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Research Article

Case Fatality Rate Components Based Scenarios for COVID-19 Lockdown

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Abstract

Objectives: The important control measure to limit the spread of the pandemic is a lockdown. Current criteria for initiating or releasing lockdown are largely subjective and debatable. Many divergent views are arguing for initiating, continuing, and ending the lockdown. This paper aims to find a unique baseline statistically derived standardized model of different options scenarios for lockdown initiation and releasing without the need for a subjective opinion.

Study Design: Twenty-one countries were chosen. The inclusion criterion was each country should have more than 1 million Covid-19 tests/ M on February 25, 2021. Data is derived regarding reported crude Covid-19 cases /million population inhabitants (CC/M) and Covid-19 deaths/ M population inhabitants (CD/M). Case fatality rate (CFR), CC/M and CD/M were used for developing a lockdown model.

Methods: Kolmogorov-Smirnov Z Test, analysis of variance of linear and non-linear regression and estimation of the Confidence Interval (C.I.).

Results: the estimated CFR critical value was 1.125. Different estimates of confidence intervals for the critical point were provided. The lower CFR point for confidence interval at 0.0005 p-value was 0.464485, while at 0.05 p-value was 0.829029.

Conclusions: A novel statistical model was developed.

Keywords: Case fatality rate; Covid-19 deaths; Covid-19 cases; Critical value

Introduction

On March 11, 2020, the World Health Organization (WHO) has declared the novel coronavirus (COVID-19) outbreak a public health emergency of international concern [1]. A prominent countermeasure implemented in numerous countries has been a “lockdown”. Lockdowns implemented in varying degrees and at different times, thought to be most effective at containing and interrupting COVID-19 widespread and transmission [2-4].

Lockdown initiated in China’s Hubei province in January 2020 and Italy in March 2020, implemented in many other countries including the entire 1.3 billion population of India [5,6].

The heterogeneity in the way that lockdowns were applied for both their timing and duration was significant. The evidence base of when, how, and how long to apply a lockdown to maximize its effect is not well reported [7].

Lockdowns have been met with opposition and protests in some parts of the world [8]. That raises the question of when lockdown measures should be relaxed. Too soon or too late relaxation is a matter of the epidemic will bounce back or there is needless economic suffering [9]. Speculation about the lifting of restrictions that are currently in place to limit the spread of the COVID-19 virus becomes a hot topic. WHO suggested that restrictions are lifted slowly and strategically, with a tapering off of restrictions that will hopefully avoid a new cycle of outbreaks [10]. The WHO has outlined six criteria that each country should meet before lifting restrictions: (1) Transmission of the virus is under control. (2) The health system can early diagnose and treat cases and trace contacts. (3) The risk of outbreak hotspots is reduced in vulnerable settings. (4) Essential places have effective preventative measures in place. (5) In place, measures are available to manage the risk. (6) Educated, engaged, and empowered communities able to adjust to the new norms [10].

We designed this study to set standards for lockdown in context of: (1) WHO criteria are difficult to measure, (2) controversies regarding current poorly quantified Covid-19 pandemic lockdown strategies and models [7], (3) most of the currently implemented models are country-specific and not considered case fatality rate (CFR), (4) increased mortalities during wave peak was attributed to the system failure to cope with increases burden rather than related to increased mortality rates (MR)s associated with increased case overload. The former assumption makes previous models adapted to hospital and ICU beds capacity rather than adapted to the total number of affected persons.

Methods

Twenty-one countries were chosen. The inclusion criterion was each country had more than 1 million Covid-19 tests/ M on February 25, 2021. Just one country was excluded due to 0 covid-19 fatality. Territories that have an administrative division, usually an area that is under the jurisdiction of a sovereign state and had its separated Covid-19 statistics were included. Data is derived regarding reported total cases /1M and deaths /1M on February 25, 2021. We calculated crude (CFR)s and (MR)s according to derived data.

Definitions

Case fatality rate (CFR): counted number of Covid-19 deaths / counted confirmed cases %.

Crude Covid-19 deaths/M (CD/M): crude Covid-19 deaths/ 1 million population inhabitant.

CC/M: crude confirmed cases/ 1 million population inhabitant.

Case fatality rate components based scenarios: the model designed by authors to put standards for lockdown options.

Study Design

Algorithm of the suggested technique includes:

1. Transfer by using standard degrees of z-score for the studied markers (i.e. numbers of morbidity and mortality of studied countries per one million population inhabitants accredited to conduct the critical-degree calibration process.
2. Examine the fitted of the optimal model in light of the analysis of variance of linear and non-linear regression under assumed models between standard z-scores of (morbidity and mortality) separately as an independent variable and CFR as a dependent variable.
3. Unifying the units of measurement for the standard z-score on the horizontal axis, taking into account the importance of unifying the ideal model that achieves the highest levels of fitness, whether that is with the standard degrees of morbidity or mortality.
4. Standardizing the units of measurement for the CFR according to the previous step by providing the units of measurement for the most appropriate model, either registered by morbidity or mortality.
5. Using the option of “Aggregation and Re-Aggregation” procedures on the Excel application to combine the long-term trends of the two graphs which are crossed in the front of the critical-degree calibration process at the CFR axis.
6. In this step, it is possible to estimate the Confidence Interval (C.I.) after a Kolmogorov-Smirnov test to prove the validity of the assumptions of the normal distribution function of CFR readings and under determination of confidence levels for the estimation with intervals with the adoption of the critical degree as a center point.

Application of the Suggested Technique

Among surveyed of chosen 21 countries, with calculated the crude case CFR as it is on February 25, 2021, and the MR, as well as z-score for preceding markers, as shown in the Appendix 1 and Table 1.

Table 1 represents a one-sample “Kolmogorov-Smirnov” test procedure comparing the observed cumulative distribution function for studied readings with a specified theoretical distribution, which proposed a normal shape (i.e. bell shape) for the studied markers.

Table 1: Normal distribution function test (goodness of fit test) for studied markers.

One-Sample Kolmogorov-Smirnov Test			
Statistics	**Markers**		
	Covid-19 CC/M	Covid-19 MR /M.	CFR February 25, 2021
Kolmogorov-Smirnov Z	1.018	0.951	0.576
Asymptotic Sig. (2-tailed)	0.251	0.327	0.894
C.S. (*)	NS	NS	NS
Statistical Hypothesis: Ho: Markers are followed normal distribution function. Test distribution is Normal. *NS: Non Sig. at P>0.05.			

The results show that the test's distribution was normal for studied reading's markers since no significant levels are accounted ($P>0.05$), and that could enable us of applying the z-score transformation as shown in Table 2, using estimations by points and intervals, such as (mean, standard deviation, standard error, 95% confidence interval for the population mean value) which supposed that underlying data having normal distribution function.

Table 2: Z-Score transform of studied markers concerning the studied countries.

Item	Countries	Z-score		
		AR /1M	MR /1M	CFR
1	USA	1.101	-0.373	0.810
2	UK	1.392	-0.714	2.235
3	Israel	-0.091	0.403	-0.492
4	UAE	-0.72	0.539	-1.027
5	Denmark	-0.359	-0.574	-0.02
6	Bahrain	-0.553	1.342	-0.96
7	Singapore	-0.864	1.569	-1.351
8	Luxembourg	0.395	-0.051	0.022
9	Cyprus	-0.63	-0.471	-0.564
10	Hong Kong	-0.837	-0.958	0.814
11	Malta	0.017	-0.549	0.364
12	Andorra	0.924	0.706	-0.148
13	Iceland	-0.763	-0.52	-0.815
14	Gibraltar	2.577	-0.261	1.284
15	Channel Islands	-0.249	-0.836	1.237
16	San Marino	1.84	-0.322	1.089
17	Monaco	-0.134	-0.473	0.078
18	Bermuda	-0.626	-0.887	0.706
19	Faeroe Islands	-0.845	0.132	-1.227
20	St. Barth	-0.743	3.092	-1.196
21	Cayman Islands	-0.832	-0.795	-0.839
Introduced by the Authors depending on the (One-Sample Kolmogorov-Smirnov Test).				

After examining a fitted of the optimal models in light of the analysis of variance of linear and non-linear regression under the assumed models between the standard of z-scores of (morbidity and mortality) separately as an independent variable, and (CFR) as the dependent variable, polynomial of quadratic forms were accounted the best-fitted model for the studied functions, and as illustrated in the Table 3.

Table 3: Impact the Covid-19 MR /M and CC/M on the CFR as it is on Feb 25, 2021 separately.

Predicted Equation of CFR-By Polynomial of Quadratic Model					
Correlation Coefficient	0.70847 (HS)	Meaningful Non Linear regression Tested in two tailed alternative Statistical hypothesis			
R- Square	0.50193				
F Statistic of Reg. ANOVA	9.06991	Sign. F =	0.0019(HS) (*)		
Variables in the Equation					
Independent Variable (X)	$\hat{B}$	SE. $\hat{B}\hat{B}$	Beta	t-test	Sig. level (*)
CD/M	0.714149	0.217590	0.886323	**3**.282	0.0041
$(CD/M)^2$	-0.131295	0.143724	-0.24669	-0.914	0.3730
(Constant)	1.262420	0.189325	--	6.668	0.0000
Predicted Equation of CFR - By Polynomial of Quadratic Model					
$(\widehat{CFR}) = (1.26242) + (0.714149)X - (0.131295)X^2$					
Correlation Coefficient	0.63880 (HS)	Meaningful Non Linear regression Tested in two tailed alternative Statistical hypothesis			
R- Square	0.40806				
F Statistic of Reg. ANOVA	6.20427	Sign. F =	0.0089 (HS) (*)		
Variables in the Equation					
Independent Variable (X)	$\hat{B}$	SE. $\hat{B}\ \hat{B}$	Beta	t-test	Sig. level (*)
CC/M.	-0.709407	0.238390	-2.88044	-2.976	0.0081
$(CC/M.)^2$	0.138242	0.115589	0.353849	1.196	0.2472
(Constant)	0.056518	0.029426	-	5.583	0.0000
$(\widehat{CFR}) = (0.056518) - (0.709407)X + (0.138242)X^2$					
(*)HS: Highly Sig. at P<0.01. CC/M: Crude Covid-19 cases /million population inhabitants, CM /M : Covid-19 crude deaths /million population inhabitants ,CFR; case fatality rate %					

Figure 1 shows long term trends of scatter diagrams impact of the Covid-19 CD/M and CC/M on the CFR: as it is on February 25, 2021 separately.

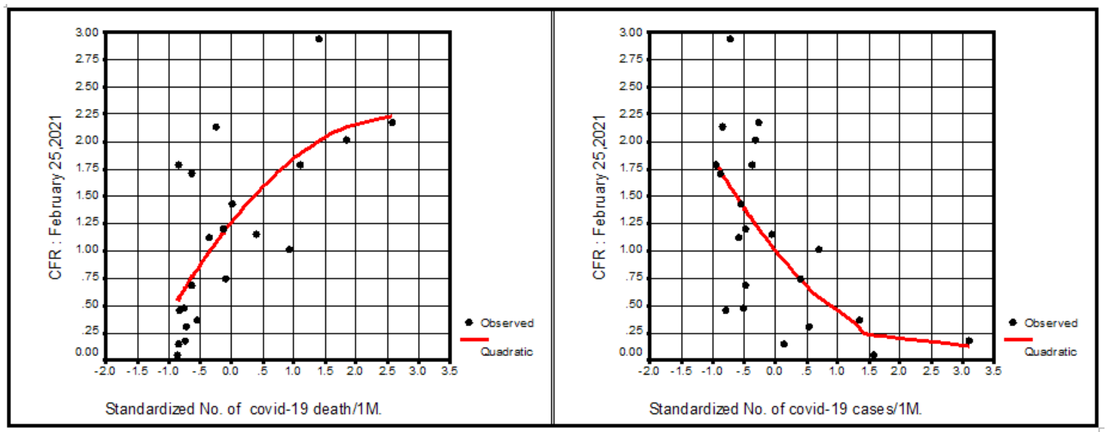

Figure 1: Long-term trend of the scatter diagram concerning the impact of Covid-19 CD/M and CC/M on CFR as it is on Feb. 25, 2021, separately. CC/M: Crude Covid-19 cases /million population inhabitants, CM /M: Covid-19 crude deaths /million population inhabitants, CFR; case fatality rate %.

The implementation of steps for the suggested algorithm's technique (Figure 2) represents procedures on the Excel application to combine the long term trends of the two preceding graphs which are crossed in the front of the critical-degree calibration process at the CFR axis.

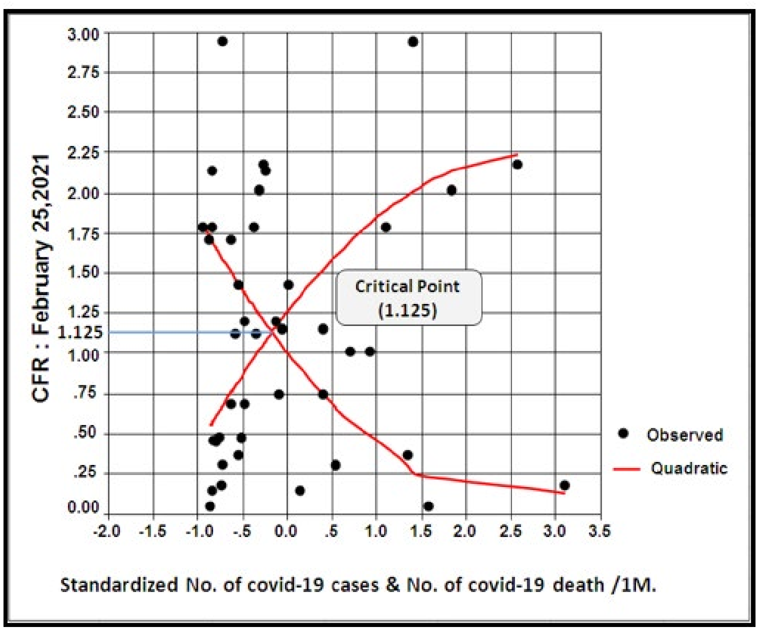

Figure 2: Combining the long term trends of the two graphs which are crossed in the front of the critical-degree calibration process at the CFR axis. CC/M: Crude Covid-19 cases /million population inhabitants, CM /M: Covid-19 crude deaths /million population inhabitants, CFR; case fatality rate %.

Finally, due to assumptions of the normal distribution function of CFR readings and under determination of the confidence levels for the estimation of intervals with the adoption of the critical degree as a center point. Table 4 displays the final results of the estimates of the confidence interval, and according to common levels of significant, which is the scientific evidence that needs to be taken into the consideration when it comes to making any decision about the seriousness of the spread of COVID-19.

Table 4: Determine common confidence intervals take on the critical degree due to different levels of significant.

Level of Significant (*) (Error Type I) P-value	Types of Confidence	Confidence Intervals for population parameter of the critical degree	
		L.b.	U.b.
0.400	One side	1.080948	1.169052
	Two sided at (P=0.200)	0.977418	1.272582
0.300	One side	1.033551	1.216449
	Two sided at (P=0.150)	0.942410	1.307590
0.200	One side	0.977418	1.272582
	Two sided at (P=0.100)	0.897569	1.352431
0.100	One side	0.897569	1.352431
	Two sided at (P=0.050)	0.829029	1.420971
0.050	One side	0.829029	1.420971
	Two sided at (P=0.025)	0.767028	1.482972
0.010	One side	0.691178	1.558822
	Two sided at (P=0.005)	0.636727	1.613273
0.005	One side	0.636727	1.613273
	Two sided at (P=0.0025)	0.560945	1.689055
0.001	One side	0.515486	1.734514
	Two sided at (P=0.0005)	0.464485	1.785515

*Error Type I: Probability of rejection the statistical hypothesis when it's true.

Discussion

Limitations: Underestimation of the number of cases leads to delay lockdown according to currently implemented models, while our model could lead to early lockdown because this leads to higher than actual CFR estimates. High CFR is a common finding in countries with low detection rates. For this reason, proper estimations and adjustments of the number of Covid-19 cases/M (CC/M) are crucial to avoid such bias [11]. Another drawback is the concurrent reduction in economic activity.

Deaths caused by COVID-19 may be misclassified as deaths caused by pneumonia or influenza or misattributed to others. According to CDC three different measures of death counts are used: a count of deaths attributed to COVID-19; an excess death estimates attributed to respiratory illnesses; and an excess death estimate of all deaths [12].

A critical value is a crossed point of two CC/M curves one with CFR, other with CD/M curve. It lies at the front of the critical-degree calibration process at the CFR axis (Figure 2). As CFR decreases with an increase in CD/M, the increased CD/M tends to increase CFR. The net CFR could be high if CD/M is high and CC/M is high [13]. These findings might explain Covid-19 pandemic behavior and epidemics in general.

Results of this study make it easy to define lockdown effectiveness as the ability to keep the CFR as far as possible below the critical level (1.125) and to reduce the total incidence of the disease.

This research introduces a novel idea by estimating CFR critical value. This critical value constitutes a cornerstone for designing lockdown CFR multiple levels of confidence intervals that give a high degree of precision through multiple levels of confidence intervals in making decisions regarding a lockdown time and duration without any doubts.

The timing of lockdown and reopening depends on desired CFR confidence interval for the critical value. This model can be applied at the country level or district/region level when the outbreak is local.

This model will help policymakers in making their decision based on a standardized uniform statistical model. An IT package will help these authorities in different countries to start or release lockdown. An advance option to set further critical points and further CFR coefficient intervals as a desired option to expand the application to (non-listed) options is a desirable option to be added to this package. The latter can be used alternatively when the critical value is re-estimated with more coverage rates and according to statistical re-estimations. This model when adopted will enable authorities all over the world to make strait forward decisions with no debates or objections whether created by the public or by opinions of other experts or authorities. The theoretical background for critical CFR in initiating lockdown is that it is CFR increases with the increase of CD/M (Figure 1 and Table 3), this is consistent with a recent study in this field [13]. This study shows that increased CC/M can lead to an increase in CD/M [13].

Important explanations for increasing CFR is the failure of the health system when the case overload is high [14-16]. A recent study revealed no significant association between the number of hospital beds/100,000 and COVID-19 deaths and suggests other factors [15,17].

Anyhow, increased fatality rates have been described in local settings and clusters cannot be explained by the capacity of health resources. Cluster infections can play critical roles in the widespread of COVID-19 and exponentially increases the number of cases. These findings and suggestions make increase CC/M an important factor that can lead to increase CFR even in robust health systems.

Conclusions

This paper is designed for decisions about COVID-19 lockdowns. The aim of initiating a lockdown is to limit social contact to reduce the number of people getting the disease and to decrease the burden of mortalities. Our model is based on a critical CFR value which was found 1.125. In many countries, the number of COVID-19 patients needing intensive care treatment exceeded the intensive care capacity, especially when MR and CFR exceed a certain level so this aspect is included in this model.

This model set a point for the complete lockdown that is the critical value. The optimal desired interval and partial lockdown set up point can be applied according to the stage of pandemic, herd immunity status, intensive care capacity constraint, and impact on economic activity.

These set points and intervals can minimize large debates raised about initiating or releasing lockdown decisions. Furthermore, it helps decision-makers to announce emergency state and drive the appropriate budget to the health system or to redistribute it to a certain sector.

The novel findings are relevant at a community level since the model is not constrained to impose specific group lockdowns. The model is beyond geographical boundaries and politics. The options for decision-makers will be not been biased and will be beyond personal opinions and doubts.

Data Availability Statement

The original data presented in the study are included in this article/ Supplementary appendices.

Author's Contributions

This work was carried out in collaboration between authors: (Abdulkhaleq A. Ali Ghalib Al-Naqeeb) Find the idea of the research, Designed the study, and formulation the title of the research with the aim of the study in cooperation (with the second author), methodology (i.e. the algorithm of the research), analysis and findings results for the application. (Tareef Fadhil Raham) Gathered the initial data, Wrote introduction, carried out discussion of results (in collaboration with the first author regarding data management) . Both authors read and approved the final manuscript.

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Appendix 1: Data by Country or Territory collected on 25/2/2021(Initial datasheet).

	Country	**CC/M**	**CD/M**	**CFR**	**Test/M**	**Population**	**Total Cases/ total deaths**
1	USA	87,241	1,562	1.79	1,061,640	332,267,383	28,987,289/ 518,951
2	UK	60,990	1,792	2.938	1,297,549	68,118,443	4,154,562/122070
3	Israel	83,227	617	0.741	1,289,359	9,197,590	765,492/5637
4	UAE	38,289	119	0.310	3,016,341	9,968,017	381,662/1182
5	Denmark	36,118	405	1.121	2,853,050	5,805,508	209,682/2351
6	Bahrain	68,904	251	0.364	1,744,847	1,739,498	119,858/437
7	Singapore	10,187	5	0.049	1,239,864	5,880,292	59,900/29
8	Luxembourg	86,742	1,002	1.155	3,306,272	632,578	54,871/634
9	Cyprus	27,789	190	0.683	1,496,689	1,213,082	33,710/231
10	Hong Kong	1,450	26	1.793	1,058,962	7,536,568	10,927/**198**
11	Malta	49,115	703	1.431	1,555,411	442,310	21,724/311
12	Andorra	139,619	1,422	1.018	2,502,974	77,346	10,799/110
13	Iceland	17,652	85	0.481	1,455,688	342,686	6,049/92
14	Gibraltar	125,727	2,731	2.172	5,472,895	33,684	4,235/92 deaths
15	Channel Islands	23,053	492	2.134	2,089,591	174,905	4,032/86
16	San Marino	106,569	2,148	2.015	1,217,935	33,978	3,621/73 deaths
17	Monaco	48,601	583	1.2	1,317,835	39,423	1,916 cases 23 death
18	Bermuda	11,316	193	1.706	2,786,775	62,127	658 cases 1 death
19	Faeroe Islands	13,433	20	0.149	4,704,332	48,984	658 1 death
20	St. Barth	57,896	101	0.174	1,814,287	9,897	573 1 death

21	Cayman Islands	6,508	30	0.461	1,100,328	66,223	431 2 deaths
22	Falkland Islands*	15,233	0	0	1,977,151	3,545	54 cases total no death

*Falkland Islands was excluded due to zero deaths as it is on February 25, 2021. CC/M: Crude Covid-19 cases /million population inhabitants, CM /M: Covid-19 crude deaths /million population inhabitants, CFR; case fatality rate %.

Appendix 2: Countries and territories according to Covid-19 CC /M, CM/1M and crude case fatality rate as it is on February 25, 2021.

Item	Countries	CC/M	CD/M	CFR February 25, 2021
1	USA	87241	1562	1.790
2	UK	60990	1792	2.938
3	Israel	83227	617	0.741
4	UAE	38289	119	0.310
5	Denmark	36118	405	1.121
6	Bahrain	68904	251	0.364
7	Singapore	10187	5	0.049
8	Luxembourg	86742	1002	1.155
9	Cyprus	27789	190	0.683
10	Hong Kong	1450	26	1.793
11	Malta	49115	703	1.431
12	Andorra	139619	1421	1.018
13	Iceland	17652	85	0.481
14	Gibraltar	125727	2731	2.172
15	Channel Islands	23053	492	2.134
16	San Marino	106569	2147	2.015
17	Monaco	48601	583	1.200
18	Bermuda	11316	193	1.706
19	Faeroe Islands	13433	20	0.149
20	St. Barth	57896	101	0.174
21	Cayman Islands	6508	30	0.461

CC/M: Crude Covid-19 cases /million population inhabitants, CM /M: Covid-19 crude deaths /million population inhabitants, CFR; case fatality rate %.

Appendix 3

No.	Country	References for data collection as it was on February 25, 2021
-	ALL	1- COVID-19/Coronavirus Real Time Updates With Credible Sources in US and Canada 2- COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU)". ArcGIS. Johns Hopkins University. 3- WHO Coronavirus Disease (COVID-19) Dashboard https://covid19.who.int/?gclid=CjwKCAiA1eKBBhBZEiwAX3gql_TD3cUixzIROXwHFdS3yNhCxcF79FAYNtFC8mgHVXewA13pOFhEQxoCV1IQAvD_BwE
Further Country - specific References as it was on February ,25,202		
1	USA	1-Track the U.S. COVID-19 Outbreak in Real Time https://www.medpagetoday.com/infectiousdisease/covid19/85354 2- COVID-19 Dashboard. HEALTH CARE FOR THE HOMELESS COMPARATIVE DATA. https://nhchc.org/covid-dashboard/
2	UK	Coronavirus (COVID-19) in the UK. coronavirus.data.gov.uk.
4	UAE	UAE CORONAVIRUS (COVID-19) UPDATES". National Emergency Crisis and Disaster Management Authority (UAE).

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