COVID-19 endemicity: a taste of the future

The COVID-19 pandemic, which started in December 2019, is still raging in the world. It has been reported from 213 countries and two satellite territories[1], and had started from late December 2019 to March–April 2020 (ref. 2).

In March, one of us (T.J.J.) had projected the natural evolution of the pandemic to an endemic disease in all regions of the world, and named it as a state of 'pan-endemic'[3]. The transmission dynamics with basic reproduction number (R_0) and effective reproduction number, R, and their relationships with epidemic and endemic states were also described. In several countries that had already seen the epidemic curve peak and decline, the disease continues to have a low-level incidence that fits well with the concept of persistent endemic prevalence.

When weekly numbers are low and steady, the number of daily new infections approximates the number of daily births in the country and the prevalence is endemic. The weekly numbers of ascending and descending limbs rise and fall respectively, not having reached a steady state. In the steady state of endemicity, following the descending limb of the epidemic curve, the weekly numbers of infected individuals should remain at a steady low level. This represents a state wherein hitherto uninfected subjects are exposed in small numbers to the virus. We do not know what proportion of the population remains uninfected and is susceptible to infection; however, we expect a large pool of susceptible individuals to remain after the epidemic and sustain endemic transmission. The number of susceptible subjects will also increase as a function of time through new births.

When weekly numbers are low and steady, the prevalence is endemic and $R = 1$. For endemic seasonal diseases like influenza, R may fluctuate in a cyclical fashion between >1 and <1, but the annual average of R remains about 1. We have chosen seven weeks starting on 1 June in four countries that already show low incidence and steady-state prevalence, indicating $R = 1$. We assume that a seven-week period is long enough to assess steady state.

It is important to know whether this endemic state is reached in some countries and the proportion of the population affected in the endemic state to aid healthcare planning. The purpose of this correspondence is to illustrate how the steady endemic state has already been reached in countries that have transitioned from epidemic phase to endemic phase. In countries with a large and heterogeneous population demography it is possible that there may be more than one peak in the epidemic curve, the first or primary wave due to rapid urban spread is usually large and a secondary wave may occur after urban cases have decreased but cases in small towns and villages increase in number. Sometimes the second wave may just merge with the first wave and be represented as a hump on any part of the epidemic curve or even after reaching endemic phase as outbreaks. Countries that succeeded in 'flattening' the epidemic curve early, will have larger proportion of uninfected persons by the end of the first wave. In such cases the second wave may be larger than the first.

We obtained information on the weekly number of new cases from Worldometer coronavirus for the countries whose epidemic curve indicates a clear peak followed by a descent and a low level of incidence of new cases thereafter. The four countries which showed this pattern were Germany, Italy, Republic of Korea and Taiwan[4–7]. The total population of these countries was also obtained from the same source. The mean numbers during the phase of endemic persistence were expressed as a percentage of the number of cases during the peak week and as a percentage of the population.

In Germany, with a population of 84 million, the epidemic began in the first week of March, reached a peak in the last week of the month (number – 26 March to 1 April: 40,658) and declined to low numbers in the last week of May. From 1 June till 18 July, the weekly number of cases was: 1931, 1551, 3545, 3114, 2554, 2254 and 2395 (mean 2478)[4]. These numbers show a relatively steady state of prevalence without wide fluctuations, wherein $R = \sim 1$. The mean weekly infection during endemic persistence was 6% of the peak week (2478/40,658) and incidence 29 per million (0.0029%) population.

In Italy (population 60 million) the epidemic started in February (or even earlier), peaked in the last week of March (number – 21 to 27 March, 39,437) and declined to relatively low numbers by the end of May. From 1 June till 18 July, the weekly number of cases was 1607, 1655, 1687, 1250, 1109, 1218 and 1155 (mean 1383)[5], showing steady state and $R = \sim 1$. The mean weekly infection during endemic persistence was 3.5% of the peak week (1383/39,437) and incidence 23.05 per million (0.0023%) population.

In South Korea (population of 51 million), the epidemic started in mid-February, reached a peak in the first week of March (number – 28 February to 5 March: 4224) and declined to low numbers by the third week of April. From 1 June till 18 July, the weekly number of infections was 216, 275, 288, 232, 315, 282 and 294 (mean 271)[6], showing steady state and $R = \sim 1$. The mean weekly infection during endemic persistence was 6.4% of the peak week (271/4224) and incidence 5.3/million (0.00053%) population.

In Taiwan (population 23 million) the epidemic started in mid-February, peaked in the third week of March (number – 21 to 26 March: 144) and declined to very low numbers in mid-May. From 1 June till 18 July, the weekly number of cases was 0, 0, 3, 1, 2, 2 and 3 (mean 1.57)[7], showing steady state and $R = \sim 1$. The mean weekly infection during endemic persistence was 1.1% of the peak week (1.57/144) and incidence 0.07/million (0.00007%) population.

The shape of the epidemic curve in these four countries clearly shows that after a peak, there was a progressive decline followed by a steady state of weekly incidence of infections without major fluctuations, features of the curve which indicate that the epidemic has entered a persistent endemic state.

Table 1 summarizes the data. The mean weekly number of infections during the seven-week period of endemic persistence is presented, expressed also as a percentage of the number of infections during the peak week. Further, the mean number of weekly new infections during the seven weeks of endemic persistence is expressed as number per million population. It is apparent that the two countries which had higher incidence in the peak week had higher

Table 1. Comparison of weekly new cases from the four countries studied[4–7]

Country	Population (million)	Number of people infected at peak seven days	Infections at peak per million population	Average numbers during endemic persistence	Infections during endemicity/infections at peak %	Infections during endemicity per million population
Germany	84	40,658	484	2,478	6	29.5
Italy	60	39,437	657	1,383	3.5	23.05
South Korea	51	4,224	83	271	6.4	5.31
Taiwan	23	144	6.3	1.57	1.1	0.07

incidence during the seven weeks of endemic persistence, than the other two countries with lower incidence at peak and endemicity.

Table 1 presents the total population, number of infections at peak week, average number of infections per week during endemic persistence (actual numbers and as percentage of the peak) and the number of new infections per million population during endemic persistence.

Our analysis shows that the four countries with populations ranging from 23 to 84 million that had experienced peak of the epidemic during March have now evolved to a state of endemic prevalence of COVID-19 over seven consecutive weeks from 1 June to 18 July. It is reasonable to assume that this is likely to be the natural history of the epidemics in these and other countries. We may therefore anticipate similar endemic persistence in all countries over the next weeks to months, modified only by control measures such as lockdown and other personal protective measures adopted by the citizens.

In the early days of the pandemic, R_0 was calculated to be between 2 and 3.9 (ref. 8). Accepting it to be 2.5, herd immunity between 50% and 75% has been assumed to be sufficient to stop the spread of SARS-CoV-2, using the formula $1 - 1/R_0$ (ref. 9). The authors define herd immunity as 'a level of population immunity such that disease spread will decline and stop even after all preventive measures have been relaxed' (ibid). Others have called the herd immunity level required for stopping transmission as the 'herd immunity threshold'[10].

No infection has ever stopped from transmission spontaneously after reaching high level of herd immunity. The concept of herd immunity threshold applies only to vaccine-induced herd immunity[10]. While a proportion of individuals (100 – herd immunity level) remain non-immune and susceptible to infection, and, births continuously add infection-naïve children to the community (globally 140 million annual birth cohort), SARS-CoV-2 will continue as an endemic infection.

After the first major epidemic evolves as an endemic phase, the risk of minor outbreaks will remain on account of the presence of both the endemic virus and large number of susceptible people – those who escaped the first wave of the epidemic and the new birth cohorts. Such outbreaks are now occurring in three of the four countries in this study – Germany, Italy and South Korea[4–6].

We must anticipate that in the absence of a safe and effective vaccination strategy, the high risk of severe disease and high case-fatality rate of >5% among those above 65 years of age and subjects of any age with chronic non-communicable diseases (diabetes, hypertension, chronic lung, heart, kidney, liver diseases) will continue even during endemic prevalence. Continuing use of the mask and cocooning of the elderly[11] and vulnerable should continue till universal vaccination is achieved and the disease eradicated.

The current vaccination platforms in developing countries are the expanded programme on immunization and the antenatal vaccination programme. Vaccination of all others are generally on a voluntary basis in all countries. With the endemic persistence of the COVID-19 epidemic, the world needs to invent and implement innovative vaccination approaches to protect senior citizens and others vulnerable to severe COVID-19. If such an innovative vaccination platform is put in place, global eradication of COVID-19 is an attractive and feasible proposition[12].

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Received 29 July 2020; accepted 21 November 2020

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