the effect of environmental variables on SARS-CoV-2 (Wang et al., 2020, Sajadi et al., 56 2020) and forecasting monthly scenarios of the spread of the new virus based on climate 57 suitability (Araújo & Naimi 2020, but see Chipperfield et al., 2020). Although temperature and 58 humidity are known to affect the spread and survival of other coronaviruses (i.e., SARS-CoV 59 and MERS-CoV, Tan et al., 2005, Chan et al., 2011, Doremalen et al., 2013, Gaunt et al., 2010) 60 61 using the current occurrences of SARS-CoV-2 cases to build correlative climatic suitability

62 models without taking into consideration connectivity among different locations and
63 socioeconomic conditions might be inadequate.

Many factors might influence the distribution of diseases at different spatial scales. 64 Climate might affect the spread of viruses given its known effect on biological processes that 65 influences many biogeographical patterns, including the distribution of diseases and human 66 67 behavior (e.g., Murray et al., 2018). Geographic distance represents the geographical space where the disease spread following the distribution of hosts and has also been found to explain 68 biogeographic patterns (Pulin 2003, Nekola & White 2004, Warren 2014). Socioeconomic 69 characteristics of countries could be viewed as a proxy for the ability to identify and treat 70 infected people and for the governability necessary to make fast political decision and avoid the 71 spread of new diseases. Finally, the global transportation network might surpass other factors as 72 it can reduce the relative importance of geographic distance and facilitate the spread of viruses 73 and their vectors (Brockmann & Helbing 2013, Pybus et al., 2015). According to the 74 International Air Transport Association (2019) more than 4 billion passengers traveled abroad in 75 2018. This amount of travelers reaching most of our planet's surface represents a human niche 76 construction (i.e. global transportation network; Boivin et al., 2016) that facilitates the global 77 78 spread of viruses and vectors (Brockmann & Helbing 2013) in the same way it facilitated the spread of invasive species and domesticated animals over modern human history (Boiving et al., 79 80 2016).

The spread of SARS-CoV-2 from central China to other locations might be strongly associated with inter-country connections, which might largely surpass the effect of climate suitability. Thus, at this point of the pandemic, there is still a distributional disequilibrium that can generate very biased predictions based on climatic correlative modeling (De Marco et al.,

2008). Thus, here we used an alternative macroecological approach (Burnside et al., 2012), based
on the geographical patterns of exponential growth rates of the disease at country level, to
investigate variations on the growth rates of SARS-CoV-2. We studied the effect of
environment, socioeconomic and global transportation controlling for spatial autocorrelation that
could bias model significance. By analyzing these factors, we show that the exponential growth
of COVID-19 at global scale is explained mainly by country's importance in global
transportation network (i.e., air transportation).

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93 Material & Methods

We collected the number of people infected by the COVID-19 per day from the John
Hopkins (Dong et al., 2020) and European Centre for Disease Prevention and Control (ECDC,
2020). This data is available for 204 countries, for which 65 had more than 100 cases recorded
and for which time series had at least 30 days after the 100th case. We also performed the
analysis considering countries with more than 50 cases, but it did not qualitatively change our
results. Thus, we only show the results for countries with more than 100 cases.

In our analysis, we only used the exponential portion of the time series data (i.e. number of people infected per day) and excluded days after stabilization or decrease in total number of cases. We empirically modelled each time series using an exponential growth model for each country and calculated both the intrinsic growth rate (r) and the regression coefficient of the log growth series to be used as the response variable in our models. Because both were highly correlated (Person's r = 0.97), we used only the regression coefficient to represent the growth rate of COVID-19 in our study.

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107	To investigate potential correlates of the virus growth rate, we downloaded climatic and
108	socioeconomic data of each country. We used climatic data represented by monthly average
109	minimum and maximum temperature (°C) and total precipitation (mm) retrieved from the
110	WorldClim database (https://www.worldclim.org) (Fick & Hijmans 2017). We used monthly
111	available data for the most recent year available in WorldClim. We extracted climatic data from
112	the months of January, February, March, and December to represent the climatic conditions of
113	the winter season in the Northern Hemisphere and the summer season in the Southern
114	Hemisphere. From these data, we computed the mean value of climatic variables across each
115	country. Finally, minimum and maximum temperatures were combined to estimate monthly
116	mean temperature for December, January, February, and March, which was used in the model
117	along with total precipitation for the same months. However, using different combinations of
118	these variables (i.e., using means of minimum or maximum temperatures, as well as minimum or
118 119	these variables (i.e., using means of minimum or maximum temperatures, as well as minimum or maximum for each month) did not qualitatively affect our results.
118 119 120	these variables (i.e., using means of minimum or maximum temperatures, as well as minimum or maximum for each month) did not qualitatively affect our results. We extracted socioeconomic data for each country. Human Development Index (HDI)
118119120121	these variables (i.e., using means of minimum or maximum temperatures, as well as minimum or maximum for each month) did not qualitatively affect our results. We extracted socioeconomic data for each country. Human Development Index (HDI) rank, mean number of school years in 2015, gross national income (GNI) per capita in 2011,
 118 119 120 121 122 	these variables (i.e., using means of minimum or maximum temperatures, as well as minimum or maximum for each month) did not qualitatively affect our results. We extracted socioeconomic data for each country. Human Development Index (HDI) rank, mean number of school years in 2015, gross national income (GNI) per capita in 2011, population size in 2015 and average annual population growth rate between 2010-2015 were
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 118 119 120 121 122 123 124 125 	these variables (i.e., using means of minimum or maximum temperatures, as well as minimum or maximum for each month) did not qualitatively affect our results. We extracted socioeconomic data for each country. Human Development Index (HDI) rank, mean number of school years in 2015, gross national income (GNI) per capita in 2011, population size in 2015 and average annual population growth rate between 2010-2015 were used in our study and downloaded from the United Nations database (http://hdr.undp.org/en/data). We also obtained a mean value of health investment in each country by averaging the annual health investments between 2005-2015 obtained from the World
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 118 119 120 121 122 123 124 125 126 127 	these variables (i.e., using means of minimum or maximum temperatures, as well as minimum or maximum for each month) did not qualitatively affect our results. We extracted socioeconomic data for each country. Human Development Index (HDI) rank, mean number of school years in 2015, gross national income (GNI) per capita in 2011, population size in 2015 and average annual population growth rate between 2010-2015 were used in our study and downloaded from the United Nations database (http://hdr.undp.org/en/data). We also obtained a mean value of health investment in each country by averaging the annual health investments between 2005-2015 obtained from the World Health Organization database (http://apps.who.int/gho/data/node.home). Due to the strong collinearity among some of these predictors, HDI rank and mean number of school years were

Finally, we also downloaded air transportation data from the OpenFlights (2014) database 129 regarding the airports of the world, which informs where each airport is located including 130 country location (7,834 airports), and whether there is a direct flight connecting the airports 131 (67,663 connections). We checked the Openfligths database to make the airports and connections 132 compatible by including missing or fixing airport codes and removing six unidentified airport 133 134 connections resulting in a total of 7,834 airports and 67,657 connections. We used this information to build an air transportation network that reflects the existence of a direct flight 135 between the airports while considering the direction of the flight. Thus, the airport network is a 136 unipartite, binary, and directed graph where airports are nodes and flights are links (Fig 1, Fig 137 S1). In the following step, we collapsed the airports' network into a country-level network using 138 the country information to merge all the airports located in a country in a single node (e.g., 139 United States had 613 airports that were merged in a single vertex representing the country). The 140 country-level network (Fig 1, Fig S1) is a directed weighted graph where the links are the 141 142 number of connections between 226 countries which is collapsed for the 65 countries that had more than 100 cases and for which time series data had at least 30 days after the 100th case. 143 Afterward, we measured the countries centrality in the network using the Eigenvector Centrality 144 145 (Bonacich, 1987), hereafter centrality, that weights the importance of a country in the network considering the number of connections with other countries and how well connected these 146 147 countries are to other countries – indirect connections. All networks analyses were generated 148 using package igraph (Csardi & Nepusz, 2006).

We evaluated the relationship between the predictors (climatic, socioeconomic and transport data) and our growth rate parameter using a standard multiple regression (OLS) after taking into consideration the distribution of the original predictors as well as the normality of

model residuals. Moreover, OLS residuals were inspected to evaluate the existence of spatial
autocorrelation that could upward bias the significance of predictor variables on the model using
Moran's L correlograms (Legendre & Legendre 2013). Prior to the analysis, we applied
logarithmic (mean precipitation, total population size, and network centrality) and square root
(mean health investments) transformations to the data to approximate a normal distribution.

158 Results

The models used to estimate COVID-19 growth rate on different countries showed an average R^2 of 0.91 (SD = 0.04), varying from 0.78 to 0.99, indicating an overall excellent performance on estimating growth rates. The geographical patterns in the growth rates of COVID-19 cases do not show a clear trend, at least in terms of latitudinal variation, that would suggest a climatic effect at macroecological scale (Fig. 2A).

We build one model including only climate and socioeconomic variables, which 164 explained only 14% of the variation on growth rates. This model did not have spatial 165 autocorrelation in the residuals. When we added country centrality (i.e. country importance in 166 global transportation network) as a predictor, the R² increased to 48.6%. In this model, annual 167 population growth and precipitation had positive and significant effects (Table 1, P = 0.036, P 168 =0.041, Fig 2), while health investments had a negative and significant effect on growth rate 169 (Table 1, P=0.035, Fig 2). Here, exponential growth rates increased *strongly* in response to 170 countries importance in the transportation network which has more than two times the effect size 171 of any significant variable (Table 1). However, it is also important to note that growth rates of 172 173 COVID-19 weakly increases with increases of annual population growth and precipitation, and

- decreases with higher investments in health (Table 1). Statistical coefficients were not upwardbiased by spatial autocorrelation.
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177 Discussion

The pandemic state of SARS CoV-2 is killing hundreds of thousands of people, put the 178 world in guarantine and is causing an unprecedented economic crisis. The rates of increase of 179 new cases of COVID-19 is faster in some countries than others. To understand why growth rates 180 are different among countries we investigate the effect of climatic, socioeconomical and human 181 transportation variables that could have important roles on the exponential phase of COVID-19. 182 At global scale, temperature, population size and Gross National Income had no significant 183 184 effect on the exponential phase of COVID-19. However, annual population growth, health investments and precipitation show significant, but weak effects on growth rates. Countries' 185 importance in the global transportation network has a key role on the severity of COVID-19 186 pandemic in different countries as it is strongly associated with the growth rates of the disease 187 188 (Fig 2).

The centrality measure is widely used to discover distinguished nodes on many networks, 189 including epidemiological networks (e.g., Madotto & Liu 2016). Our findings reinforce the 190 importance of propagule pressure on disease dissemination (Tian et al., 2017, Chinazzi et al., 191 2020). Aerial transportation is an important predictor of COVID-19 dissemination in China 192 (Kraemer et al., 2020), in Brazil (Ribeiro et al., 2020), and in Mexico (Dátillo et al., 2020). It is 193 quite likely that further phases of COVID-19 spread, in terms of peak of infections and decrease 194 195 in mortality rates, will be better related to socioeconomics characteristics of each county and their political decisions when secondary transmissions were identified. We can already clearly 196

identify the effects of adopting strong social isolation policies in China (see Kraemer et al., 197 2020) and, on the opposite side of this spectrum, in European countries like Italy, Spain and 198 England (Enserink & Kupfershmidt 2020). Our analyses call attention to the case of Brazil, a 199 well-connected tropical country that presents one of the highest increase rates of COVID-19 in 200 the tropics in its exponential phase (Fig 2A). If decision makers take into consideration yet 201 202 unsupported claims that growth rates of COVID-19 in its exponential phase might be lower in warmer and humid countries, we might observe terrible scenarios unrolling in tropical countries, 203 especially in those with limited health care structure, such as Brazil. As our results also show, 204 those countries that invested less in health are also the ones with faster growth rates of covid-19 205 in its exponential phase (Fig 2, Table 1). 206

When discussing and modelling the effect of climate on SARS CoV-2 it is important to 207 remember that modern human society is a complex system composed of strongly connected 208 societies that are all susceptible to rare events. It is also critical to consider the negative 209 210 correlations between climate and local or regional socioeconomic conditions (i.e., inadequate sanitary conditions and poor nutritional conditions) that could easily counteract any potential 211 climatic effect at local scales, such as lower survival rates of viruses exposed to high humidity, 212 213 temperatures and high UV irradiation (Wang et al., 2020, Duan et al., 2003). Tropical regions will experience mild climate conditions in a couple of months. Thus, regardless of the influence 214 215 of local environmental conditions, tropical countries could still expect high contagious rates. In 216 addition, our results points to a positive effect of precipitation on growth rates, which is the contrary of what has been suggested by climate suitability models. Finally, climatic suitability 217 218 models might be ephemeral for very mathematized modelling fields of science such as 219 epidemiology and virology that developed over time very realistic models that enables the

possibility of learning with parameters of similar viruses (i.e. SARS) that can definitely help andinstruct decision makers to take actions before it is too late.

Here we showed that countries' importance in the global transportation network has a key 222 role on COVID-19 growth rates in its exponential phase. Our results reinforce board control 223 measures in international airports (Bitar et al., 2009, Nishiura & Kamiya 2011) during 224 225 exceedingly early stages of pandemics to prevent secondary transmissions that could lead to undesired scenarios of rapid synchronically spread of infectious diseases in different countries. 226 The rapid international spread of the severe acute respiratory syndrome (SARS) from 2002 to 227 2003 led to extensively assessing entry screening measures at international borders of some 228 countries (Bell et al., 2003, John et al., 2017). The 2019-2020 world spread of COVID-19 229 highlights that improvements and testing of board control measures (i.e. screening associated 230 with fast testing and quarantine of infected travellers) might be a cheap solution for humanity in 231 comparison to health systems breakdowns and unprecedented global economic crises that the 232 233 spread of infectious disease can cause. However, it is important to note that board control of potentially infected travellers and how to effectively identify them is still a hotly debated topic in 234 epidemiology and there is still no consensus on accurate methodologies for its application (Sun 235 236 et al., 2017).

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238 Conclusions

Here, we show that countries' importance in the global transportation network has a key role on the severity of COVID-19 pandemic in different countries as it is strongly associated with the growth rates of the disease (Fig 2). We do not expect that our results using a macroecological approach at a global scale would have a definitive effect on decision-making in

243	terms of public health in any particular country, province, or city. However, we expect that our					
244	analyses show that current claims that growth of COVID-19 pandemics may be lower in					
245	developing tropical countries should be taken very carefully, at risk to disturb well-established					
246	and effective policy of social isolation that may help to avoid higher mortality rates due to					
247	collapse in national health systems.					
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Figure 1

Air transportation network

Fig 1. Air transportation network among 65 countries that had more than 100 cases and for which time series data had at least 30 days after the 100th case. Different colours represent modules of countries that are more connected to each other. Different sizes of each node represent the growth rate of COVID-19 estimated for each country (See results Fig 2).



Figure 2

Geographical patterns of response and significant predictor variables

Fig 2. Geographical patterns of growth rate of covid-19 in the exponential phase (**A**), the Eigenvector Centrality that represents countries' importance in global transportation network (**B**), Annual population growth (**C**), health investments (**D**) and mean precipitation (**E**). The relationship between growth rate and the log transformed eigenvector centrality is showed in **F**. **G**, **H** and **I** are partial plots showing the relationship between the residuals of growth rates vs log transformed eigenvector centrality and annual population growth, health investments and mean precipitation.

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Table 1(on next page)

Model Statistics

Table 1. Model statistics for all variables used in the study.

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	Standardized				
	Estimate	Estimate	Std Error	t value	P-value
Intercept		0.149	0.026	3.547	< 0.001
Eigenvector Centrality	0.758	0.016	0.002	6.124	< 0.001
Gross National Income	0.16	0.000	0.000	1.491	0.141
Population Size	-0.096	-0.004	0.004	-0.953	0.344
Annual population growth	0.306	0.008	0.003	2.139	0.036
Heath investment	-0.287	-0.0004	0.000	-2.155	0.035
Mean Temperature	-0.127	-0.0003	0.000	-0.908	0.367
Mean Precipitation	0.253	0.007	0.003	2.091	0.041