Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the Editor

Case fatality rate in patients with COVID-19 infection and its relationship with length of follow up☆

Dear Editor,

In their systematic review on the clinical characteristics of COVID-19, Wu and colleagues report a 3.2% case fatality rate (CFR), ranging from 2% to 4% [1] with strong heterogeneity between studies (I^2 =100%). One study from the initial phase of the epidemic in Wuhan showed higher CFR and was responsible of the heterogeneity of results [2]. The authors suggest that higher complication and fatality rate in Wuhan could be due to the limited clinical experience in the initial phase of the epidemic.

When comparing data from China to those from Italy, CFR is the most impressive difference, with data from Italy, and now also from other European countries [3], reporting rates three to ten times higher than in China [1,4].

Other studies tried to justify this difference as due to the extremely old Italian population and provided similar age-specific CFR in the two countries [5]. But this was in an initial phase of the epidemic, when official statistics reported 7.2% CFR in Italy. Now overall CFR reported by routine statistics in Italy, Spain, UK, The Netherlands and France is over 10% [1] and it is difficult to justify the difference only with the older age of patients. Here we propose a simple explanation: the length of follow up.

We report data from the COVID-19 information system set up in Italy by the National Institute of Health and described elsewhere [5,6], diagnosed from February 20 to March 29 and followed up to April 5 in Emilia-Romagna region (approximately 4.5 million inhabitants). Briefly the dataset collects individual information on date of symptom onset, RT-PCR test, hospitalization, intensive care admission, death or recovery for all SAR-2-CoV RT-PCR positive patients in Italy.

The CFR increases with the length of follow up of cases, from 8% for cases diagnosed between March 23 and March 29, to about 20% for those diagnosed from February 20 to March 8 (Table 1). Including only cases with symptom onset (or laboratory diagnosis, when symptom onset was not reported) before March 15, ie with at least 22 days of follow up, we constructed a frequency distribution of the distance from symptom onset to death (Fig. 1a). The median in this subpopulation is 12 days.

The definition of clinically recovered patients includes patients with two consecutive negative swabs and those who had no symptoms in the preceding three days at least. The median time to recovery is 20 days. Given that the minimum follow up in this cohort is 22 days, we are by far underestimating the median time to recovery.

Our data show that, according to the Italian definition of COVID-related death [5,6], the CFR can reach about 20% if we follow up patients for a long enough time to observe the vast majority of deaths. These findings are identical to those in other Italian regions [6]. It is possible that Italian surveillance is now testing only severe cases, thus overestimating CFR, but the increase with increasing observation time

Table 1
cases, deaths and case fatality rate, by calendar period and, for patients with at least 22 days of follow up, by age and sex. Emilia-Romagna region, 2020.

All cases	cases	deaths	Case fatality rate	95% confidence interval
calendar period				
February 10 to March 1	1361	277	20.4	(18.2–22.6)
March 2 to March 8	2133	423	19.8	(18.2–21.6)
March 9 to March 15	4070	595	14.6	(13.5–15.7)
March 16 to March 22	4561	492	10.8	(9.9–11.7)
March 23 to March 29	2897	208	7.2	(6.3–8.2)
Restricted to period from 10/02/2020 to 8/03/2020[a]				
Age				
< 50	771	7	0.9	(0.3–2.6)
50-59	625	27	4.3	(3.1–6.9)
60-69	660	83	12.6	(10.4–16.0)
70-79	775	257	33.2	(30.7–37.9)
> =80	662	326	49.2	(45.0–53.2)
Sex				
males	2129	507	23.8	(22.0–25.7)
females	1290	182	14.1	(12.3–16.1)

[a] One case with missing age and 75 missing sex.

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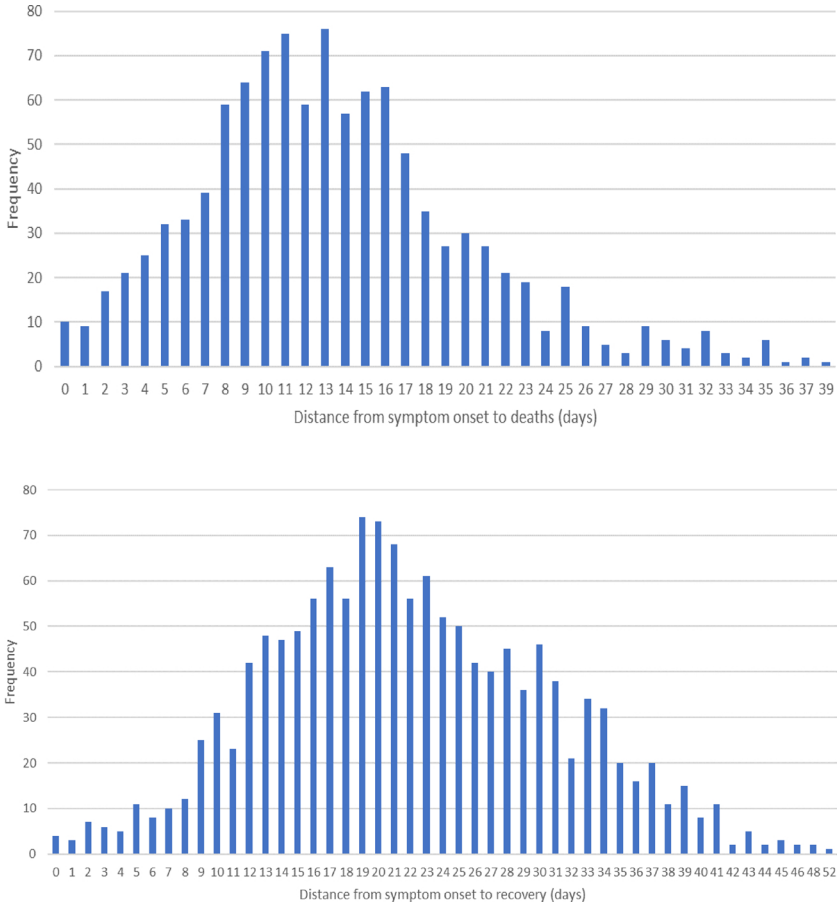

Fig. 1. Frequency distribution of deaths (upper) and recoveries (clinical or virological) (lower) by time since symptom onset or diagnosis (if symptoms are not reported) of COVID-19. Here are included only cases with at least 22 days of follow up, ie with disease onset before March 15. 1064 deaths (52% of the total deaths as of April 5) and 1392 recoveries (63.2% of the total recoveries as of April 5).

is probably generalizable to other case definitions. Unfortunately, previous studies did not focus on this point.

Declaration of Competing Interest

None.

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