Decreased Case Fatality Rate of COVID-19 in the Second Wave: a study in 53 countries or regions

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Abstract: The raw case fatality rate (CFR, reported number of COVID-19 deaths divided by the number of cases) is an important indicator to quantify the severity or treatment efficacy. In many countries, the pandemic had two waves to date. To our knowledge, no studies have compared the

CFR between the two waves. In this work, we report that of 53 countries or regions with the highest death tolls, 43 had lower CFR estimates in the on-going second wave than in the first wave . We discussed the possible reasons. Also, we compared the two-wave pattern of COVID-19 with those of influenza. Influenza activities in the pre-pandemic era provided an indicator for seasonality of climate in a country. The sharp drop in 2020 influenza activity is an indicator of the effects of social distancing.

Main Text

The ongoing COVID-19 pandemic has caused a serious health threat globally. Many countries have seen a wave pattern of reported cases, namely a second wave followed the first wave. To our knowledge, there are no studies to date to compare the case fatality rate between these two waves.

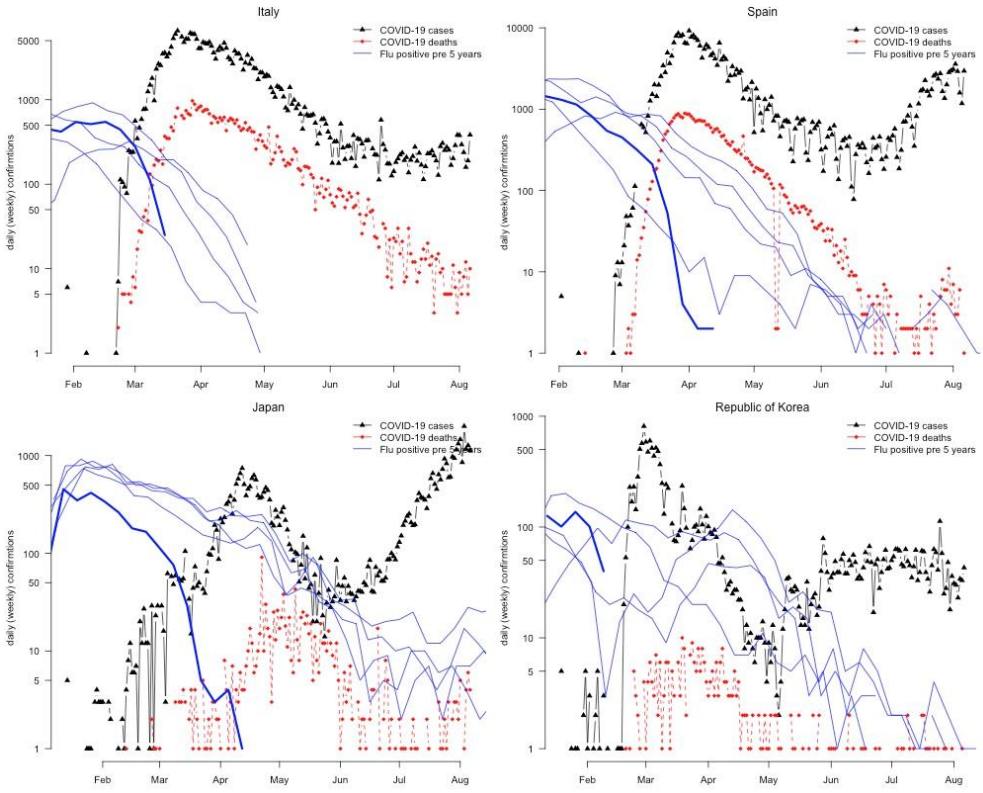

Figure 1. Time series plots of daily confirmed COVID-19 cases (in black), COVID-19 deaths (in red), and influenza positive cases in 2015-2019 (in light blue) and in 2020 (in dark blue).

We obtained the daily confirmations of COVID-19 cases and deaths for 216 countries or regions, during February 2020 - August 2020, and weekly influenza confirmations during 2015 to current week, from the World Health Organization [1,2]. We showed data of four countries (two from Europe and two from Asia which caught a lot of attention in the early phase of the pandemic) in Figure 1. Research of other 49 countries or regions are listed in the supplementary. The time series (in common log scale on vertical axis) of confirmed cases showed two waves. Based on this observation, we divided the transmission of the disease into two phases: Phase I before June 1 and Phase II after June 1 for confirmed cases; and Phase I before June 10 and Phase II after June 10 for deaths. For deaths, we choose the truncated time ten days later to account for the delay between confirmation and deaths [3]. We compared the raw case fatality rate (CFR) of Phase I and Phase II for all countries or regions.

In our supplementary data in the appendix, for each country, we break down the data for Phase I or Phase II. The column "case_pre" is the total of confirmed cases before June 1 and the column "case_post" is the total of confirmed cases after June 1 up to July 26. Accordingly, the column of "death_pre" is the infection death before June 10 and the column "death_post" is the infection death after June 10 up to August 6. We define the raw case fatality rates (CFR) as $r_1=\frac{death\_pre}{case\_pre}$ and $r_2=\frac{death\_post}{case\_post}$. Then the change in CFR is reduction= $\frac{r_1-r_2}{r_1}$. Based on our analysis, among all 53 most affected countries or regions (supplementary Table 1), 43 had an apparent reduction in CFR, the rest ten had an increase in CFR in opposite. The median of the 53 reductions is 0.383 and the first quantile is 0.194. The decrease of CFR might indicate the decreasing severity of the global pandemic, and the potential reasons warrant further investigations. We propose the following hypotheses that could contribute to the decrease of CFR in the second phase. First, the lower CFR in the second phase than in the first phase could be a harvest effect. In other words, a large number of the elderly and those with health conditions (the vulnerable groups) likely had died in the first wave, especially in these countries with a high infection rate. By contrast, if a country or region (such as Hong Kong) was spared from the first phase, it might have an increase in CFR when the virus attacked again. Second, the test capacities and healthcare system in many countries could have been better prepared in the second phase. As a result, mild and asymptomatic cases were more likely reported in the later outbreaks, and severe cases could have

received timely and treatments to greatly reduce the CFR. Third, the age structure of infected could have changed from the first wave to the second wave due to a variety of reasons, e.g. social movement in many countries might involve more healthier young individuals. Fourth, the virus might have evolved to increase its transmissibility in young healthy adults and children, which could be further facilitated by low compliance of social distancing in young people. Last but not least, favourable environmental factors might have led to a reduced CFR (e.g. warmer weather in the Northern Hemisphere and improved air quality due to city lockdown as reported in many studies [4-6]). The current evidence remains limited to suggest which of the above hypotheses is more plausible. Nevertheless, according to the classical epidemiologic triangle model, the interactions of the host, pathogen and environment determine the characteristics of outbreaks, rather than one or two factors alone.

We show the time series plots of eight countries in supplementary figures S1&S2, and summarizes the results of 53 countries or regions in supplementary figure S3, and Table 1. Majority of (43 out of 53) countries or regions had a decrease in the raw CFR. 10 countries showed increased raw CFR, which could be due a variety of reasons, e.g. being in south hemisphere (Peru and Chile), milder first wave. The weekly influenza laboratory confirmations for the previous five years may be used as a proxy of the seasonality of climate and population global travel pattern in a country [7]. Thus we may wonder whether favourable weather may contribute to a reduce CFR for COVID-19. The sharp drop in influenza cases in 2020 (dark bold curve), compared to those in previous years, may be due to social distancing and possible interference with COVID-19 infection. Thus it is informative to compare the COVID-19 and influenza in these plots. Individual or age specific data are needed to further investigate the reasons behind changing CFR. The finding is nevertheless of significance to inform the public and policy makers. Although the lower CFR in the second phase is a positive sign to suggest the decrease severity of COVID-19 infections, the shift to younger age groups could bring more difficulty in containing the pandemic. We also need to stay vigilant for the potential rebound of influenza outbreaks as many countries or regions are planning to lift social distancing control measures.

Declarations

List of abbreviations

COVID-19: coronavirus disease 2019

CFR: case-fatality-rate

Ethics approval and consent to participate

The ethical approval or individual consent was not applicable.

Consent for publication

Not applicable.

Availability of data and materials

All data and materials used in this work were publicly available.

Conflict of interests

DH was supported by an Alibaba (China) Co. Ltd. Collaborative Research project. Other authors declare no competing interests.

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Authors' Contributions

All authors conceived the study, carried out the analysis, and drafted the first manuscript. All authors discussed the results, critically read and revised the manuscript, and gave final approval for publication.

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Not applicable.

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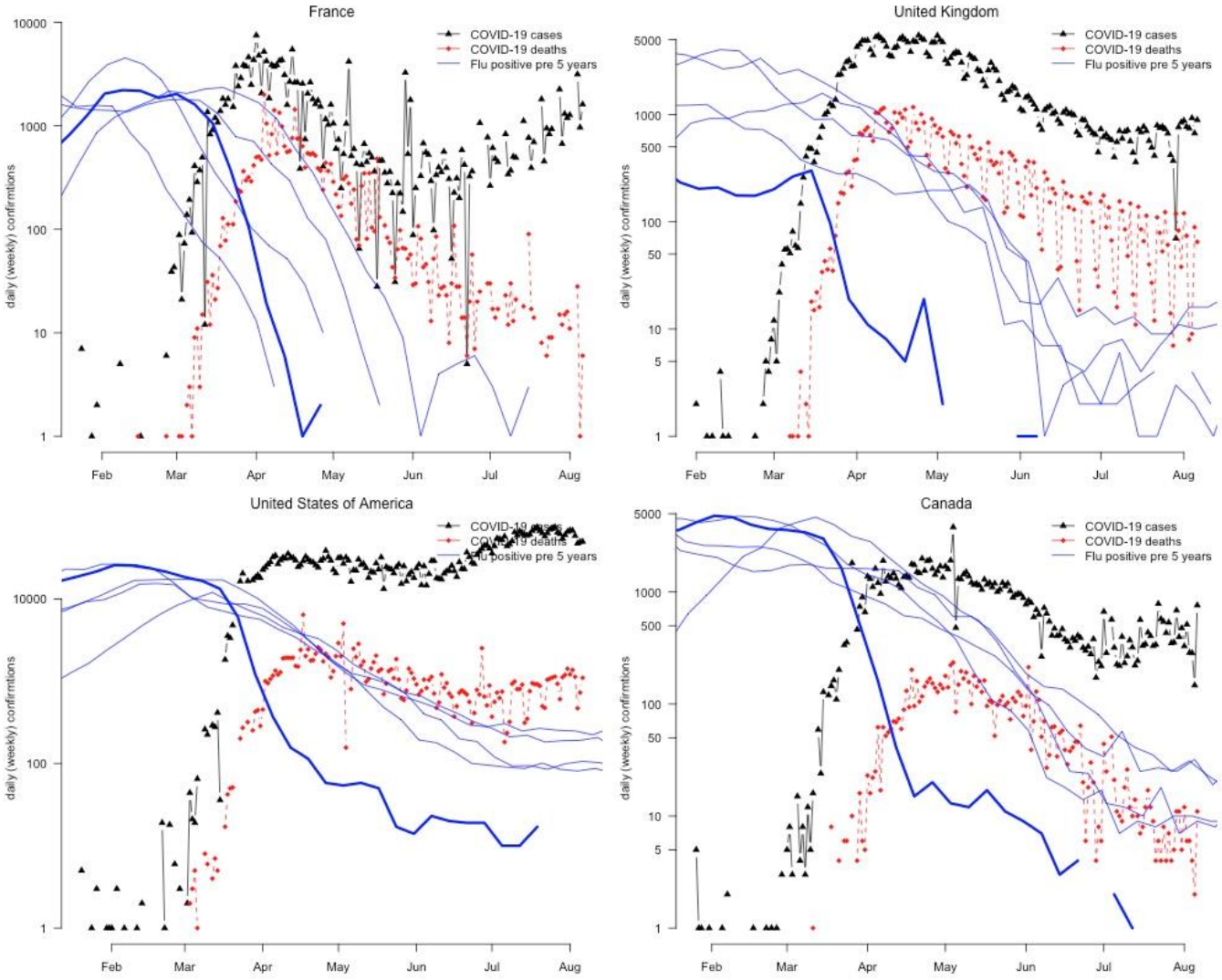
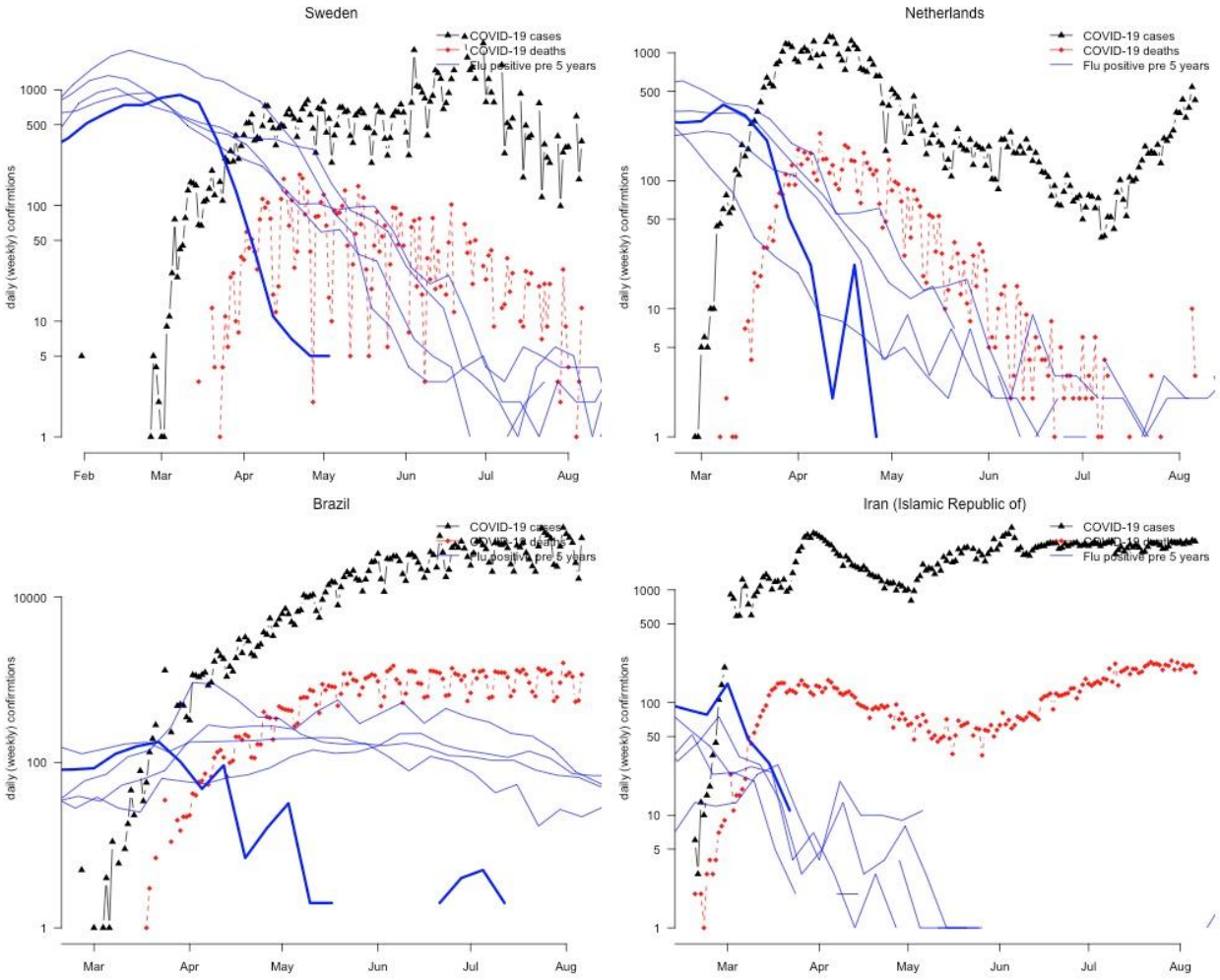
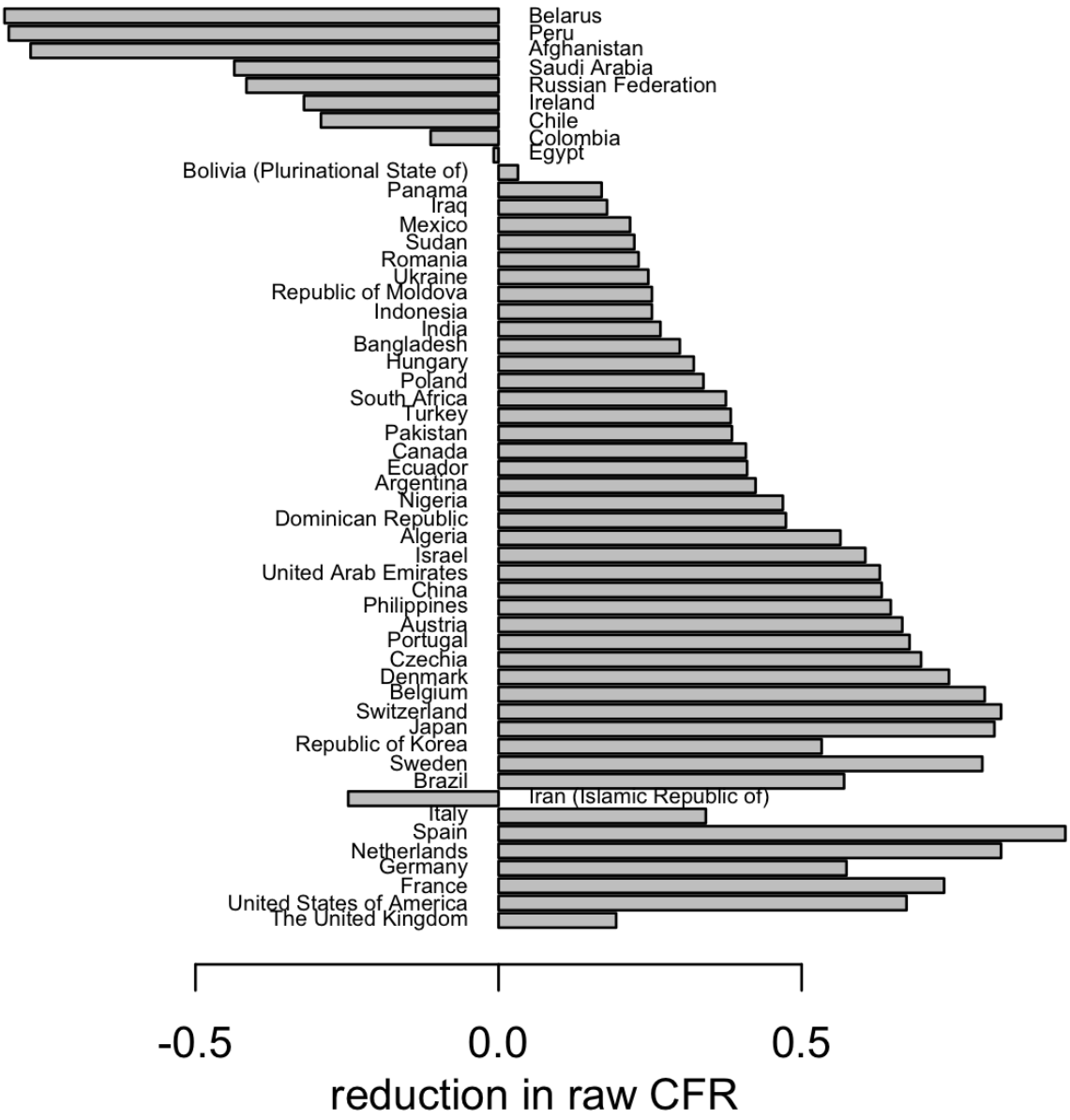
1. Supplementary Figure S1



2 Supplementary Figure S2



3 Bar plot of the reduction (or increase) in raw CFR in 53 countries or regions



4 Supplementary Data by Aug. 6, 2020

In the following table, for each country, we break down the data for Phase I or Phase II. The column “case_pre” is the data of confirmed cases before June 1 and the column “case_post” is the data of confirmed cases after June 1. Accordingly, the column of “death_pre” is the infection death before June 10 and the column “death_post” is the infection death after June 10. For the data after June, the end time of our data is Aug. 6,

2020. We define two raw case fatality rates as r_1=$\frac{death\_pre}{case\_pre}$ and r_2=$\frac{death\_post}{case\_post}$. In addition, we calculate the reduction in case fatality rate as reduction= $\frac{r_1-r_2}{r_1}$ and place the result in the last column.

Table S1. The data breakdown for Phase I and Phase II

Country or region	case_pre	death_pre	case_post	death_post	reduction
The United Kingdom	254394	40686	44042	5678	0.194
United States of America	1734040	110220	2204054	45830	0.673
France	148436	29149	19855	1033	0.735
Germany	181482	8711	22701	464	0.574
Netherlands	46257	6016	6147	137	0.829
Spain	239650	28232	34846	267	0.935
Italy	232664	33964	12674	1217	0.342
Iran (Islamic Republic of)	148950	8351	135084	9451	-0.248
Brazil	465166	36455	1762348	59364	0.57
Sweden	37113	4694	41650	1066	0.798
Republic of Korea	11468	274	2511	28	0.533
Japan	16851	916	11105	110	0.818
Switzerland	30789	1676	3124	29	0.829
Belgium	58751	9628	7117	231	0.802
Denmark	11633	593	1757	23	0.743
Czechia	9230	328	5570	60	0.697
Portugal	32203	1485	17176	255	0.678
Austria	16638	672	3484	47	0.666
Philippines	18086	1011	56304	1112	0.647
China	84570	4645	1930	39	0.632
United Arab Emirates	33896	281	24092	74	0.629
Israel	17071	295	39373	269	0.605
Algeria	9267	715	16217	546	0.564
Dominican Republic	16908	539	40707	683	0.474
Nigeria	9855	361	29093	566	0.469
Argentina	14702	670	127198	3339	0.424
Ecuador	38571	3642	39577	2205	0.41
Canada	89741	7800	22499	1158	0.408
Pakistan	69496	2172	200904	3863	0.385
Turkey	163103	4711	60212	1073	0.383
South Africa	30967	1080	377085	8218	0.375
Poland	23571	1166	18009	590	0.338

Hungary	3867	548	531	51	0.322
Bangladesh	47153	930	168957	2337	0.299
India	182143	7466	1105802	33233	0.267
Indonesia	26473	1883	67184	3569	0.253
Republic of Moldova	8098	359	14007	464	0.253
Ukraine	23672	810	39151	1009	0.247
Romania	19133	1334	22142	1187	0.231
Sudan	4800	372	6502	391	0.224
Mexico	84627	13699	277647	35170	0.217
Iraq	6179	370	96047	4724	0.179
Panama	12531	393	43375	1129	0.17
Bolivia (Plurinational State of)	8731	465	55404	2855	0.032
Egypt	23449	1271	66964	3660	-0.008
Colombia	26688	1259	191740	10056	-0.112
Chile	94858	2264	243901	7528	-0.293
Ireland	24929	1683	897	80	-0.321
Russian Federation	405843	6142	395006	8464	-0.416
Saudi Arabia	83384	746	177010	2274	-0.436
Afghanistan	15094	376	20887	922	-0.772
Peru	148285	5465	218265	14542	-0.808
Belarus	41658	276	25030	301	-0.815