Asymptomatic infectives and R_0 for COVID

Giuseppe Gaeta
Dipartimento di Matematica, Universita' degli Studi di Milano
via Saldini 50, 20133 Mlano (Italy)
and
SMRI, 00058 Santa Marinella (Italy)
giuseppe.gaeta@unimi.it
(Dated: 31/3/2020)

We discuss how the presence of a large set of asymptomatic infectives changes our estimate of the COVID-19 basic reproduction number, also known as R_0.

The most basic tool for modeling epidemic behavior is the SIR model [1–5], partitioning the population into Susceptibles, Infected and Infectives, and Removed; in the COVIDcontext, Removed means either healed (or dead) or isolated. The SIR model is – in physicists' language – a mean field one: all individuals are assumed to be equal and interact in the same way with any other one. These assumptions are of course not realistic, but the model ins an important tool to get some intuition about general mechanisms, also present in more refined ones [2].

The SIR equations are

$$\begin{aligned} dS/dt &= -\alpha S I \\ dI/dt &= \alpha S I - \beta I \\ dR/dt &= \beta I \ . \end{aligned} \tag{1}$$

The parameter β is the removal rate, and can be thought of as the inverse of the infection time (time from infection to removal); the parameter α takes into account many factors, such as the capacity of the virus to infect an organism it gets in contact with, the individual protection measures, and the intensity of social contacts.

The number of infectives will raise as long as

$$S(t) > \frac{\beta}{\alpha} := \gamma \ ; \tag{2}$$

this number γ is thus the *epidemic threshold*.

In the SIR equations, the term αSI represents the new infected per unit of time; this means that each infective gives origin to

$$\delta I = \alpha S (\delta t)$$

new infections in the time δt. As each infective is active, on the average, for a time β^{-1}, and in the early phase we can take $S \approx S_0$, this means that each infective will give raise in this phase to

$$R_0 = \frac{\alpha}{\beta} S_0 = \frac{S_0}{\gamma} \tag{3}$$

new infections. This number is the *basic reproduction number* for the model. (The notation R_0 is maybe unfortunate, as it may seem to refer to the initial datum for $R(t)$, but it is traditional and we will keep to it;moreover in the case of COVID – as far as we know – there is no natural immunity, so $R(0) = 0$ and no confusion can arise.) In the case of COVID-19, estimates of R_0 from epidemiological data suggest $R_0 \simeq 2.5 - 3$; this can be compared with R_0 for standard seasonal flu, which is about half.

It is by now clear that in the case of COVID there is a large set of *asymptomatic infectives*. We want to discuss how this affects our estimate of R_0.

In a recent contribution [6] I have introduced a modified version of the SIR model, taking into account the relevant presence of asymptomatic infectives and thus called A-SIR model. In this, there are two classes of infected/infectives individuals, I and J, and two classes of removed ones, R and U. Here I represents the known infectives, J the unknown (in particular, asymptomatic) ones; similarly R represents the registered recovered individuals, while U the unregistered ones – basically those who went through an asymptomatic infection and are removed from the epidemic dynamics only once they are naturally healed. The model assumes that both classes of infectives are equally infective (it would be easy to formulate a variation removing this assumption, but we want to deal with the simplest model accounting for asymptomatic infectives); on the other hand, while symptomatic infectives are promptly removed from the dynamics by Hospital or home isolation, asymptomatic ones stay around for all the infective period. Thus the A-SIR equations are

$$\begin{aligned} dS/dt &= -\alpha\, S\,(I+J) \\ dI/dt &= \alpha\xi\, S\,(I+J) - \beta I \\ dJ/dt &= \alpha\,(1-\xi)\, S\,(I+J) - \eta J \\ dR/dt &= \beta I \\ dU/dt &= \eta J \ . \end{aligned} \tag{4}$$

Note that the last two equations (like the last one for SIR) amount to direct integrations, $R(t) = R_0 + \beta \int_{t_0}^{t} I(y)dy$, $U(t) = U_0 + \eta \int_{t_0}^{t} J(y)dy$.

Here the parameter β represents again the inverse of the removal time for registered infectives, while η represents the removal time for unregistered infectives. In practice, β^{-1} corresponds to incubation time (first COVID symptoms appear usually after about 5 days)

plus some delay for these to be recognized as such; our fitting of early data for the epidemics in Northern Italy gave the value $\beta^{-1} \simeq 7$ days. On the other hand, η^{-1} represents the removal time for undetected infectives; this corresponds to the incubation time plus the time needed for the organism to spontaneously cancel the infection, and our (clinically reasonable) working hypothesis in [6] was $\eta^{-1} \simeq 21$ days.

Here the number of new infected per unit of time is $\alpha S(I+J)$, and again in the early phase of the epidemic we can assume $S \approx S_0$. Thus each infective will give origin in the time span δt to $\alpha S_0 \delta t$ new infectives; we assume that each of these will be registered – and thus isolated after an average time β^{-1} – with probability ξ, while it will remain undetected – and thus disappear from the epidemic dynamic – with a probability $1-\xi$. Current estimates of ξ range from $\xi = 1/10$ to $\xi = 1/7$ [7], albeit smaller values have also been suggested (see [8]; see also [9] in this context).

Thus we should look at the *average removal rate* B or equivalently to the *average infective time* B^{-1} in the early phase of the epidemic; in there the ratio between registered and total infectives is simply

$$x \;:=\; \frac{I}{I+J} \;=\; \xi \;, \tag{5}$$

while in later stages the proportion between I and J changes, as individuals stay longer in the J class than in the I class.

The average removal rate is

$$B \;=\; \xi\,\beta \;+\; (1-\xi)\,\eta \;. \tag{6}$$

This means that each (symptomatic or asymptomatic) infective individual will give direct origin, across its infective and non-isolation period, not to $R_0 = \alpha S_0/\beta$ but instead to

$$\widehat{R}_0 \;=\; \frac{\alpha}{B}\,S_0 \;=\; \frac{\beta}{B}\,R_0 \tag{7}$$

new infectives. As $\beta < B$, this means that the actual basic reproduction number $\widehat{R}_0$ is larger –and possibly substantially larger – than the value which is estimated solely on the basis of registered infections.

A trivial computation on the basis of the values given above – i.e. $\beta^{-1} \simeq 7$, $\eta^{-1} \simeq 21$, $\xi \simeq 1/10$ – provides

$$\widehat{R}_0 \;=\; \frac{5}{2}\,R_0 \;. \tag{8}$$

This could explain why all Health Systems were surprised by the rapid growth of the number of COVID-19 infections; in fact, the presence of a large set of asymptomatic infectives was not realized when the epidemic attacked the first countries, and is becoming clearly established only now [7], also thanks to the large scale epidemiological studies recently conducted in Italy [10].

Acknowledgements

I thank L.Peliti (SMRI), M. Cadoni (Cagliari) and E. Franco (Roma) for useful discussions. The work was carried out in lockdown at SMRI. I am also a member of GNFM-INdAM.

[1] W.O. Kermack and A.G. McKendrick, "Contributions to the Mathematical Theory of Epidemics", *Proc. R. Soc. Lond. A* **138** (1932), 55-83; *Proc. R. Soc. Lond. A* **141** (1933), 94-122

[2] J.D. Murray, *Mathematical Biology. I: An Introduction*, Springer (Berlin) 2002

[3] H.W. Hethcote, "The Mathematics of Infectious Diseases", *SIAM Review* **42** (2000), 599-653

[4] L. Edelstein-Keshet, *Mathematical Models in Biology*, SIAM 2005

[5] N.F. Britton, *Essential Mathematical Biology*, Springer 2003

[6] G. Gaeta, "A simple SIR model with a large set of asymptomatic infectives", `arXiv:2003.08720`

[7] R. Li et al., "Substantial undocumented infection facilitates the rapid dissemination of novel coronavirus (SARS-CoV2)", *Science* 10.1126/science.abb3221 (2020)

[8] J. Lourenco *et al.*, "Fundamental principles of epidemic spread highlight the immediate need for large-scale serological survey to assess the stage of the SARS-CoV-2 epidemic", `https://www.medrxiv.org/content/10.1101/2020.03.24.20042291v1`

[9] `http://www.eecs.qmul.ac.uk/ norman/papers/Coronavirus-death-rates-causal-model.pdf`

[10] E. Lavezzo *et al.*, "Suppression of COVID-19 outbreak in the municipality of Vò, Italy", submitted paper