

## Commentaries

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## The COVID-19 Epidemic as a Dynamic System: A Robust, Hypothesis-Free Approach

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The global diffusion of COVID-19 made apparent the many points of friction between scientific modelling (at both the mathematical and the biological levels) and the social and clinical 'empirical' consequences of the crisis. As aptly stressed by Mazzocchi (2020) in referring to the COVID-19 pandemic: "These crises are the result of multiple causes, which interact at different scales and across different domains. Therefore, investigating their proximate causes is not enough to fully understand them."

The need to face the COVID-19 pandemic's economic, political, and psychological consequences requires simple, albeit informative, estimates of the entity of the problem along both space and time dimensions. The classical SEIR (Susceptible, Exposed, Infected, Recovery) compartmental models with the consequent estimation of the Basic Reproduction Number (R) has been proven to generate severely biased estimates of epidemic spreading. The use of R in both popular media and governmental communication has led to misunderstandings and distortions of the real state of affairs. These distortions derive from many 'anomalies' with respect to the ideal case from where the SEIR model stems. These anomalies encompass the lack of ergodicity (the presence of 'super-spreaders', the marked spatial heterogeneity of the disease, the uncertainty of initial data) and the simple fact that R can only register the 'increase of new cases' without explicitly considering the 'healed' compartment, i.e., the 'exit' from the 'infectious basin'. This situation can be equated to the estimate of the level of a hydrographic basin, taking into consideration the in-fluxes without considering the out-fluxes constituted by the emissaries. The situation turns out to be more critical due to the relatively low lethality and morbidity of the virus with a great majority of asymptomatic cases that (especially in the initial period of the epidemic) get unnoticed with a consequent bias in the estimation of



both the actual number of infected persons and lethality of the disease.

Italy is a paradigmatic case of such problems that present a marked spatial and temporal heterogeneity of the epidemic with the much larger number of both fatalities and infections concentrated in Lombardy and, more in general, in the northern part of the country.

The authors thus shifted the attention from the actual number of infected persons (from where classical R-like statistics depend) to the dH/dI ratio (RI) being dH and dI the daily variation of healed and infected numbers. This index was demonstrated to correctly 'catch' the tipping-point of the epidemic, i.e., the discrete time points preceding the transitions of the epidemic going thru initial growth, exponential rise, plateau, and decline phases. Two very simple albeit powerful features of the index allow for reaching this result: 1. The daily differential is much less affected than the absolute number by the uncertainty and fatally non-random sampling of the population, and 2. The 'healed' status is acquired after three negative tests, then is fatally delayed with respect to acquiring the 'infected' condition, so giving to the dH/dI ratio the meaning of an 'acceleration' (positive or negative), acting as a 'second order' derivative of the dynamics catching the inflectionpoints of the time series.

The authors demonstrate the sensitivity of the RI index to such inflection-points (transitions) that go completely unnoticed by the R index.

On the other hand, the recognition of a strict linear relation between the number of accesses to intensive care units (ICUs) and fatalities (both the indexes known without any relevant uncertainty) and their ability to follow the epidemic dynamics allows for simultaneously getting a cross-check of the epidemic dynamics and of the stress on the nation's health system. Finally, yet importantly, a simple logistic model fed with the initial epidemic figures allowed for correctly predicting the timing of the plateau phase of infection. This demonstrated that even largely biased and preliminary evidence permits a reliable forecasting for the subsequent evolution of the crisis.

The authors know very well the difficulty of the task to go from science to the acquisition of the new perspective by regulators. At the same time, however, the huge social consequences of such a crisis asks for a correct assessment of the situation for both regulators and public opinion.

## References

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