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Letter to the Editor

Herd immunity – estimating the level required to halt the COVID-19 epidemics in affected countries

Dear Editor,

Previous workers have attempted to predict the cumulative number of cases of Coronavirus Disease 2019 (COVID-19) in China.[1] However, since then, the epidemic has rapidly evolved into a pandemic affecting multiple countries worlwide.[2] There have been serious debates about how to react to the spread of this disease, particularly by European countries, such as Italy, Spain, Germany, France and the UK, e.g. from closing schools and universities to locking down entire cities and countries. An alternative strategy would be to allow the causal virus (SARS-CoV-2) to spread to increase the population herd immunity, but at the same time protecting the elderly and those with multiple comorbidities, who are the most vulnerable to this virus.[3]

Before initiating either of these strategies, we need to estimate the *basic* reproductive number (R_0), or the more 'real-life' *effective* reproductive number (R_t) for a given population. R_0 is the number of secondary cases generated by the presence of one infected individual in an otherwise fully susceptible, well-mixed population. R_t is a more practical real-life version of this, which uses real-life data (from diagnostic testing and/or clinical surveillance) to estimate the reproductive number for an ongoing epidemic.

For this anaylsis, we will estimate R_t, and we can do this by applying the exponential growth method,[4] using data on the daily number of new COVID-19 cases, together with a recent estimate of the serial interval (mean = 4.7 days, standard deviation = 2.9 days),[5] at a 0.05 significance level, with the mathematical software R (v3.6.1.).

Using these values of R_t, we can then calculate the minimum ('critical') level of population immunity, P_{crit}, acquired via vaccination or naturally-induced (i.e. after recovery from COVID-19), to halt the spread of infection in that population, using the formula: $P_{crit} = 1-(1/R_t)$. So, for example, if the value of $R_t = 3$ then $P_{crit} = 0.67$, i.e. at least two-thirds of the population need to be immune.[6]

As of 13 March 2020, there were 32 countries outside China with over 100 COVID-19 cases.[7] The seven countries with the highest number of infections were: the United States ($n = 2294$), France ($n = 3671$), Germany ($n = 3675$), Spain ($n = 5232$), Korea ($n = 8086$), Iran ($n = 11,364$) and Italy ($n = 17,660$). The number of confirmed cases in the other 25 countries were less than 1200 (Table 1).

Exploring these parameters and their implications further, the difference between R_0 and R_t is related to the proportion of individuals that are already immune (either by vaccination or natural infection) to that pathogen in that population. So another way of calculating R_t for a pathogen in a given population is by multiplying R_0 by the proportion of that population that is non-immune (i.e. susceptible) to that pathogen.[6] Hence, R_0 will only equal R_t when there are no immune individuals in the population (i.e. when all are susceptible). This means that any partial, pre-existing immunity to the infecting agent can reduce the number of expected secondary cases arising.

Although SARS-CoV-2 is a new coronavirus, one source of possible partial immunity to is some possible antibody cross-reactivity and partial immunity from previous infections with the common seasonal coronaviruses (OC43, 229E, NL63, HKU1) that have been circulating in human populations for decades, as was noted for SARS-CoV.[8] This could also be the case for SARS-CoV-2 and might explain why some individuals (perhaps those who have recently

Table 1
Estimates of SARS-CoV-2 effective reproduction number (R_t) of 32 study countries (as of 13 March 2020,[7]), and the minimum proportion (Pcrit, as% of population) needed to have recovered from COVID-19 with subsequent immunity, to halt the epidemic in that population.

Study countries	Population infected by COVID-19	Estimates of effective reproduction number (R_t) (95% CI), ($n = 32$)	Minimum proportion (%) of total population required to recover from COVID-19 to confer immunity (P_{crit})
R_t >4			
Bahrain	210	6.64 (5.20, 8.61)	85.0
Slovenia	141	6.38 (4.91, 8.38)	84.3
Qatar	320	5.38 (4.59, 6.34)	81.4
Spain	5232	5.17 (4.98, 5.37)	80.7
Denmark	804	5.08 (4.60, 5.62)	80.3
Finland	155	4.52 (3.72, 5.56)	77.9
R_t (2–4)			
Austria	504	3.97 (3.56, 4.42)	74.8
Norway	996	3.74 (3.47, 4.04)	73.3
Portugal	112	3.68 (2.86, 4.75)	72.8
Czech Republic	141	3.57 (2.88, 4.45)	72.0
Sweden	814	3.44 (3.20, 3.71)	70.9
The United States	2294	3.29 (3.15, 3.43)	69.6

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Table 1 (*continued*)

Study countries	Population infected by COVID-19	Estimates of effective reproduction number (R_t) (95% CI), ($n = 32$)	Minimum proportion (%) of total population required to recover from COVID-19 to confer immunity (P_{crit})
Germany	3675	3.29 (3.18, 3.40)	69.6
Switzerland	1139	3.26 (3.05, 4.78)	69.3
Brazil	151	3.26 (2.99, 3.55)	69.3
Netherlands	804	3.25 (3.02, 3.51)	69.2
Greece	190	3.12 (2.67, 3.67)	67.9
France	3661	3.09 (2.99, 3.19)	67.6
Israel	143	3.02 (2.56, 3.59)	66.9
The United Kingdom	798	2.90 (2.72, 3.10)	65.5
Italy	17,660	2.44 (2.41, 2.47)	59.0
Canada	198	2.30 (2.07, 2.57)	56.5
Iceland	134	2.28 (1.90, 2.75)	56.1
R_t (1–2)			
Iran	11,364	2.00 (1.96, 2.03)	50.0
Australia	199	1.86 (1.71, 2.03)	46.2
Belgium	559	1.75 (1.55, 1.97)	42.9
Malaysia	197	1.74 (1.61, 1.88)	42.5
Iraq	101	1.67 (1.41,1.97)	40.1
Japan	734	1.49 (1.44, 1.54)	32.9
Korea	8086	1.43 (1.42, 1.45)	30.1
Singapore	200	1.13 (1.06, 1.19)	11.5
Kuwait	100	1.06 (0.89, 1.26)	5.66

recovered from a seasonal coronavirus infection) have milder or asymptomatic infections.[9]

Finally, returning to the concept of enhancing herd immunity to control the COVID-19 epidemic, given that the case fatality rate (CFR) of COVID-19 can be anything between 0.25–3.0% of a country's population,[10] the estimated number of people who could potentially die from COVID-19, whilst the population reaches the P_{crit} herd immunity level, may be difficult to accept.[3]

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Kin On Kwok*
JC School of Public Health and Primary Care, The Chinese University of Hong Kong, Hong Kong Special Administrative Region, China

Florence Lai
Department of Cardiovascular Sciences, University of Leicester, United Kingdom

Wan In Wei, Samuel Yeung Shan Wong
JC School of Public Health and Primary Care, The Chinese University of Hong Kong, Hong Kong Special Administrative Region, China

Julian W.T. Tang*
Respiratory Sciences, Clinical Microbiology, University of Leicester, 5/F Sandringham Building, Leicester Royal Infirmary, Leicester LE1 5WW, United Kingdom

*Corresponding authors.
E-mail addresses: kkokwok@cuhk.edu.hk (K.O. Kwok), Julian.Tang@uhl-tr.nhs.uk (J.W.T. Tang)

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