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Can commercial trade represent the main indicator of the COVID-19 diffusion due to human-to-human interactions? A comparative analysis between Italy, France, and Spain

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ABSTRACT

The main goal of this study is to analyze the relation between commercial trade and pandemic severity in society, in order to support new hypotheses which can explain transmission dynamics of COVID-19, as well as promote policy responses to cope with future epidemics similar to COVID-19. This study considers the role of trade in the dynamics of pandemic diffusion, within and between countries, which has not been investigated yet in this emerging field of research. We focus on three large countries in Europe: Italy, France, and Spain. The analysis is performed at regional level (involving in total 52 European regions). Results suggest that the association between trade and pandemic severity seems to be supported by empirical evidence, making it possible to introduce new hypotheses for explaining transmission dynamics of COVID-19 within and between countries. In particular, international trade data is supposed to be used as a comprehensive indicator accounting for population density, economic dynamism, and human mobility. The statistical analyses, also in a multivariate context, strongly support this hypothesis and suggest that crisis management has to focus in the very first place on infections occurring outside the national boundaries, in order to cope with pandemic threat of new waves of COVID-19 and future similar epidemics/pandemics.

1. Introduction

Understanding the determinants that contributed to the initial diffusion of the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), the novel virus that causes coronavirus disease 2019 (COVID-19), is critical for different reasons, such as to provide suitable scientific responses to the still-controversial proposed mechanism of airborne virus transmission and to support appropriate policy responses to cope with this environmental threat to the health of the world's population and in general to our socioeconomic systems (Coccia, 2020, 2021). Indeed, even though literature has already provided evidence that the aerosol generated by infected people can contribute to the indoor spread of SARS-CoV-2, there is some uncertainty concerning outdoor airborne transmission, also due to the possibility of bioaerosol travelling for several meters (Bontempi, 2020; Bontempi et al., 2020).

In this context, several studies postulated a direct correlation between air pollution and the virus spread (defined as environment-to-human pollution or air pollution to human transmission by Coccia, 2020), suggesting that mechanisms other than human-to-human transmission have an active role in the COVID-19 diffusion (Chirizzi et al., 2021; Coccia, 2021; Copat et al., 2020). Other studies (Wang et al., 2020; Bontempi, 2020b) recognized the fundamental role of the human-to-human interactions, supported by an increased international exchange in the COVID-19 infection global spread, that happened at an impressive and unexpected rate (Anand et al., 2021). For example, human mobility was recognized to be the source of the early epidemic growth rate in China (Kraemer et al., 2020). Menkir et al. (2021) argued that predictions of international outbreaks were mainly based on imported cases from Wuhan (China), potentially missing imports from other cities. The model used by these scholars suggests that some COVID-19 cases were imported to African destinations and 90% of imported cases arrived between the 17th of January and the 7th of February 2020, before the first case detections. In short, the dynamic role of source locations can support surveillance and response efforts.

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The spread of COVID-19 has been very difficult to study partly because of lockdown periods that have interrupted and changed its dynamics (Cocker et al., 2020; De Angelis et al., 2021). Coccia (2021) explains how COVID-19 was transmitted so rapidly in northern Italy, analyzing the underlying relationships between infected people and environmental, demographic, and geographical factors that influenced its spread. In particular, cities with little wind, high humidity and frequently high levels of air pollution — exceeding safe levels of ozone or particulate matter — seemed to have higher numbers of COVID-19 infected individuals and deaths (cf. Coccia, 2020). Ahmed et al. (2020) focus on different demographic, socioeconomic and lifestyle health factors in countries, to explain the variety of COVID-19 effects in societies. The risk of vulnerability of cities to future epidemics and pandemics similar to COVID-19 may be caused by some factors, such as (Coccia, 2020) high air pollution, little wind, high density of population and social interaction, and previous incidence of lung and bronchi cancer.

However, a suitable way to consider the human-to-human interactions due to people mobility (accounting, for example, for exchanges among different countries) is still not considered in the modeling of the different aspects of SARS-CoV-2 diffusion. In particular, detailed analyses of possible global commercial trade scenarios due to the pandemic have been proposed (Guan et al., 2020) but an inverse inspection, investigating the role of commercial trade in the dynamics of pandemic diffusion, within and between countries, being it a comprehensive indicator of population density, economic dynamism and human mobility, has not been explored yet in this emerging field of research. The analysis of past epidemic diffusions shows that viruses diffused faster during economic booms (Adda, 2016). This can be attributed to the increase of people travelling, with consequent increase of interpersonal contacts. Then it becomes possible to use commercial trade as an indicator of people mobility.

In addition to this, over the last couple of centuries, a positive economic growth took place almost all around the world. This process was coupled with a corresponding increase in global trade, with an evolution of the economy toward a global dimension. Today, about one fourth of total global production is exported (The Economy ebook, 2017).

As shown in supporting information S1 (see the Supporting), a strong correlation between economic growth and commercial trade is established: countries with higher rates of GDP growth also tend to have higher rates of growth in trade as a share of output. This allows to suppose that international trade can be considered also an indicator of GDP.

Bontempi (2020b) suggests that a more exhaustive and comprehensive approach to the explanation of transmission dynamics of the COVID-19 can be achieved by considering different parameters that may be not strictly related to sanitary implications. In these topics, there is a possibility to apply a trans-disciplinary approach to analyze such a complex system, which, for its nature, encompasses many factors.

The main goal of this study is to analyze the relation between commercial trade and pandemic severity in society, in order to support new hypotheses which can explain the transmission dynamics of COVID-19, as well as promote policy responses to cope with future epidemics similar to COVID-19.

2. Study design

2.1. Research setting and sample

This study focuses on all the regions of three large countries in Europe: Italy, Spain, and France (totally 52 regions, listed in the Supporting). These three countries have a similar socioeconomic background for appropriate comparative analyses. In particular, considering that these countries have applied similar lockdown policies, the evolution of the local (in all the countries' regions) transmission can be investigated comparing the available data of their international trade exchanges, just before the pandemic's outbreak. In particular, this study performs a comparative analysis, using data at regional level, in order to carry out appropriate comparisons of the relation between possible determinants and effects of COVID-19 in society.

2.2. Measures

To account for the SARS-CoV-2 spread differences that can be found in different geographical areas (also of the same country), it is necessary to choose first a suitable indicator. It must be indicative of human-to-human interactions, given the basic recognized mechanism of initial virus diffusion (Ferretti et al., 2020). Then, it must be correlated with the human mobility factor, since the virus requires high levels of humans' interactions. This measure can be validated by considering different countries. Notably, commercial relationships, related to the globalization of companies' value chains and markets, are based on persistent mobility patterns across different countries, and, differently from vacation travels, they often need close social interaction among individuals (Bontempi et al., 2020). Hence, they can be considered as the synthetic expression of social relationships, which are created by economic activities, requiring human contacts due to business collaborations. In fact, globalization has been accompanied by a growing share of international trade. The increase of imports of resources is also indicative of increasing living standards (Rodrigue, 2020; Oster, 2012) and GDP (see supporting information S1). In addition, recent literature has already proposed a correlation between COVID-19 case incidence and GDP (Aycock, 2021) in several countries, showing that economic development facilitates infectious disease spread, due to advanced transportation system, better domestic and international travel for businesses, and more group activities. In the present study, the indicator selected to be representative of living standard, economic dynamics, and globalization level of a region is the sum of the total amount of import and export international trade (see Fig. 1). These data were collected considering the last reported available international trade data (2019) for each region of Italy, Spain, and France (in total 52).

Concerning the spread of contagion, the reported epidemiological data are generally considered as an approximation, since they may be different in the selected regions. Indeed, the documented and detected infections depend on testing capability (less testing causes a lower reporting of asymptomatic positives, thus leading to under-estimation; cf., Bertuzzo et al., 2020). Also, fatality rates can depend on several factors, such as the criteria used for its evaluation (Giordano et al., 2020) and the stress suffered by healthcare facilities (Bertuzzo et al., 2020). On the contrary, the number of hospitalized patients in Intensive Care Units (ICU) can be assumed to be a strong indicator of pandemic severity,

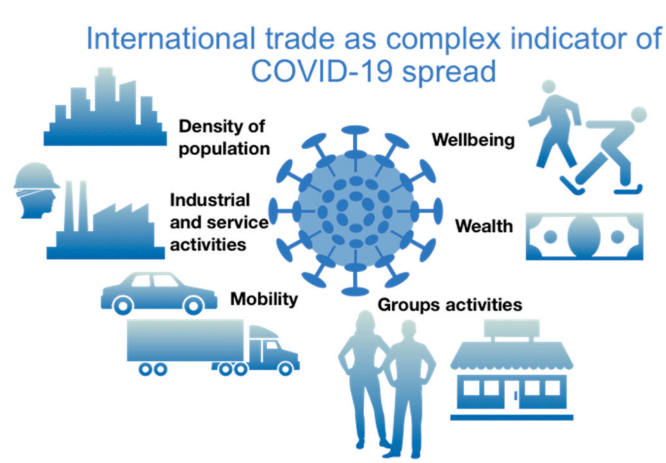

Fig. 1. Import-export trade data is considered a complex indicator including manifold drivers of human-to-human interactions, responsible of COVID-19 transmission dynamics in geo-economic areas.

being it a suitable parameter also for comparisons between different regions in different countries. Considering the number of hospitalized patients in ICU at the peaks of the contagion makes all the data comparable, also because they do not depend on the local temporal difference of regional virus diffusion.

To systematize, the measures applied in this study, using data at regional level in Italy, France, and Spain (the 52 total regions studied are listed in the Supporting), are the following ones:

- Gross Domestic Product per capita (GDP PC) for all the regions of Italy, France, and Spain (2019 per Italy, 2016 per France, 2018 per Spain; these data are the latest available at regional level). The data were downloaded by the national statistics websites of the three countries considered (Datacomex, 2021) (Lekiosque, 2021) (Istat, 2021).
- 2019 Import and export, total value in Euros (€), for all the regions of Italy, France, and Spain. The data were downloaded by national statistics websites of the three countries considered (Datacomex, 2021) (Lekiosque, 2021) (Istat, 2021).
- ICUs during the 1st peak in April 2020, 2nd peak in November 2020, 3rd peak in January 2021 or thereabouts, for all the regions of Italy, France, and Spain. The data were downloaded by national websites devoted to pandemic data publication (RTVE, 2021) (Cascoronavirus, 2021) (Protezione Civile, 2021).
- Hospitalization of people (included ICUs) during the 1st peak in April 2020, 2nd peak in November 2020, 3rd peak in January 2021 or thereabouts, for all the regions of Italy, France, and Spain. The data were downloaded by national websites devoted to pandemic data publication (RTVE, 2021) (Cascoronavirus, 2021) (Protezione Civile, 2021).
- Confirmed cases during the 1st peak in April 2020, 2nd peak in November 2020, 3rd peak in January 2021 or thereabouts for all the regions of Italy, France, and Spain. The data were downloaded by national websites devoted to pandemic data publication (RTVE, 2021) (Cascoronavirus, 2021) (Protezione Civile, 2021).
- Deaths during the 1st peak in April 2020, 2nd peak in November 2020, 3rd peak in January 2021 or thereabouts for all the regions of Italy, France, and Spain. The data were downloaded by national websites devoted to pandemic data publication (RTVE, 2021) (Cascoronavirus, 2021) (Protezione Civile, 2021).
- Fatality rate (+14 days from ICUs admission) during the 1st peak in April 2020, 2nd peak in November 2020, 3rd peak in January 2021 or thereabouts for all the regions of Italy, France, and Spain. The data were downloaded by national websites devoted to pandemic data publication (RTVE, 2021) (Cascoronavirus, 2021) (Protezione Civile, 2021). The lag of about 14 days from initial symptoms to deaths is based on empirical evidence of some studies (Zhang et al., 2020).
- Population density, expressed as the number of people per Km^2 of land area for all the regions of Italy, France, and Spain. The data were downloaded by national websites devoted to population statistic data publication (INE, 2021) (INED, 2021) (Istat, 2021).

2.3. Data analysis procedure

2.3.1. Statistical analyses per country

Comparative analysis is performed investigating the relationships between the studied variables with descriptive statistics (arithmetic mean and standard deviation) within countries, using regional data, and with non-parametric correlation Kendall's tau b considering the small sample within countries with regional data (Supporting for regions studied here). Kendall's tau-b (τ_b) correlation coefficient (Kendall's tau-b) is a nonparametric measure of the strength and direction of association that exists between two variables, alternative to the Pearson's correlation when data has failed one or more of the assumptions of this test.

These two assumptions of Kendall's tau-b are:

1. Variables are measured on a continuous scale.
2. Kendall's tau-b determines whether there is a monotonic relationship between two variables.

To confirm these results, the Pearson correlation is used as well. Finally, to analyze the effects of the COVID-pandemic across regions, the number of hospitalized patients (log scale) in Intensive Care Units (ICU) at the peaks of the contagious curves in France, Italy, and Spain regions (data refer to 13th April for France* and Spain$^+$ and to 1st April for Italy°) is studied as a function of the sum of total amount of import and export international trade (data are reported in €, in log. Scale for each region).

2.3.2. Statistical analyses using regional aggregated data for the three countries under study

This statistical analysis considers all provinces of three countries (Italy, France, and Spain) under study with N = 52 regions. Bivariate Pearson correlations were used to verify relationships between variables, with the degree of association determined by the coefficient of correlation. One-tailed tests of significance for correlation were computed to consider the associations between variables in the most recent year available in the databases.

The correlation is also performed using as control variables the density of population (inhabitants per km^2) and GDP PC, to verify if the association between variables is consistent, removing the factors of other variables.

Multivariate analysis is performed with multiple regression with the following models, specified as follows:

$$\log yt = \alpha + \beta 1 \log x1,\ t-1 + \beta 2 \log x2,\ t-1 + \beta 3 \log x3,\ t-1 + \beta 4 \log \mathrm{INTER}x4,\ t-1 + u \quad [1]$$

where:

y = dependent variable (ICUs, Hospitalization, Confirmed cases) in April 2020, November 2020, and January 2021

x 1 = explanatory variables of total Import -Export

x 2 = explanatory variables of density of population per (inhabitants per km^2)

x 3 = explanatory variables of Gross Domestic Product per capita

x 4 = explanatory variables of Interaction density of population × Gross Domestic Product per capita

α is a constant; βi = coefficient of regression i = 1, 2, 3, 4; t = time; u = error term.

Statistical analyses are performed with the Statistics Software SPSS® version 26.

3. Results and discussion

3.1. Results for Italy, France and Spain

Table 1 shows the descriptive statistic data for all the countries considered, reported as mean values, at the regional basis. Then, Table 1 allows to have a global vision of the data for all the countries. It shows that the volume of export and import is high in Italy and very high in France. The highest density of population in Italy is 182.10 inhabitants per km^2, whereas in France is about 173, and in Spain 170. France and Spain have total confirmed cases, hospitalization and ICU admissions during the first, second and third peaks of COVID-19 pandemic always higher than Italy. The ratio between total cases and population confirms roughly these results. The total hospitalization divided by total cases in the first peak is higher in France and Spain, while in the second peak it's higher in Italy and in the third peak higher in Spain. Finally, fatality rate shows that Italy tends to have higher values in all of the three peaks.

Table 2 presents Kendall's tau-b correlation coefficient, τb, which shows the association between the total value of import - export and confirmed cases in the first, second and third peaks ($\geq$0.75, p-value < .01). The magnitude of the Kendall's tau-b correlation coefficient, τ_b,

Table 1
Descriptive statistics reporting the mean values for the considered countries (Italy, France, and Spain).

	Italy		France		Spain	
	Mean	Std. Error	Mean	Std. Error	Mean	Std. Error
GDP per capita (GDP PC)	30758.78	335799037.00	313787177.00	223590643.00	24651.37	1168.86
Import Export Total per million	43944.06	13747.32	81936.66	18257.43	31968.96	9542.49
Population density (inhabitants per km^2)	182.10	25.56	173.14	71.47	170.03[a]	47.47
Confirmed cases 1 peak	5528.70	2232.58	7544.31	2978.68	12961.68	4506.57
Total cases 1pk/population[a]100	.18		.15		.53	
Confirmed cases 2 peak	63617.60	17353.80	147884.92	34651.45	69938.53	19916.35
Total cases 2pk/population [a]100	2.11		2.96		2.82	
Confirmed cases 3 peak	125775.35	28971.70	240817.62	45514.83	142368.47	36493.40
Total cases 3pk/population [a]100	4.18		4.82		5.74	
Hospitalizations 1 peak	1621.90	664.28	2446.69	966.01	4639.53	1927.99
Total/total cases 1pk [a]100	29.34		32.43		35.79	
hospitalization 2 peak	1858.70	492.98	2494.85	584.58	1065.21	283.52
Total/total cases 2pk [a]100	2.92		1.69		1.53	
hospitalizations 3 peak	1153.20	237.79	2072.77	391.76	1617.16	428.44
Total/total cases 3pk [a]100	.92		0.86		1.14	
ICUs 1 peak	201.75	66.63	511.46	186.70	412.58	149.83
ICUs 2 peak	183.50	45.60	372.00	87.15	150.68	39.18
ICUs 3 peak	114.40	23.37	236.15	49.09	242.53	62.90
Deaths 1 peak	274.06	65.16	263.31	72.04	1494.11	503.27
Deaths 2 peak	182.97	65.01	202.89	103.80	247.21	73.38
Deaths 3 peak	131.02	55.09	91.07	76.05	133.93	56.07
Fatality 1 peak	14.20	1.19	14.77	0.94	10.45	0.97
Fatality 2 peak	3.93	0.31	1.74	0.18	3.03	0.28
Fatality 3 peak	3.43	0.23	1.67	0.10	2.34	0.20
Valid N (listwise)	20		13		19	

[a] Except Melilla and Ceuta that create distortions as outliers.

Table 2
Correlation Kendall's tau τ_b, using confirmed cases evaluated at national level, considering all regions of Italy, France, and Spain.

		Italy	N = 20				
		Import Export	GDP PC	Density of population	Confirmed cases 1 peak	Confirmed cases 2 peak	Confirmed cases 3 peak
Import Export	Correlation Coefficient	1	.295[a]	.599**	.747**	.779**	.853**
GDP PC	Correlation Coefficient	.295[a]	1	0.143	.400**	0.263	0.253
Density of population	Correlation Coefficient	.599**	0.143	1	.557**	.695**	.706**
		France	N = 13				
Import Export	Correlation Coefficient	1	0.256	.462[a]	.641**	.641**	.667**
GDP PC	Correlation Coefficient	0.256	1	.487[a]	0.103	0.205	0.231
Density of population	Correlation Coefficient	.462[a]	.487[a]	1	0.256	.359[a]	0.333
	Spain	N = 19					
Import Export	Correlation Coefficient	1	.298[a]	−0.041	.684**	.754**	.754**
GDP PC	Correlation Coefficient	.298[a]	1	0.006	.357[a]	.287[a]	0.24
Density of population	Correlation Coefficient	−0.041	0.006	1	−0.216	−0.099	−0.099

[a] Correlation is significant at the 0.05 level (1-tailed). ** Correlation is significant at the 0.01 level (1-tailed).

between these variables is higher than GDP PC and density of population, and confirmed cases in the peaks.

Tables 3 and 4, using hospitalizations and ICU admissions, confirm the higher level of Kendall's tau-b correlation coefficient, τ_b when using the variable of total import and export. The international trade data and ICU hospitalized patients for all Italy, Spain, and France regions (concerning first wave peak) are reported in Fig. 2. This Figure allows a visual inspection of data, clearly highlighting a correlation, that is quantified in Table 5.

In particular, Table 5, reports the Pearson correlation concerning the first and second pandemic peaks for all the countries considered. In addition, Table 5 also reports the Pearson correlation between the ICU hospitalized patients and the density of population of the corresponding regions.

It is very interesting to highlight that the results show a strong positive correlation between the international trade data and the ICU hospitalized patients, for both pandemic peaks for all countries. A correlation between ICU hospitalized patients and the density of population is also evident but only for Italy and France. The increase in population density is expected to raise the possibilities of social contacts, then the virus spread. Instead, surprisingly, the correlation is already established considering international trade. The lack of correlation between pandemic data and population density considering the Spanish regions, highlights that virus diffusion mechanism is very complex, because social interactions can be higher in some regions, even if with reduced people density, in comparison to other regions with higher

Table 3
Correlation Kendall's tau b, using hospitalization.

		Italy	N = 20				
		Import Export	GDP PC	Density of population	Hospitalization 1 peak	Hospitalization 2 peak	Hospitalization 3 peak
Import Export	Correlation Coefficient	1.000	.295[a]	.599**	.737**	.768**	.832**
GDP PC	Correlation Coefficient	.295[a]	1.000	.143	.411**	.253	.232
Density of population	Correlation Coefficient	.599**	.143	1.000	.589**	.642**	.684**
		France	N = 13				
Import Export	Correlation Coefficient	1.000	.256	.513**	.590**	.692**	.667**
GDP PC	Correlation Coefficient	.256	1.000	.487[a]	.103	.205	.231
Density of population	Correlation Coefficient	.513**	.487[a]	1.000	.256	.359[a]	.333
	Spain	N = 19					
Import Export	Correlation Coefficient	1.000	.298[a]	-.041	.614**	.743**	.708**
GDP PC	Correlation Coefficient	.298[a]	1.000	.006	.380[a]	.228	.146
Density of population	Correlation Coefficient	-.041	.006	1.000	-.193	-.158	-.123

[a] Correlation is significant at the 0.05 level (1-tailed). ** Correlation is significant at the 0.01 level (1-tailed).

Table 4
Correlation Kendall's tau b, using ICUs admission.

		Italy Import Export	N = 20 GDP PC	Density of population	ICUs Admission 1 peak	ICUs Admission 2 peak	ICUs Admission 3 peak
Import Export	Correlation Coefficient	1	.295[a]	.599**	.723**	.758**	.768**
GDP PC	Correlation Coefficient	.295[a]	1	0.143	.406**	0.242	0.253
Density of population	Correlation Coefficient	.599**	0.143	1	.553**	.610**	.706**
		France	N = 13				
Import Export	Correlation Coefficient	1	0.256	.462[a]	.744**	.684**	.692**
GDP PC	Correlation Coefficient	0.256	1	.487[a]	0.154	0.245	0.256
Density of population	Correlation Coefficient	.462[a]	.487[a]	1	0.308	.400[a]	.359[a]
	Spain	N = 19					
Import Export	Correlation Coefficient	1	.298[a]	−0.041	.743**	.774**	.645**
GDP PC	Correlation Coefficient	.298[a]	1	0.006	0.275	0.27	0.129
Density of population	Correlation Coefficient	−0.041	0.006	1	−0.018	−0.106	−0.106

[a] Correlation is significant at the 0.05 level (1-tailed). ** Correlation is significant at the 0.01 level (1-tailed).

population density. Then, this parameter can be unsuitable to model pandemic diffusion. On the contrary, international trade data results more robust. This is evident from the data inspection (see Fig. 2) and analysis (see Tables 4 and 5).

Fig. 2 allows to present a new picture of the pandemic in the EU countries considered, enabling us to learn a new lesson about SARS-CoV-2 diffusion in the society. To the best of our knowledge, the approach is unique not only for the data that are reported, but also in pooling and comparing information from multiple regions of different countries at once. In particular, despite the role of international trade has already been proposed (Bontempi, 2020b; Bontempi et al., 2020), the already published data only concerned Italian regions and their import and export trade data with China. In the present case, the analysis was extended to all the regions of other countries (France and Spain) and to data concerning the total international trade of all the regions (i.e. with all their foreign partners).

In conclusion, Fig. 2 shows that the evolution of the infection must be inspected by a multilevel analysis, highlighting the potential of a transdisciplinary vision, crossing the disciplines' borders to better focus on what emerges from the data (Rigolot, 2020). What clearly appears is that the complexity of such a system cannot be described only considering a strict virology perspective, but it requires the involvement of global connectivity of cultural, social, and economic systems, with the possibility of different variables interdependence (Bontempi, 2021).

3.2. Results of aggregated data using all regions of Italy, France and Spain

Table 6 shows partial correlation, controlling for the density of population and GDP PC. Results reveal that the association between total import and export and ICUs, hospitalization and confirmed cases is

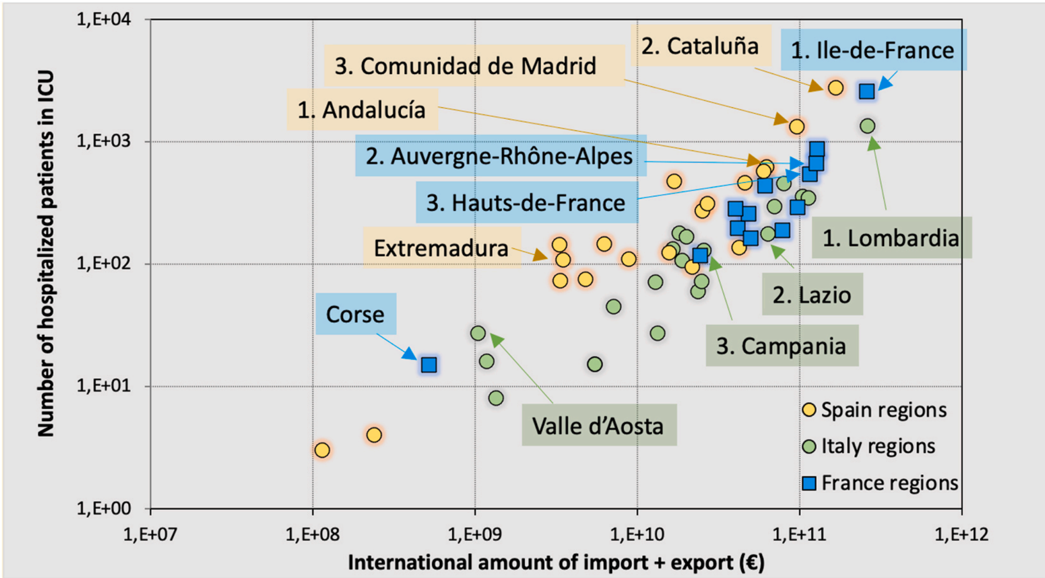

Fig. 2. Number of hospitalized patients (log. Scale) in Intensive Care Units (ICU) at the first peak of the contagious curves in France, Italy, and Spain regions (data refer to the 13th of April for France and Spain and to the 1st of April for Italy) as a function of the sum of the total amount of import and export international trade (data are reported in €, in log. Scale for each region). The first three most populated regions for each country are highlighted with the number corresponding to the relative ranking, that allows underlining a lack of (expected) correlation between the population and the number of hospitalized patients in ICU. Also, the least populated regions of each country are highlighted.

Table 5
Pearson correlation (R) between the international trade (the sum of total amount of import and export) and hospitalized patients in Intensive Care Units (ICU) in France, Italy, and Spain regions.

	ICU occupancy first wave		ICU occupancy second wave	
	R (95% CI)	p-value (2 sided)	R (95% CI)	p-value (2 sided)
International trade Italy	0.967 (0.917–0.987)*	3.60E-12*	0.943 (0.859–0.978)*	4.93E-10*
International trade France	0.933 (0.787–0.980)**	3.20E-06**	0.899 (0.689–0.970)**	2.96E-05**
International trade Spain	0.957 (0.890–0.984) ***	1.42E-10***	0.920 (0.799–0.969) ***	2.60E-08***
Population density Italy	0.605 (0.222–0.826)*	4.69E-03*	0.712 (0.394–0.878)*	4.27E-04*
Population density France	0.945 (0.821–0.984)**	1.16E-06**	0.778 (0.398–0.930)**	1.72E-03**
Population density Spain	−0.168 (−0.578 - 0.310)***	4.92E-01***	−0240 (−0.626 - 0.240)***	3.22E-01***

Note: The correlation is reported also between the density of population and ICU occupancy for all the regions. First wave ICU data refer to 13th April for France** and Spain*** and to 1st April for Italy*. Second wave ICU data refer to 13th November for France**, 6th November for Spain*** and to 18th November for Italy*.

rather strong, with a coefficient of correlation r in the range .78–.94 (p-value <.001). This result suggests how total import and export is interrelated with the main variables associated with the health of people in April and November 2020 and January 2021 (cf., Tables 1S and 2S in the Supporting).

Table 7 shows the estimation of parameters of multivariate analyses for aggregated data, including all the regions of Italy, France, and Spain. The first coefficient of regression in the model indicates that an increase of 1% total import and export (controlling for the density of population, GDP PC and interaction variable), it increases (Table 7):

- the expected ICUs in April 2020 by 0.69% (p-value < .001)
- the expected ICUs in November 2020 by 0.67% (p-value < .001)
- the expected ICUs in January 2021 by 0.72% (p-value < .001)
- the expected Hospitalization in April 2020 by 0.71% (p-value < .001)
- the expected Hospitalization in November 2020 by 0.69% (p-value < .001)
- the expected Hospitalization in January 2021 by 0.76% (p-value < .001)
- the expected Confirmed cases in April 2020 by 0.62% (p-value < .001)
- the expected Confirmed cases in November 2020 by 0.68% (p-value < .001)
- the expected Confirmed cases in January 2021 by 0.71% (p-value < .001)

The coefficient R^2 in Table 7 indicates that about 69–90% of the variables of the health of population can be attributed (linearly) to total import and export (controlling for the density of population, GDP PC and interaction variable), suggesting a consistent and robustness of the model in a multivariate context.

4. Concluding remarks and future perspectives

The association between commercial trade and pandemic severity that seems to be established in Fig. 2 as well as statistical analyses of data correlation and regression can support new conclusions and/or new hypotheses about the pandemic diffusion and data modeling, needing a trans-disciplinary level of analysis.

First, analyzing the number of hospitalized patients in ICU versus a non-conventional reference indicator makes it possible to deduce that the severity of the SARS-CoV-2 infection was actually comparable in different EU regions (also considering different countries). In particular, those regions that are most active in the commercial activities are generally the richest areas, with an expected higher population mobility, economic dynamism, and more group activities. These considerations allow justifying the choice of commercial trade as a variable, accounting for several determinants of virus diffusion (see Fig. 1), due to human-to-human interactions (cf., Chang et al., 2020; Coccia, 2021a). This

Table 6
Partial Correlation with two control variables for aggregated data, including all regions of Italy, France and Spain.

Control Variables, Log GDP PC and Population Density	Log Import Export	LogICUs April 2020	LogICUs November 2020	LogICUs January 2021	LogHosped April_June 2020	LogHosped November 2020	LogHosped January 2021	Log Confirmed cases April_June 2020	Log Confirmed cases November 2020	Log Confirmed cases January 2021
Log Import Export	1.000	.873	.927	.849	.786	.912	.919	.781	.921	.939
Significance (2-tailed)	.	.001	.001	.001	.001	.001	.001	.001	.001	.001
Log ICUs April 2020	.873	1.000	.885	.914	.950	.846	.911	.942	.922	.923
Significance (2-tailed)	.001	.	.001	.001	.001	.001	.001	.001	.001	.001
Log ICUs November 2020	.927	.885	1.000	.880	.797	.978	.947	.778	.962	.960
Significance (2-tailed)	.001	.001	.	.001	.001	.001	.001	.001	.001	.001
Log ICUs January 2021	.849	.914	.880	1.000	.884	.849	.962	.871	.902	.936
Significance (2-tailed)	.001	.001	.001	.	.001	.001	.001	.001	.001	.001
Log Hosped April_June 2020	.786	.950	.797	.884	1.000	.776	.863	.979	.859	.864
Significance (2-tailed)	.001	.001	.001	.001	.	.001	.001	.001	.001	.001
Log Hosped November 2020	.912	.846	.978	.849	.776	1.000	.937	.755	.946	.949
Significance (2-tailed)	.001	.001	.001	.001	.001	.	.001	.001	.001	.001
og Hosped January 2021	.919	.911	.947	.962	.863	.937	1.000	.845	.945	.980
Significance (2-tailed)	.001	.001	.001	.001	.001	.001	.	.001	.001	.001
Log Confirmed cases April_June 2020	.781	.942	.778	.871	.979	.755	.845	1.000	.839	.846
Significance (2-tailed)	.001	.001	.001	.001	.001	.001	.001	.	.001	.001
Log Confirmed cases November 2020	.921	.922	.962	.902	.859	.946	.945	.839	1.000	.981
Significance (2-tailed)	.001	.001	.001	.001	.001	.001	.001	.001	.	.001
Log Confirmed cases January 2021	.939	.923	.960	.936	.864	.949	.980	.846	.981	1.000
Significance (2-tailed)	.001	.001	.001	.001	.001	.001	.001	.001	.001	.

Note: df = 48.

analysis shows that regions with higher international trade activities (that are representative of living standard, economic dynamics, and globalization level) are more susceptible to be in contact with foreign populations, with an increased risk to import the virus in their communities and spread the diffusion. This is in line with studies reported by Li et al. (2020) that estimated how a large number of undocumented infections originated from China, before travel restrictions, was the source of fast spreading of SARS-CoV-2 around the world. In particular, accelerating events or situations are expected to occur with higher probability in most rich (productive) areas, thus justifying a different growth of the infection rate, also starting from local differences in the origins (Adam et al., 2020).

Another implication regarding the reported data is that globalization appears to be a problem for other future pandemic events. It is evident that, also considering a single country, regions with limited international relationships result less exposed to the virus spread and may turn out to be protected in the eventual condition of a possible undetected infection. The monotone trend of data shown in Fig. 2 may also allow estimating the regions that are more (or less) susceptible to contagious diffusion, identifying and proposing suitable future action strategies.

Hence, statistical analyses strongly suggest that crisis management has to focus on infections occurring from outside the national boundaries, before relaxing foreign mobility limitations (Bertuzzo et al., 2020). The statistical evidence in this study is based on the relation of association between the variables under study, rather than a relation of dependence, because of manifold confounding factors that influence these variables.

Overall, then, this study has investigated the possibility to introduce only a variable to model the pandemic diffusion, due to human-to-human interactions. Preliminary data analysis involving all the Italian 107 provinces is in accord with this study (Bontempi et al., 2021). However, some other critical variables may be needed for more detailed research of other factors associated with the spread of novel infectious diseases, such as environmental factors (temperature, humidity, wind

Table 7
Multivariate regression analysis for aggregated data, including all regions of Italy, France and Spain.

	LogICUs April 2020	LogICUs November 2020	LogICUs January 2021	LogHosped April_June 2020	LogHosped November 2020	LogHosped January 2021	Log Confirmed cases April_June 2020	Log Confirmed cases November 2020	Log Confirmed cases January 2021
Constant α	−11.821[b]	−6982[b]	−2.483	−7.859	−8.014[b]	-.909	−6.320	−3.621	.193
Coefficient $\beta 1$ *ImpExp*	.691[a]	0,670[a]	.721[a]	.706[a]	.685[a]	.764[a]	.616[a]	.682[a]	.707[a]
Coefficient $\beta 2$ *Density Pop*	-.089	0,043[c]	.112	-.130	.058	.021	-.066	.057	.064
Coefficient $\beta 3$ *GDP PC*	.080	−0,431	−1.039[c]	-.145	-.169	−1.041[a]	.007	-.212	-.577*
Coefficient β *INT Density Pop × ImpExp*	6.06E-015	0,000	2.53E-015	8.15E-015	1.73E-015	2.79E-015	7.17E-015	2.81E-015	2.17E-015
R^2	.82	.88	.73	.70	.86	.86	.69	.87	.90
(St. Err. of Estimate)	.64	.47	.75	.95	.51	.54	.84	.48	.43
F-test	54.58[a]	88.32[a]	32.41[a]	26.88[a]	69.86[a]	69.61[a]	26.65[a]	81.05[a]	100.17[a]

Note: log Scale; Predictors: (Constant), Import Export, Density Population (inhabitants per km^2), GDP PC, INT=Interaction (Density Pop × Import-Export).
[a] p-value<.001.
[b] p-value<.01.
[c] p-value<.05.

speed, etc., cf., Coccia, 2021b). To conclude, this study is a beginning of a new research investigation field, based on the proposed data, to identify new approaches and sources (for example additional parameters to include in the models) and open challenges for further works, based on a trans-disciplinary path, able to cross the disciplines' border to better eviscerate the complexity of a pandemic.

Authors contribution

E. Bontempi: Conceptualization and conceiving the original idea, draft preparation and writing. M. Coccia: Statistical analysis, draft preparation and writing. A. Zanoletti: Literature survey/mining, Figure designing. S. Vergalli: Critical Review and Editing/Proofreading the manuscript.

Declaration of competing interest

The authors declare that they have no competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2021.111529.

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