Herd immunity, COVID-19 and vaccination: some propositions

Srijit Mishra

In the backdrop of the Great Barrington Declaration and the John Snow Memorandum, a critical look into the math of herd immunity for COVID-19 suggests that the goal should be to reach the threshold through multiple interventions, that any vaccine intervention should show efficacy beyond the threshold for relative and absolute risks in and beyond trials, that recognizing proximate impact, introducing public provisioning and focusing on groups with greater exposure can all reduce the proportion required for direct intervention to reach the threshold. Besides recognizing the advantages of natural immunity, the ethical imperative requires no excessive focus on a single disease or type of care and does not mandate any specific care.

Keywords: COVID-19, herd immunity, proximate impact, public provisioning, vaccination.

THE onset of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) with its murky origin[1], and its associated coronavirus disease of 2019 (COVID-19) leading to a pandemic that adversely affected lives and livelihood have brought forth two broad scientific views. The Great Barrington Declaration (hereafter, the Declaration), to minimize the adverse impact of the economy on the underprivileged and to address public health concerns beyond COVID-19, called for focused protection of the high-risk population while allowing the low-risk population to participate in their day-to-day activities with care and caution[2]. A cyclic strategy of work–exit–work taking advantage of the latent period of the virus to arrive at a balance between health and economy, can also be considered as a perspective that fits with the Declaration[3]. As against this, the John Snow Memorandum (hereafter, the Memorandum), while agreeing that lockdown restrictions have affected physical and mental health and also harmed the economy, was against opening up the economy to the low-risk population and argued for controlling community spread untill a safe vaccine or therapeutic medication was available[4].

The proponents of the Declaration indicated that the wait for a safe vaccination or administering one with emergency use authorization would have a greater adverse impact on lives and livelihood, and therefore herd immunity through natural infection along with focused protection would be better. However, proponents of the Memorandum believed that opening up without controls would take more lives, and hence one ought to vaccinate even if it is emergency use authorization to attain herd immunity[5]. Cataclysmic fear of death from COVID-19 led to some vaccines receiving country-specific as also World Health Organization (WHO) approval for emergency use authorization since late 2020/early 2021 (ref. 6).

There have been calls to ensure safe and effective vaccination against COVID-19 as a global common good[7]. In addition, there could be difficulties because vaccines do not prevent transmission, there are inequities in vaccine distribution, vaccines are ineffective with new variants, waning vaccine immunity and increased interaction after vaccination[8].

At the same time, concerns have been raised on the advantages of natural immunity after infection as with other viruses[9], possible harm due to adverse events[10] and the importance of informed consent and social beneficence[11]. Nevertheless, the vaccination drive, in line with the Memorandum, persisted and continued without the necessary checks and balances. This was aided by lies told[12], censorship of alternative views[13], methodological and ethical concerns in reporting observational data[14], and math murder[15].

Given these, what ought to be the approach for vaccination or any intervention to address the spread of an infectious disease like COVID-19? In this context, the maths of herd immunity helps derive five propositions and suggests three ethical concerns.

The maths of herd immunity

Now, the propositions. First, for an infectious disease, public health interventions to obtain herd immunity ρ, will depend on the threshold level θ, derived from the reproduction number $R_0 > 1$ (ref. 16), from which is deducted a parameter μ, depicting the impact of interventions, including network impact[17], such that

$$\rho = \theta - \mu, \tag{1}$$

Srijit Mishra is at the Indira Gandhi Institute of Development Research, General AK Vaidya Marg, Goregaon East, Mumbai 400 065, India.
e-mail: srijit@igidr.ac.in

$$\theta = 1 - R_0^{-1}, \tag{2}$$

$$\mu = \sum_i \sum_j \mu_{ij}. \tag{3}$$

In eq. (3), $i = 1, \ldots, m$ denotes public health interventions, $j = 1, \ldots, n$ denotes individuals, and μ_{ij} denotes the impact of the ith intervention on the jth individual (for analytical purposes, the impact of interventions is considered as mutually exclusive, which implies that interaction effects are considered independently and double counting is avoided; however this does not preclude a package of practices be considered as an intervention). Equations (1)–(3) give

Proposition 1: For an infectious disease with $R_0 > 1$, herd immunity would be achieved if aggregation of impact from all interventions is equal to the threshold level, $\rho = 0 \leftrightarrow \mu = \theta$.

Second, for any single intervention, the population can be divided into three categories, $k = d, p, s$, referring to three broad average policy impacts: direct impact, proximate impact on account of network externality and secluded with no impact respectively[18]. The decision to vaccinate can also depend on network-based proximate impacts[19], but in the current context, one is looking into the possible advantages of being in proximity to those receiving the direct impact. Incorporating the three impacts, eq. (3) can be written as

$$\mu_i = \sum_{k_i} \delta_{k_i} \alpha_{k_i} = \delta_{d_i} \alpha_{d_i} + \delta_{p_i} \alpha_{p_i} + \delta_{s_i} \alpha_{s_i}. \tag{4}$$

In eq. (4), the population share of the k_ith category is $\delta_{k_i} = n_{k_i}/n \le 1$, where n_{k_i} is the population of the k_ith category and n is the total population, such that

$$\sum_{k_i} n_{k_i} = n \text{ and } \sum_{k_i} \delta_{k_i} = 1.$$

It would be prudent to restrict δ_{p_i} to a range $0 \le \delta_{p_i} < R_0 \delta_{d_i}$, where the lower limit explains that there will be no proxymate impact if all those who could have benefitted are now recipients through direct impact. The upper limit suggests that advantages from proximate impact while being independent of the disease-diffusion mechanism will be constrained by it and hence $\delta_{p_i}/\delta_{d_i}$ cannot be greater than the reproduction number. The efficacy of impact on the k_ith category will be $\alpha_{k_i} \in [-1, 1]$, where a negative value refers to an adverse effect. By implication, for a positive direct impact, $\alpha_{p_i} \le \alpha_{d_i}$, and $\alpha_{s_i} = 0$. This gives

Proposition 2: For an infectious disease with $R_0 > 1$, the efficacy of direct impact of an intervention should be greater than the threshold level $\alpha_{d_i} > \theta$.

Third, superimposing from propositions 1 and 2 that $\mu = \theta$ and $\alpha_{d_i} > \theta$ respectively, and rearranging eq. (4) gives the population share.

$$\delta_{d_i} = \frac{\theta - \alpha_{p_i}(1 - \delta_{s_i})}{\alpha_{d_i} - \alpha_{p_i}}. \tag{5}$$

This gives

Proposition 3: For an infectious disease with $R_0 > 1$, given $\mu = \theta$ and $\alpha_{d_i} > \theta$, if for a combination of proximate impact $\alpha_{p_i} > 0$, and proportion secluded $\sigma_{s_i} < \theta$, the proportion requiring direct intervention is equal to the threshold $\delta_{d_i} = \theta$, then, *ceteris paribus*, the proportion requiring direct intervention will be lower than the threshold when (a) the proximate impact is greater, $\sigma_{d_i a} < \theta$ when $\alpha_{p_i a} > \alpha_{p_i}$, or (b) the proportion secluded is lower, $\delta_{d_i b} < \theta$ when $\delta_{s_i b} < \delta_{s_i}$.

Fourth, let us introduce two different policy situations, $l = q, r$. Here q allows public provisioning of the intervention leading to direct impact and does not discriminate because of paying capacity of individuals or other non-epidemiological considerations. There is no seclusion, $\delta_{s_i q} = 0$. As against this, r allows some form of discrimination based on non-epidemiological considerations, such as open market provisioning with price variation. This is likely to seclude some proportion of the population, $\delta_{s_i r} > 0$. It follows that

$$\delta_{d_i r} - \delta_{d_i q} = \frac{\alpha_{p_i} \delta_{s_i r}}{\alpha_{d_i} - \alpha_{p_i}} \ge 0. \tag{6}$$

This gives

Proposition 4: For an infectious disease with $R_0 > 1$, the proportion requiring direct intervention to reach the threshold will be greater if the intervention is discriminatory, $\delta_{d_i r} > \delta_{d_i q}$, and it leads to seclusion, $\delta_{s_i r} > 0$.

Fifth, let us introduce a two-group scenario (say $g = u, v$), where one of the groups has a greater possibility of reproduction $R_{0u} > R_{0v}$, such that $R_0 = \sum_g \delta_g R_{0g}$, $\sum_g \delta_g = 1$. It follows that

$$\tilde{\theta} = \sum_g \delta_g \theta_g < \theta; \theta_g = 0 \leftrightarrow R_{0g} \le 1, g = u, v. \tag{7}$$

This can be extended to multiple groups such that $\tilde{\theta} = \sum_g \delta_g \theta_g < \theta$; $g = 1, 2, \ldots, G$. This gives

Proposition 5: For an infectious disease with $R_0 = \sum_g \delta_g R_{0g} > 1$, if the intervention is prioritized based on R_{0g}, then the weighted threshold level will be lower than the threshold level, $\tilde{\theta} < \theta$.

In addition, there are three ethical concerns. First, $\alpha_{ij} \not< 0$; the efficacy of an intervention, direct or proximate, should not be negative for any individual. This is in line with the dictum of 'do no harm'. Second, $\sum_i \alpha_{ij} \not> 1$ $\forall j$; the aggregation of efficacy for any individual should not be greater than unity. This is in line with the judicious use of limited resources because more than the required use by some will lead to unnecessary additional expenses and could exclude others. Third, $\mu \not> \theta$; the overall efficacy should not exceed the threshold. This aligns with the effective use of resources from a public health perspective. Given the limited resources, the less we use them for a particular disease, the more we will have for other diseases or other socio-economic concerns.

Let us now discuss the propositions and ethical concerns with examples and counterfactuals. The discussion will also make a comparative assessment between the Declaration and the Memorandum.

Discussion

To aid this, quarterly data for three years, 2020–22, for six COVID-19-related indicators, viz. reproduction number (maximum), stringency index (average), cases per million, deaths per million, vaccines per 100 (cumulative), and real income (2019 = 100) are given for four selected countries, namely India, Japan, Kenya and USA (Table 1)[20–22]. Some of these are also indicated in Figures 1–3 on reproduction number (daily)[20], stringency index (average)[20], and vaccines per 100 persons (cumulative)[20,21] respectively.

First, for COVID-19, an estimate indicates $R_0 = 3$ (ref. 23). However, trends in Figure 1 and quarterly maximum data in Table 1 suggest that except for the peaks during the early months of 2020 or late 2021/early 2022, $R_0 < 2.5$, while for the latter part of 2020, R_0 was around 1.5 or lower. These suggest that the threshold level will be context-specific. For $R_0 = 3$, $\theta = 0.67$.

For India, with $R_0 = 2.5$, the threshold value will be 50%, $\theta = 0.5$. Thus, following proposition 1 and eq. (1) as a first principle, multipronged interventions can be restricted to 50%, $\mu = 0.5$, as a reasonable goal. Further, following the advantages of natural immunity[9], one can exclude those already recovered, which according to seroprevalence estimates, had reached 20% by the end of 2020 (ref. 24).

Second, independent of the advantages of natural immunity or those with lower risks, an intervention should be such that the efficacy of direct impact is greater than the threshold level $\alpha_{d_i} > \theta$, as in proposition 2. Alternatively, the proportion requiring direct intervention to reach the threshold will be $\delta_{d_i} = \theta / \alpha_{d_i}$. For this, efficacy in both relative and absolute sense matters, and should be taken into consideration by the regulatory authorities. Five COVID-19 vaccines that received emergency use authorization in early 2021 had their efficacy in terms of relative risk reduction that ranged from 67% to 95% highlighted, while their absolute risk reduction that ranged from 0.8% to 1.3% remained hidden in fine print[25].

Even if one keeps aside the possibility of lower absolute efficacy, one could look for possible proximate impact. For instance, if in a household there are two individuals who, if infected, can pass on the same to the other, but only one of them is exposed to additional risks of being infected because of occupational or other reasons, then by providing immunity through a specific intervention to the individual with a greater additional risk of being infected, one pre-empts any risk for the other individual also.

Third, the proportion receiving direct intervention can be lower than the threshold level if (a) either the proximate impact is greater or (b) the proportion secluded is lower. Now, let $\theta = 0.67$, $\alpha_{d_i} = 0.95$, $\alpha_{p_i} = 0.25$, $\delta_{s_i} = 0.2$, then $\delta_{d_i} = \theta$. For (a), if $\alpha_{p_i a} > 0.25$, we will have $\delta_{d_i a} < \theta$, such that, if $\alpha_{p_i a} = 0.30$, then $\delta_{d_i a} = 0.66 < \theta$. Similarly, for (b), if $\delta_{s_i b} < 0.2$, we will have $\delta_{d_i b} < \theta$, such that, if $\delta_{s_i b} = 0.15$, then $\delta_{d_i b} = 0.65 < \theta$. Note that the population that has been secluded from a safe and effective intervention could be for epidemiological reasons, and inability to pay, among others.

Fourth, to compare and contrast scenarios with and without public provisioning, let $\theta = 0.67$, $\alpha_{d_i} = 0.95$, $\alpha_{p_i} = 0.25$, $\delta_{s_i q} = 0$, $\delta_{s_i r} = 0.2$, then $\delta_{d_i q} = 0.60$, $\delta_{d_i r} = 0.67$ and $\delta_{s_i r} - \delta_{s_i q} = 0.07$. This shows that under public provisioning the proportion requiring direct intervention will be seven percentage points less to reach the threshold level. This also means that public provisioning gives greater space for seclusion due to epidemiological reasons, whereas absence of public provisioning not only reduces that space but also allows seclusion on account of other reasons, such as inability to pay. Thus, justifying the call for COVID-19 vaccines as a global common good[7], if they satisfy safety (including from adverse effects) and efficacy (including relative and absolute risk reductions) parameters. The space for seclusion also suggests that public provisioning or regulation should not be interpreted to mean that coercion of any form (with or without persuasion) should be used to achieve the goal. That would be ethically inappropriate.

Fifth, some sub-groups, like healthcare workers or vendors, may have greater exposure and risk and hence a higher reproduction number (say, in the range 1.3–7.7, approximately averaging to 5.0)[26]. This calls for group-specific intervention. Let $R_0 = 3$, $R_{0u} = 5$, $\delta_u = 0.2$, $\delta_v = (1 - \delta_u) = 0.8$, then $R_{0v} = 2.5$. It follows that $\theta = 0.67$, $\theta_u = 0.8$, $\theta_v = 0.6$, $\tilde{\theta} = \sum_g \delta_g \theta_g = 0.64 < \theta$; $g = u, v$. This shows that the weighted average threshold of 0.64 is lower than the base level threshold of 067. Incorporating proximate advantages and public provisioning to the two sub-groups such that $\alpha_{d_i g} = 0.95$, $\alpha_{p_i g} = 0.25$, $\delta_{s_i g} = 0 \forall g$, then $\delta_{d_i u} = 0.79$, $\delta_{d_i v} = 0.50$. Weighted average of proportion requiring direct intervention, $\tilde{\delta}_{d_i} = \sum_g \delta_g \delta_{d_i g} = 0.56$, will be less than the proportion requiring direct intervention without prioritization (recall, $\delta_{d_i q} = 0.60$).

The moot point from a discussion of the propositions is that the goal of the intervention need not be the entire population. This also means that public provisioning can go hand in hand with informed consent, an ethical imperative.

Table 1. Select COVID-19 indicators for each quarter in four countries, 2020–22

Country	Year	Quarter	Reproduction rate, maximum	Stringency index, average	Cases per million	Deaths per million	Vaccines per 100, cumulative	Real income, 2019 = 100
India	2020	Q1	2.44	31.3	1.0	0.0	0.0	102.2
		Q2	2.59	89.8	418.8	12.5	0.0	77.6
		Q3	1.27	86.1	4097.3	58.1	0.0	93.8
		Q4	1.00	67.1	2837.4	35.9	0.0	100.7
	2021	Q1	1.45	63.0	1378.7	9.9	4.6	103.7
		Q2	1.50	77.5	12936.0	168.2	23.4	93.4
		Q3	1.11	72.2	2381.6	34.7	62.9	101.1
		Q4	2.10	56.6	775.9	23.5	102.7	105.7
	2022	Q1	2.67	63.2	5775.4	28.1	130.3	108.0
		Q2	1.56	40.4	313.2	2.8	139.5	106.5
		Q3	1.16	33.4	790.8	2.5	154.1	106.9
		Q4	1.30	30.3	62.4	1.4	154.8	–
Japan	2020	Q1	2.21	27.7	18.0	0.5	0.0	98.2
		Q2	2.05	38.5	130.5	7.2	0.0	90.1
		Q3	1.82	31.7	519.1	4.8	0.0	95.0
		Q4	1.48	38.3	1217.3	15.3	0.0	99.5
	2021	Q1	1.60	47.6	1917.1	45.5	0.8	97.1
		Q2	1.33	49.2	2602.4	45.0	42.8	97.2
		Q3	1.84	51.3	7271.3	23.0	136.4	96.5
		Q4	1.59	47.2	227.0	6.0	162.4	100.4
	2022	Q1	4.08	47.0	38904.0	78.4	208.2	97.7
		Q2	1.27	43.1	22310.5	25.5	230.0	98.5
		Q3	1.81	37.1	96566.9	110.1	262.7	98.1
		Q4	1.35	31.7	64192.2	99.9	301.3	–
Kenya	2020	Q1	0.00	52.9	1.1	0.0	0.0	104.3
		Q2	1.60	88.0	121.6	2.8	0.0	95.8
		Q3	1.33	74.5	617.2	10.8	0.0	97.0
		Q4	1.49	51.1	1106.2	18.3	0.0	101.9
	2021	Q1	1.50	52.6	714.5	9.2	0.3	106.9
		Q2	1.22	70.7	947.6	28.0	2.6	106.3
		Q3	1.26	57.9	1228.5	28.0	7.1	106.5
		Q4	2.87	43.3	854.0	4.8	18.7	109.1
	2022	Q1	1.11	52.9	529.3	5.0	32.5	113.7
		Q2	1.72	48.6	190.6	0.1	34.4	112.5
		Q3	1.08	35.8	87.5	0.5	39.7	–
		Q4	1.62	25.0	74.7	0.2	42.4	–
United States of America	2020	Q1	3.61	22.5	572.8	16.0	0.0	100.8
		Q2	1.85	72.0	7316.9	363.6	0.0	91.6
		Q3	1.26	66.6	13680.1	233.6	0.0	98.0
		Q4	1.28	68.5	38564.6	430.0	1.7	98.5
	2021	Q1	1.09	67.6	30777.5	587.7	51.2	102.0
		Q2	1.09	56.6	9507.9	155.6	100.6	103.1
		Q3	1.53	51.2	28939.2	285.2	119.4	102.8
		Q4	1.68	50.8	33682.2	381.3	154.4	104.1
	2022	Q1	1.64	42.6	74994.8	466.9	168.0	105.8
		Q2	1.31	29.1	22044.2	101.5	177.2	104.9
		Q3	1.16	27.9	25661.1	124.6	184.9	104.8
		Q4	1.30	27.2	12988.8	97.9	196.4	–

Note: The population density (sq. km) for the selected countries is 450 for India, 348 for Japan, 87 for Kenya, and 36 for USA[20]. For reproduction rate, the maximum reported for any day in that quarter is given[20]. For Stringency Index, which is based on Oxford COVID-19 Government Response Tracker, the average from the days reported for that quarter is given[20]. For cases and deaths per million and for vaccines per 100, the population used is our estimate for the middle of each quarter (16 February, 16 May, 16 August and 16 November)[20,21]. For real income, indexed value benchmarked to the relevant quarter of 2019 = 100 is computed using quarterly real, seasonally adjusted, gross domestic product[22].

From another ethical perspective, the adverse effects of the vaccines also need consideration[10]. Also, data in Table 1 and Figures 1–3 show that the second peak of reproduction number in some countries and relatively higher cases/deaths per million in some others have occurred after the vaccine rollout. The relatively higher vaccine uptake and cases/deaths in Japan (also USA) compared to Kenya, to begin with, imply an inequity in global distribution, and

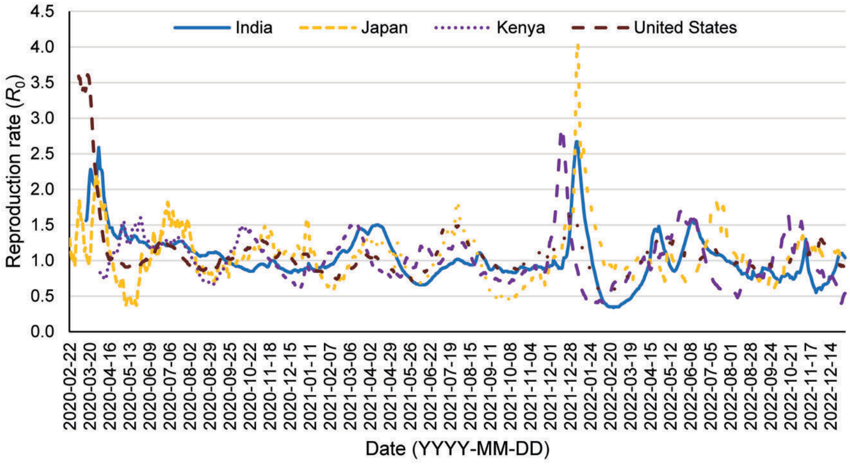

Figure 1. Trends in reproduction rate (R_0) of COVID-19. Note: In the four countries represented, the trends in reproduction rate[20] have largely remained around 1.5 or lower except for the two peaks.

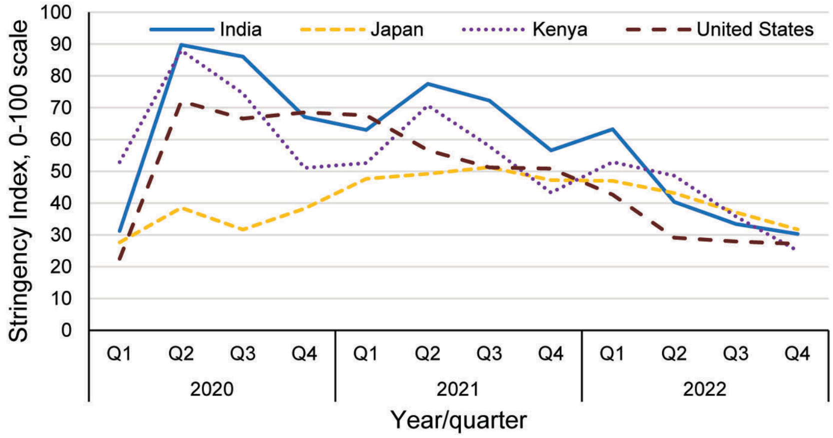

Figure 2. Stringency Index, 2020–22. Note: Stringency index[20] shows variation in Government response over time to COVID-19 across the four represented countries, which is not commensurate with the reproduction rate given in Figure 1.

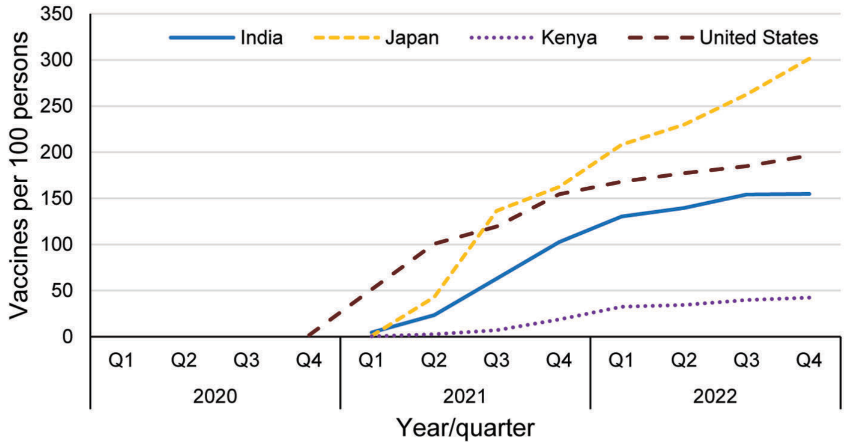

Figure 3. Vaccination against COVID-19. Note: Vaccines per 100 persons[20,21] show differences in distribution across the four countries and also raises concerns on increase in COVID-19 cases and deaths (Table 1) after the vaccinations.

then the need subsequently for additional resources to address adverse effects. Besides, excessive focus on a single disease could limit resources for other public health and socio-economic concerns.

Concluding remarks

The COVID-19 pandemic adversely affected lives and livelihoods worldwide. From a public health aspect, there have been two broad perspectives. The Great Barrington Declaration prioritized livelihood as delays would further adversely affect life, while the John Snow Memorandum favoured postponing livelihood concerns to save lives. In sync with the Memorandum, since early 2021, the world went ahead with emergency use authorization of vaccines.

In this backdrop, the math of herd immunity identified five propositions that have public policy implications for any intervention, including vaccination strategy. The first proposition suggests that the goal of public health intervention should be to reach the threshold level, which for reproduction number 3.0 is 67%. The second proposition indicates that the effectiveness of an intervention, captured through a reduction in both absolute and relative risks, should be greater than the threshold level. A concern for some vaccines was that their absolute risk reduction was at 0.8%–1.3%. The subsequent three propositions suggest that incorporating proximate impact or reducing proportion secluded, public provisioning, and prioritizing across groups based on their risks would reduce the proportion requiring direct intervention to reach the threshold level. The COVID-19 vaccine rollout per se was in line with the Memorandum, and there was public provisioning and prioritizing, which would also fit in with the Declaration. However, subsequent extension to the entire population in many countries, and disregard of natural immunity and possible harm, which was increasingly becoming evident, has not been in line with the declaration.

A caveat is in order. The reproduction number, efficacy rates and other parameters can fluctuate and need not be the ones used in our examples and counterfactuals. This, however, does not alter the fact that the goal for the intervention need not be the entire population. There is also ample space that allows public provisioning to go hand in hand with informed consent, which is also an ethical imperative. Further, an ethical public health posture also requires not having an excessive focus on a single disease, not limiting interventions for a disease to specific types of care, and not mandating any specific care.

Conflict of interest: None.

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ACKNOWLEDGEMENTS. Comments by the two anonymous reviewers, and also Jagannath Chatterjee (Member, Medico Friends Circle), and Sudhir Patnaik (Editor, *The Samadrusti*) as well as discussions in the class with students and research/teaching assistants were helpful. An earlier version (pre-print) has come out as Working Paper WP-2021-024 of Indira Gandhi Institute of Development Research. The usual disclaimers apply.

Received 20 November 2021; revised accepted 16 April 2023

doi: 10.18520/cs/v125/i4/363-368