Targeted adaptive isolation strategy for COVID-19 pandemic

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ABSTRACT

We investigate the effects of social distancing in controlling the impact of the COVID-19 epidemic using a simple susceptible-infected-removed epidemic model. We show that an alternative or complementary approach based on targeted isolation of the vulnerable sub-population may provide a more efficient and robust strategy at a lower economic and social cost within a shorter timeframe resulting in a collectively immune population.

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1. SIR model

We consider the standard susceptible-infected-removed/recovered (SIR) epidemic model (Anderson & May, 1979; Kermack & McKendrick, 1927) (1) to represent the current COVID-19 pandemic:

$$\frac{dS}{dt} = -kSI, \quad \frac{dI}{dt} = kSI - \gamma I, \quad \frac{dR}{dt} = \gamma I, \quad (1)$$

where the parameter k characterises the probability of transmission of infection from the infected (I) to the susceptible (S) fraction of the population, and γ is the rate of recovery, which is assumed to lead to immunity or death (R). The behavior of the model depends on a single non-dimensional parameter $R_0 = k/\gamma$ which is the number of new infections caused by a single infected in a fully susceptible population. The condition for an epidemic outbreak is $R_0 > 1$, otherwise the infection dies out monotonously. Typical estimates of R_0 for the COVID-19 epidemic are roughly in the range 2 – 3.5 (Jiang et al., 2020; Kucharski et al., 2020; Wang, Wang, Chen, & Qin, 2020). We will use $\gamma = 0.2\text{day}^{-1}$ consistent with a typical recovery time of around 1 – 2 weeks (Jiang et al., 2020; Kucharski et al., 2020; Wang, Wang, Chen, & Qin, 2020). A few example solutions of the model in Equation (1) for different values of R_0 are shown in Fig. 1 (a,b).

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Fig. 1. SIR model. (a,b) Solutions of the SIR model with the basic reproduction ratio $R_0 = 1.4, 1.8$, and 2.4 and $\gamma = 0.2\text{day}^{-1}$. Solutions $S(t)$ and $I(t)$ represent the fractions of the susceptible and infected populations over time, respectively. Initial conditions: $S(0) = 0.9999$, $I(0) = 0.0001$, and $R = 0$. (c) Maximum fraction of infected individuals (left axis) and time at which the fraction of infected has its peak (right axis) versus R_0 . (d) Black curve: cumulative total infected fraction $I_{total} = 1 - S(\infty)$ vs R_0 . Red curve: $1 - 1/R_0$, minimum immune proportion needed for collective immunity.

2. Social distancing

Since the large majority of the COVID-19 infected population develops very mild or no symptoms, transmission cannot be eliminated by detecting and isolating symptomatic COVID-19 patients. The so called “social distancing” strategy aims to reduce social interactions within the population decreasing the probability of transmission of the infection, represented by the parameter k in the model. A strong reduction of social interactions may thus lead to $R_0 < 1$ when the infection dies out, as $I(t) \sim \exp(-\gamma(1 - R_0)t)$. If the reduced R_0 is still larger than unity, the result is a smaller epidemic outbreak, with a lower peak value for the infected fraction, and a reduced number of cumulative infections: $I_{total} = 1 - S(\infty)$, where $S(\infty)$ is the susceptible fraction at the end of the epidemic. The total infected population is the solution of the transcendental equation: $\ln(1 - I_{total}) + R_0 I_{total} = 0$ (Fig. 1(d)). A side effect of this reduction, however, is that the duration of the epidemic outbreak increases significantly. The dependence of the peak infected fraction and the time to reach maximum infection are shown in Fig. 1(c). For example, starting with a reference value $R_0 = 2.4$, the time to peak infection is around 35 days. Reducing R_0 to 1.2, extends the time to peak infection to ~ 160 days, while the maximum infected fraction is reduced from $\sim 22\%$ to $\sim 1.5\%$ and the total infected by the end of the epidemic decreases from $\sim 90\%$ to $\sim 30\%$.

Decreasing R_0 by social distancing reduces the total infections and the peak infected fraction, which is critical due to limited hospital capacity, but it has the following possible drawbacks:

- if R_0 remains > 1 , the social distancing can significantly extend the duration of the epidemic, making it difficult to maintain the reduced transmission rate over a long time period in a large population.
- perhaps the most important problem is that there is no clear exit strategy until large scale vaccination becomes available. Since at the end of the epidemic a large proportion of the population remains susceptible to infection, after relaxation of social distancing, the population is highly susceptible to recurrent epidemic outbreaks potentially triggered by remaining undetected or newly imported infections from other regions/countries where the infection has not been eliminated yet.
- social distancing measures over extended period of time applied uniformly to a large population lead to widespread disruption of the functioning of the society and economy therefore it has a huge long term cost.

3. SIR model with vulnerable sub-population

To address these issues, we consider an alternative or complementary strategy. An essential feature of the COVID-19 infections is that it produces relatively mild symptoms in the majority of the population, while it can also lead to serious respiratory problems mainly in the older population (> 70 years of age), or in individuals with pre-existing chronic diseases (Jiang et al., 2020). For example, the hospitalization rate of the symptomatic cases in the 20 – 29 age group is 1.2% out of which 5% requires critical care and 0.03% of the infections lead to death (Zhou et al., 2020). In contrast, for the 70 – 79 age group hospitalization rate is 24.3% out of which 43.2% is critical and the fatality ratio of the infected is 5.1%. Although the transition between these extremes is gradual, a fairly sharp transition takes place around the age of 65. In addition to age, pre-

existing chronic diseases is an additional criteria for identifying a vulnerable group in the population. Based on the limited currently available data around 97 – 99% of deaths due to COVID-19 already had underlying chronic diseases, which is of course very common in the older age groups.

To take into account the markedly different age-dependent outcome of the COVID-19 infection, we extend the standard SIR model by separating the population into two compartments: the low-risk majority population with mild symptoms, and a vulnerable, mainly older population, where infection is more likely to lead to hospitalization and death; see Fig. 2(a). Properties of such multi-compartment epidemic models have been studied previously in (Ferguson et al., 2020; Heesterbeek & Roberts, 2007; Magal, Seydi, & Webb, 2016). The dynamics of the two-compartment SIR model is described by the equations:

$$\frac{dS}{dt} = -k(1-f_v)SI - \mu f_v k S I_v,$$

$$\frac{dI}{dt} = k(1-f_v)SI + \mu f_v k S I_v - \gamma I,$$

$$\frac{dS_v}{dt} = -\mu k(1-f_v)S_v I - \mu f_v k S_v I_v,$$

$$\frac{dI_v}{dt} = \mu k(1-f_v)S_v I + \mu f_v k S_v I_v - \gamma I_v$$

where f_v is the vulnerable fraction and μ is a non-dimensional parameter of a targeted isolation of the high-risk group, and $\mu = 1$ means that there is no isolation everyone mixes the same way. Numerical simulations of this model are shown in Fig. 2.

Both sub-populations follow the SIR dynamics with the important difference that while in the majority population the infections are primarily caused by transmission within this sub-population from infected to susceptible; in the vulnerable minority the dominant route of new infections is via transmission from the majority population to susceptible vulnerable. Therefore we can neglect transmission within the vulnerable population and the infection of low-risk susceptible by infected vulnerable; see Fig. 2(a), dashed transmissions. This approximation is valid when the high-risk group represents a relatively small part of the population.

When we neglect new infections caused by the vulnerable group, the majority population follows the same SIR dynamics in Equation (1) as described above independently of the vulnerable population. Then the infection rate of the vulnerable population is described by:

Fig. 2. (a) Extended SIR model with vulnerable population. S , I , and R are proportions of susceptible, infected, and recovered individuals, respectively, in the low-risk majority sub-population (unshaded) and vulnerable sub-population (shaded). Subscript v represents vulnerable individuals. Dashed curves: negligible transmissions of infection. (b,c) Numerical solutions of the two-compartment SIR model with $R_0 = 2.4$, $\gamma = 0.2\text{day}^{-1}$, $f_v = 0.15$, $\mu = 0.3$. Solutions $S(t)$ and $I(t)$ represent the fractions of the susceptible and infected populations over time, respectively. Initial conditions: $S(0) = 0.9999$, $I(0) = 0.0001$, $R = 0$, $S_v(0) = 1$, $I_v(0) = 0$, $R_v(0) = 0$. (d) Cumulative total infection in the vulnerable population: $R_v(\infty) = S_v(0) - S_v(\infty)$ versus μ and R_0 . Solid arrow: social distancing. Dashed arrow: isolation of the vulnerable population.

$$\frac{dS_v}{dt} = -\mu k(1-f_v)S_v I(t) \quad (3)$$

where μ represents the rate of transmission from the low-risk infected population (I) to vulnerable susceptible (S_v). Thus, the relative proportion of newly infected vulnerable individuals (requiring hospitalization with possibility of death) per unit time is determined by the product $\mu k(1-f_v)I(t)$.

We can also calculate the proportion of the vulnerable population infected over the whole course of the epidemic as:

$$\frac{S_v(0) - S_v(\infty)}{S_v(0)} = 1 - \exp\left(-\int_0^{\infty} \mu k(1-f_v)I(t)dt\right) = 1 - e^{-\mu(1-f_v)R_0 I_{\text{total}}(R_0)}. \quad (4)$$

where the total infected fraction of the low-risk population, I_{total} , is determined by R_0 through the standard SIR dynamics as shown in Fig. 1(d). The validity of this approximation is confirmed by comparison to numerical simulation of the full two-group model; see Fig. 2 (b).

4. Targeted adaptive isolation

Reducing the loss in S_v requires reducing the exponent in Equation (4). While social distancing aims to reduce the total infected population by decreasing R_0 , an alternative or complementary approach focuses resources to shield the vulnerable population. This could be achieved by targeted measures: restricting mobility, providing free home-delivery of food and medication, increased support addressing communication and healthcare needs, and providing separated living space where needed. Since the isolation strategy targets a sub-population, a radical isolation is likely to be more effective than uniform social distancing, and at a smaller cost for the economy and for the general functioning of the society.

The two-group SIR model helps to evaluate such strategies by representing the exposure of the vulnerable population by the parameter μ . Complete isolation and lack of specific isolation efforts correspond to $\mu = 0$ and $\mu = 1$, respectively. The overall fatality of the pandemic is primarily driven by the size of the infected vulnerable population, $R_v(\infty) = S_v(0) - S_v(\infty)$ shown in the contour plot in Fig. 2(d). Social distancing reduces R_0 (horizontal arrow), while isolation of the vulnerable population changes the parameter μ (vertical arrow).

Depending on the epidemiological situation, the public response should be a mixture of the two efforts. However, social distancing may extend the duration of the epidemic (which may affect the sustainability of efficient isolation) and results in insufficient overall immunity of the majority population against a recurrence of the epidemic outbreak.

The targeted intervention likely allows a more substantial reduction in μ , and hence in the total size of the infected vulnerable population. With limited resources available, when the strategy is primarily based on drastic targeted isolation over a shorter time, the end result is a collectively immune population resistant to further infections (“herd immunity”).

It is also apparent that the integral in Equation (4) can be reduced by decreasing μ in a time-dependent manner. This kind of adaptive measure can be implemented by monitoring the progression of the infection $I(t)$ via statistically representative testing of different regions and cities, and intensifying/relaxing the isolation of the vulnerable population accordingly.

Let us consider the case when the low-risk population is $\sim 75 - 80\%$ of the total, and when infected 3% is hospitalized, with 0.2% requiring intensive care (Zhou et al., 2020). Assuming that the intensive care capacity is around $10-20$ per 100000 , this allows for $\sim 5\%$ infected at the peak of the epidemic in the low risk population, as $5\% \times 3\% \times 0.2\% = 3$ per 100000 . An infection peak of 5% corresponds to $R_0 \sim 1.4$ (Fig. 1(b)). By the end of the epidemic, this results in $I_{\text{total}} \sim 0.6$ within the low-risk population (Fig. 1(d)) so that the immunity in the total population is $(1 - f_v) \times 0.6 \approx 45\%$. Assuming that after the epidemic the transmission rate increases back to $R_0 = 2.4$, the minimum immune fraction needed for herd immunity is around 60% . Therefore, relaxing social distancing should happen before the end of isolation to allow for further increase of the immune proportion in the low-risk group and to avoid the spread of infections into the high-risk population.

Our model and conclusions rely on the separation of the population based on age and health into two compartments with very different outcomes and applying differentiated protective measures to a minority high-risk group while allowing for the development of immunity in the rest of the population.

At the time of writing, certain countries follow various combinations of social distancing and isolation. In Sweden, only moderate social distancing is implemented which will likely lead to development of immunity in the population. This strategy, however, without introducing efficient targeted measures to protect the vulnerable population may lead to high mortality and over-saturation of the health care system.

Italy and Spain, on the other hand, implemented severe social distancing, but so far this seems to be unable to stop the progress of the epidemic and may in fact be on track towards achieving large scale infection and immunity in the population. However, with too much focus on the implementation of uniform social distancing and no clear targeted measures for identifying and efficiently protecting the vulnerable sub-population can lead to a scenario with high mortality in spite of the high social and economic costs of an extended and potentially recurrent epidemic.

Another interesting observation is the striking difference between the mortality within the confirmed infected patients in Italy ($\sim 10\%$) compared to Germany ($\sim 1\%$). While there can be multiple reasons for this difference, it is possible that the closer

social and family interactions between the older and younger generations in Italy, indicates a higher baseline value of μ , and/or the current exposure of the disease targets mainly the younger population in Germany with policies in place to decrease the exposure of the vulnerable population.

Declaration of competing interest

We declare that we have no conflict of interest of any kind in relation to the research described in this manuscript. On behalf of the authors, (Zoltan Neufeld, Hamid Khataee and Andras Czirok) Zoltan Neufeld

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