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Letter to the Editor

Flattening-the-curve associated with reduced COVID-19 case fatality rates- an ecological analysis of 65 countries

Dear Editor,

Zhang et al., recently provided evidence in this journal that the timely supply of adequate medical resources can reduce COVID-19 related mortality[1]. They found that the case fatality rate was 4.5% in Wuhan (where the epidemic was most intense and hospitals overrun) compared to 0.5% in the rest of China where services were not as stretched[1]. Dramatic interventions to increase hospital capacity in Wuhan were associated with a subsequent decline in the case fatality rate in this city.[1] They and others have suggested that high COVID-19 mortality is partly related to hospital capacity being exceeded and as a result patients receiving suboptimal care.[2] A 'flattening the curve' approach has been advocated to prevent this from happening.[2–4] This refers to a combination of strategies to slow the spread of COVID-19 which would in turn spread out the peak of the epidemic and prevent hospital capacity being overrun.[3,4] There has however been considerable heterogeneity in the extent to which countries have attempted to slow the spread of SARS CoV-2.[2,3,5] The United Kingdom, for example, initially favored encouraging the development of herd-immunity[5].

We tested the flattening-the-curve hypothesis by using linear regression to assess the country-level association between crude case fatality rate and cumulative number of COVID-19 infections/100,000 inhabitants controlling for the age of the epidemic (number of days between first case reported and 29 March) and COVID-19 testing intensity (number of tests/100 000 inhabitants; Model 1). In Model 2, health expenditure per capita was also controlled for, and in Model 3 a dummy variable for WHO world region was added. The data was obtained from sources including the European Centre for Disease Prevention and Control (ECDC) data repository (see online supplement for origin and definitions of variables used). The most recent data available as of 29 March 2020 was used.

Complete data was available for 65 countries. Case fatality rate varied between 0.08% and 10.8% (median 1.5%, IQR 0.7–2.9%; STable 1). There was also a considerable variation in the number of COVID-19 cases per capita (median 103, IQR 20–374 cases/100,000) and intensity of testing (median 1236, IQR 332–3822 tests per 100,000).

In all three multivariate models, the case fatality rate was positively associated with the cumulative number of cases (Model 1: Coef. 0.037, 95% CI 0.021–0.052) and negatively associated with the intensity of testing (Model 1: Coef. −0.003, 95% CI −0.004- −0.002; Table 1). The strength of this association did not vary when controlling for health expenditure per capita (Model 2) or WHO world region (Model 3; Table 1).

A parsimonious way to interpret these results is that the countries that have succeeded in slowing the spread of COVID-19 have been able to reduce its mortality via preventing hospitals from being overrun.[1] As such these findings could be interpreted as being supportive of flatten-the-curve campaigns. It is important to note that the estimates of the crude case fatality ratio can be biased upwards by under-reporting of cases and downwards by the failure to account for the delay from diagnosis to death.[6,7] We adjusted for the former and later via controlling for testing intensity and age of the epidemic, respectively. We acknowledge that this method is imperfect. We did not control for other variables such as the age structure and prevalence of comorbidity which may have influenced mortality.[6] Finally, we cannot be certain which component of the flatten-the-curve response was responsible for the reductions in case fatality.

Table 1
Country level, multivariate linear regression of factors associated with COVID-19 case fatality rate.

	Model 1		Model 2		Model 3	
	Coef. (95% CI)	P-Value	Coef. (95% CI)	P-Value	Coef. (95% CI)	P-Value
N	65		59		59	
Cumulative cases	.037 (0.021–0.052)	<0.001	0.040 (0.023–0.056)	<0.001	0.043 (0.023–0.063)	<0.001
Testing intensity	−0.003 (−0.004- −0.002)	<0.001	−0.003 (−0.004- −0.001)	<0.001	−0.003 (−0.004- −0.001)	<0.001
Age of epidemic	−0.0205 (−0.0470–0.0061)	0.129	−0.034 (−0.063- 0.005)	0.019	−0.0300 (−0.0679- 0.0080)	0.119
Health expenditure			−0.0002 (−0.0005- 0.0000)	0.072	−0.0002 (−0.0005- 0.0001)	0.135
Region*						
Asia					Ref.	
Europe					−0.376 (−2.209- 1.457)	0.682
Americas					−0.298 (−2.234–1.640)	0.759
Eastern mediterranean					0.609 (−2.211–3.430)	0.666

* There was only one country from sub Saharan Africa (SSA) and this was therefore combined with the Eastern Mediterranean region. The Western Pacific and South East Asian regions were combined into one Asian region.

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Despite these methodological weaknesses, this study provides further support for the concept that interventions that slow the spread of SARS CoV-2 will reduce case fatality rates.

Authors' contributions

CK conceptualized the study, was responsible for the acquisition, analysis and interpretation of data and wrote the analysis up as a manuscript.

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Ethical approval

The analysis involved a secondary analysis of public access ecological level data. As a result, no ethics approval was necessary.

Informed consent

Not applicable

Declaration of Competing Interest

The author declares that he/she has no competing interests.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jinf.2020.04.007.

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