COVID-19’s lethality in Italy is a highly discussed figure. When compared with other major countries, Italy’s 9.9% case fatality rate (CFR) as of 24 March 2020 is the highest by far. But relying on this figure is misleading. By itself, the CFR tells us almost nothing about COVID-19’s plausible lethality (infected fatality rate, or IFR). On the opposite, recent studies place China’s IFR at 0.7%. By relying on this figure, ISPI’s best estimate for COVID-19’s plausible lethality in Italy is 1.1%.

The gap between the IFR and the CFR figures can be largely attributed to the number of infected persons that have not been tested and, therefore, escape counting. ISPI estimates that the number of active cases in Italy is at around 530,000 as of 24 March 2020, or almost ten times larger than the official count of 55,000 active cases.

This paper shows that the CFR is an unreliable indicator of COVID-19’s plausible lethality, and there is not enough evidence to suggest that Italy’s IFR is much higher than expected. On the opposite, a direct comparison between the CFR and the IFR is much better placed to paint a more realistic picture of the evolution of the ongoing epidemic.

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Over the past weeks, scholars and observers alike have debated figures around COVID-19, the infectious disease caused by the novel coronavirus (SARS-CoV-2), and Italy has been under the spotlight. At the start of the epidemic in Italy, many wondered why so many cases were surfacing in Italy rather than in other European countries, and why so fast. Today, instead, many ask why the disease appears to have a much higher severity in Italy than elsewhere. By 24 March 2020, Italy’s case fatality rate (CFR) was nearing 10%, while China’s hovered at around 4% and Germany recorded a much lower figure, at 0.5% (Fig. 1).

**Figure 1**

COVID-19: Case fatality rates as of 24 March 2020

As the debate progressed, some even attempted to formulate causal theories to explain why Italy’s CFR was so high, and the disease so widespread. The list ranged from the stress on the national healthcare system to a more lethal strain of the virus, from differences in temperature and humidity to intergenerational ties (i.e., Italians live more often and for longer with their parents and other older relatives, who are at higher risk of being infected).¹

¹ On the virus having mutated, see L. Cuppini, “È vero che in Lombardia si muore di più perché il virus è mutato?”, Corriere della Sera, 21 March 2020. On climate conjectures, see M.M. Sajadi, “Temperature, Humidity and Latitude Analysis to Predict Potential Spread
Are these theories and hypotheses plausible? Given the available data as of today, not much. The issue often stems from the confusion between the case fatality rate (CFR) and the infection fatality rate (IFR). During the evolution of a new epidemic, the only way to understand who is infected is to test for the presence of the virus, and it is only natural that we cannot test the whole population of potentially infected persons. There are at least two reasons why this is so. First, a share of the population can be asymptomatic or paucisymptomatic: they do not know that they are infected, and so do not ask to be tested in the first place. Second, when the epidemic is in its initial phases the number of infected persons grows exponentially or quasi-exponentially, and this makes it necessary to restrict testing to a subset of symptomatic persons, sometimes even restricting it to severe and critical cases.

**Figure 2**

![COVID-19: The “pyramid” of the infected](source)

In a nutshell, in every epidemic there is a pyramid of infected people (Fig. 2). The CFR is based on the share of a “tip”, in that it divides the number of confirmed deaths for the number of confirmed cases. Instead, the IFR is an attempt at estimating the “base” of the pyramid, i.e. the total number of infections, and then divide the number of confirmed deaths by this estimate. Naturally, calculating the IFR is much harder, because it requires to find plausible evidence on the overall prevalence of the disease in a population. However, this estimate is also crucial if we want to get to a realistic figure of the share of people who will die if infected.

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2 We leave aside the case of infected persons who die but who have not been able to be tested, and therefore escape our counts. We assume this number to be low, barring periods of high stress on the healthcare system. The latter did indeed take place and are taking place in Italy, in particular in some cities of the Lombardy region.
CASE FATALITY RATE OR INFECTION FATALITY RATE? ITALY AS A CASE STUDY

In case you need evidence showing that the CFR is not a good estimate for the lethality of a disease, just look at the Italian case (Fig. 3).

In the first days of the epidemic, Italy’s CFR hovered at around 3%, and between 25 February and 1 March 2020 it gradually declined to 2%. After then, it abruptly started to climb, until reaching 9.9% on 24 March.

What explains this trend? A change in testing policy in Italy, that the Italian government asked Italian regions to enforce in order to fall in line with the recommendations of the World Health Organization. If we go back to the start of the epidemic, many were wondering why, in the week following 21 February (the day Italy discovered its own “patient one”), confirmed cases in the country were growing exponentially while other European countries were still lagging behind (Fig. 4).

One obvious answer is that Italy was already far ahead of the other European countries along the epidemic curve. But another factor had been key: between 21 and 28 February, affected Italian regions had conducted a vast number of tests on a wide sample of the population, in particular testing close contacts and relatives of confirmed cases. This testing policy increased the likelihood that infected persons would be found, even if they were asymptomatic. After February 28, instead, Italian regions started to comply with the government’s requests, by limiting testing only to symptomatic cases. Given a lag between tests and results, the effect of this change in testing policy started to have an impact on Italy’s CFR from February 1st onwards.
Another piece of evidence that the CFR is not a good measure of plausible lethality of COVID-19 in Italy is shown in Fig. 5. If we calculate the CFR for the 20 Italian regions, we find that this does not hover close to the national average of 9.9%, but varies widely, from Lombardia’s 13.6% to Basilicata’s 11%. It is hard to believe that the virus could mutate so swiftly from place to place, and that it kills 1 person for every 7 infected in Lombardia, and just 1 person for every 91 infected in Basilicata. This is all the more so because regions with a low CFR can be found both in Italy’s North (Veneto, Valle d’Aosta, Trentino-Alto Adige) and South (Sicilia, Calabria, Sardegna).

This variability between Italian regions is probably the best evidence to date showing that the CFR varies markedly due to differences in testing policies. Remember that, according to the Italian Constitution, healthcare policies are exclusive competence of regions, and therefore regions had ample latitude in deciding their own testing policies, especially in the initial phases of the epidemic in Italy.

Fig. 6 shows the 11 Italian regions with at least 1,000 cases so far, plotting their regional CFRs and the share of confirmed cases found with each test. When the latter figure is low, it indicates that the region has a wide-testing policy, because asymptomatic cases are harder to find (famously, Veneto is one such region, and it is found at the far left of the spectrum). Conversely, when this number is high, it means that the region is testing only symptomatic or highly symptomatic cases. As Fig. 6 shows, there is a clear-cut relationship between testing policies and the CFR, showing that when a region only tests more severe cases, leaving aside mild cases, the CFR will increase linearly. This is crucial evidence indicating that the CFR is not a good measure of the actual lethality of COVID-19 in Italy.
WHAT IS ITALY’S IFR? AND HOW MANY ARE THE INFECTED?

Once established that the CFR is not a reliable measure, we could not go progress any further, unless we find reliable estimates for the IFR. Recently, a number of studies has been published, with converging findings. In one such recent paper, Verity et al. (2020) estimate that COVID-19’s IFR for China is 0.66% (95% CI: 0.38% – 1.33%).[3] This already shows how far plausible lethality rates are from the 4% CFR for China shown in Fig. 1.

On this basis, Ferguson at al. (2020) estimate for the United Kingdom an IFR of 0.9% (95% CI: 0.4% – 1.4%).[4] The British IFR is higher than China’s because Britain’s population is older and, as with many other viruses, COVID-19 appears to be much more deadly for older and more fragile age classes (Fig. 7).

By following in the footsteps of Ferguson et al., we decided to replicate their study by adapting it to the Italian case. As shown in Fig. 8, Italy’s age distribution is a bit older than the UK’s, therefore Italy’s estimated IFR is somewhat higher. We estimate Italy’s IFR to be 1.14% (95% CI: 0.51% – 1.78%).

This leads us to the last part of this paper: while the CFR is an unreliable estimate of how deadly COVID-19 really is, and it does not allow reasonable comparisons across countries, we can still use each countries’ CFR to do something very useful.

Namely, we can compare the CFR with the IFR in order to estimate how many infected people are being missed due to each country’s testing policies or any other reasons. In its rawest form, it is sufficient to divide the CFR by the IFR every day, and then multiply the number obtained by the number of confirmed cases in the
country. When we take this figure and subtract an estimate of plausibly recovered cases (to stay on the safe side, we use the share of recovered persons among confirmed cases, which will likely be an underestimate due to the lower severity of cases that are missed by official counts), we can calculate the number of infected and active cases in each country.

**CONCLUSION**

Good start with the good news. First: Italy’s or any other countries’ high CFR does not mean that COVID-19 is more deadly there than elsewhere, after correcting the country-specific age distribution. With current available evidence it is very hard to argue that COVID-19 is more or less lethal anywhere, due to any host of factors such as the country’s climate, different strains of the virus, or the effect of intergenerational ties.

Second: the CFR is very useful in order to estimate the (plausible) extent of the epidemic in any country. Official case counts are inevitably lagging behind the epidemic, and given that the healthcare system will be focussed on responding to the emergency, there will be little time left to test the many asymptomatic cases that might be around. Having a simple, straightforward way to estimate how much we do not know is crucial.

There are some bad news, as well. First, given that CFRs the world over are almost always above 1%, and very much so in most cases, this means that almost every country has lost touch with the true extent of the epidemic. Again, this is only natural given that governments are under a lot of stress to respond to the

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3 More accurate estimates would take into account that 50% of COVID-19-related deaths occur between the first and fifth day since hospitalization. In Italy, this also tends to be the moment when testing takes place; see Istituto superiore di sanità (2020)
“Characteristics of COVID-19 patients dying in Italy: Report based on available data on March 24th, 2020”, 26 March 2020. We can therefore correct the CFR by accounting for the (lognormal) distribution of likely deaths after a specific number of days after hospitalization. This requires a few more assumptions, but leads to an estimate of plausible active cases in Italy as of 24 March 2020 of 775,000, varying between a minimum of 500,000 and a maximum of 1,350,000<. 
emergency. But, if governments want to stop the contagion from growing uncontrollably, lockdown measures become almost inevitable. When designing interventions for a post-emergency period, there will be an urgent need to map the true extent and geographical distribution of the epidemic, through sampling techniques for testing and “zooming in” on potential outbreaks in order to stop them in their tracks.

Second, despite the contagion being more widespread than originally thought, neither Italy nor any other country is nowhere near reaching the extent of the epidemic that would slow the virus down or even stop it. In fact, if recent estimates of COVID-19’s potential contagiousness are right (R0 = 2.5), “herd immunity” can only be achieved after 60% of the population has been infected and has recovered. For Italy, this is equivalent to 36 million people; but our highest estimates of the infected population, at 1.2 million, are just 3% of that figure.

The fight against the virus will still be long and perilous. Hopefully, this study provided a few useful tools to face this fight head on.