

Exit strategy of COVID-19 crisis and pathways of Vaccination

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October 20, 2023

Abstract

There is a strong coordinated effort by vaccination groups all over the world to put an end to the current crisis of COVID-19. The Mass vaccination first started in the UK on 8th December 2020 and soon afterward covered all of the globe. Now sufficient data are available to analyse and compare some results to explore many aftereffects of vaccination. Some influence variables on transmissions of the disease were discussed e.g., mass vaccination, lockdown and seasonality. To address seasonality, similarities between COVID-19 and seasonal Flu are discussed to gain useful insight. Like Flu, seasonality was shown to play a dominant role in transmissions of COVID-19 in the Eu-rope and US. In terms of mass vaccination, adverse reactions after vaccination received attention, as health and safety issues of the general public are of prime importance. Apart from direct side effects, the secondary effect of mass vaccination needs attention too. After the initiation of vaccination programme, almost all countries experienced a sudden surge of transmission and most countries had to impose strict lockdown measures. Many countries, those showed a low prevalence of the disease, suddenly showed a steep jump after the onset of mass vaccination. Some countries even followed a synchronized pattern between the rate of transmissions and the variation of vaccine doses; the pattern seemed distinct with the sudden steep rise/fall in vaccine doses (e.g., countries India, Indonesia among others). In that context, fast mutation of the virus and new variants after mass vaccination and possible mechanisms/consequences were discussed.

Balanced discussion, critical and open analyses are desperately needed in the current crucial stage. Debating, questioning and criticism are always the foundation of good science and the main pillars to its progress. Following that objective, it is an effort to explore pragmatically, areas relating to the effectiveness of the COVID-19 vaccine and the exit strategy via the pathway of vaccination. Policymakers, academics, patients and common people will be greatly benefitted from such critical, transparent and balanced analyses.

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Balanced discussion, critical and open analyses are desperately needed in the current crucial stage. Debating, questioning and criticism are always the foundation of good science and the main pillars to its progress. Following that objective, it is an effort to explore pragmatically, areas relating to the effectiveness of the COVID-19 vaccine and the exit strategy via the pathway of vaccination. Policymakers, academics, patients and common people will be greatly benefitted from such critical, transparent and balanced analyses.

Keywords: COVID-19; Seasonality; Vaccine; Flu; Temperature; Peer-review; Clinical Trial, Solutions

1. Introduction

The recent pandemic of COronaVirus Disease 2019 (COVID-19) was first originated in the Wuhan Province of China and the first reporting was made during December 2019. At a very rapid rate, it spread all over the globe and more than 5,348,990 people died till 15th December 2021 [1]. The virus responsible for the disease is Severe Acute Respiratory Syndrome CoronaVirus 2 (SARS-CoV-2) (WHO, 2020) and detailed discussions on the nature of the disease and characteristics of the virus is outlined in recent research [2,3].

The disease is highly contagious in nature and hence at the beginning of the outbreak, most countries worldwide imposed strict lockdown. Initial lockdown started from around the third week of March 2020 [4] and continued the whole of April. As no proven cure for the disease is found yet, the economy and mental health are suffering tremendously. Mass vaccination started on 8th Dec' 20, but there are many limitations. Regarding exit pathways via vaccination one concise comment from the journal Lancet: 'rapid regulatory approval and roll-out of several vaccines have ignited much optimism. However, this optimism has been dampened by the emergence of several new virus variants that are more transmissible and less sensitive to vaccine-induced antibodies' [5]. At least 4 principally different covid-19 vaccines are in place: i) inactivated virus from China and India, ii) m-

RNA Vaccines, iii) vector-borne vaccines (Astra-Zeneca), and iv) viral surface proteins and are discussed in details in recent literature [6a]. This analysis is an effort to explore pragmatically, areas relating to the exit strategy and various consequences associated with the COVID-19 mass vaccination programme. It also analyzed proclaimed apparent vaccine success stories with a critical mindset. In fact, some success stories suggested contradiction and lacked uniformity.

Adverse effects on people after vaccine and how those are monitored, scrutinized and attended by respective authorities are one of the most crucial areas before the launch of any mass vaccination programme. Some adverse effects of vaccines were reported in CDC, US and other government regulatory bodies over the globe e.g., Anaphylaxis, Thrombosis with thrombocytopenia syndrome (TTS), Guillain-Barré Syndrome (GBS), Myocarditis and pericarditis among others [6]. A recent review nicely discussed scientific basis of many adverse reactions of the COVID-19 vaccine in an excellent manner [6a]. Apart from direct side effects, indirect effects after mass vaccination which were often overlooked also need attention. In this regards, questions were raised via Rapid Response BMJ on the indirect effect of mass vaccination [7] and few points raised are as follows: i) 'After initiation of the vaccine programme, almost all countries experienced a sudden surge and most countries had to impose strict lockdown measures.' ii) 'Even for UK/ Israel, where massive vaccination started first, total deaths in three months after vaccination reached overall deaths of past 10 months before vaccination.' iii) 'A highly populated country India was having a steady decrease for five months. India passed major festive seasons where social distancing was very difficult to be maintained, still cases and deaths continued to decline. Vaccination started on 16th January and from around 16th February, India started showing a rise in cases and thereafter deaths.' iv) 'For Brazil, vaccination started in mid-January and a sharp rise in cases is observed since mid-February. Such a steep rise in deaths in Brazil that happened after that never happened in the whole period of the pandemic.'

To develop useful timely urgent Insight resemblance with Flu and COVID-19 need attention too. Every winter, tens of thousands of people die in the UK, Europe and northern America from Influenza (Flu), a virus borne respiratory disease. In spite of many differences there are striking similarities between these two virus-borne respiratory diseases, COVID-19 and Flu and discussed here [8]. 'Flu season occurs in the fall and winter. In the U.S., that means October-March, and in the southern hemisphere, June-September. Although the reason for this seasonality is not entirely understood, the influenza virus has been shown to survive longer at low temperatures and low humidity. Other suggested explanations include weakened host immunity due to decreased sunlight and vitamin D and increased exposure to the virus due to indoor cohabitation in the winter' [Amer. Soc. for Microbiology, 8]. People mainly from old and vulnerable groups are vaccinated against Flu virus at the beginning of every winter in affected countries, but still, it is not yet been possible to eradicate Flu. On the contrary, it became more destructive and powerful in later years. The main reason is that the virus is mutating over space and time, in spite of several new vaccines that were developed over time. Hence the obvious question arises, could it be similar for COVID-19?

Between COVID-19 vaccine and other known vaccines (polio, smallpox, etc.) there are enough dissimilarities too. Unlike other vaccines, if people are vaccinated for COVID-19, they still can be infected and transmit the disease and even can die [9]. People can be a carrier of the disease even after 15 days of the second dose [9]. Breakthrough cases and deaths among vaccinated are now observed of very high percentage in all countries [10, 11, 12]. 'Breakthrough cases' happen when people test positive even after 14 days of the 2nd vaccine dose. Moreover, it is worth mentioning that vaccines have not yet been invented for many virus-borne diseases too, e.g. AIDS, etc. Hence attention to varied research and exploration of alternate solutions for COVID-19 other than the vaccine is equally necessary. A recent review also discussed drug effectiveness studies and clinical therapeutics [12a].

Considering an emergency situation in mind some urgent, simple solutions were also **proposed as early as 17th March 2020** [Fig.1] and a series of research afterwards [13, 13a, 14, 15, 16] purely based on Science. Those solutions were proposed based on the following: i) exploring results of statistical analyses on global transmission of COVID-19 [13,13a,14-16, 17]; ii) observed behaviours of similar category viruses [18-22]; iii) clinical trial experiments [20,21, 23] and iv) biological mechanism/response in human bodies [24]. These solutions are heat-based and practically without side effects, can be practiced in own home and there is no vested Interest involved.

Here are little elaborations on the rationales for proposing heat-based solutions. Studies explored the role of global temperature in the spread and vulnerability to COVID-19 [13a, 14, 15, 17] and indicated that global temperature played an important role. The risk from the virus was reduced significantly for warm places and countries; whereas, a moderately cool environment was the most susceptible for the spread of the virus [14-16]. The dependency of temperature is true for similar generic categories Coronavirus MERS (Middle East Respiratory Syndrome) and SARS (Severe Acute Respiratory Syndrome) ([18],[19]) and also correct for similar other seasonal air-borne Flu viruses [20]. In low temperatures, the virus remains active for a long time [18] and low temperature significantly contributes to its transmission and survival ([19], [21], [22]). Clinical trial experiments were also conducted to study the effect of temperature further. Research using seasonally dependent endemic virus [20] noted that when the temperature was 5°C and relative humidity between 35% to 50%, the infection rate was as high as 75 to 100%; whereas, if the temperature was only increased to 30°C, keeping relative humidity still at 35%, surprisingly, the infection rate decreased to zero. A laboratory experiment, using a variable temperature, with a similar generic Coronavirus (viz. SARS-CoV) [21] indicated that inactivation of the virus was faster at all humidity levels if the temperature was simply raised to 20°C from 4°C. The inactivation was much faster if the temperature was further increased from 20°C to 40°C.

a)

Solutions : General Measures

- **Using Sauna facilities:** Usually hotels, gyms, leisure centres contain existing Sauna facilities. Also, mobile and Caravan Sauna facilities can be thought of in future. After Sauna, if surfaces of outside public places are touched, hand washing should be mandatory.
- **Portable Convector Room Heater:** Stay close to a convector room heater and inhale hot air at least two times a day for around half an hour each time (keeping comfort level). It would be very useful at the initial stages of the disease.
- **Disinfect any place using High Temperature:** Before start of office, school or business, temperature of premises may be kept very high, (say, 60°C) for half an hour. For airports, train and bus, the same method of disinfecting could be thought of. *Optimum temperature and duration can be tested easily.* For any external object or material, disinfecting using high temperature could be a useful solution.
- **Using Blow Dryer/ Hair Dryer:** For minor symptoms, inhaling hot air intermittently through the nose (keeping comfort level) even for five minutes, say two/three times a day, will also be useful to kill virus in the nasal cavity.
- **Hot Drinks:** For very mild symptoms, take hot drinks (could be tea, coffee, warm milk, hot water with lemon etc.) few times a day to destroy virus in the mouth and throat. Gargle with warm salt water at least three/four times a day will be very beneficial. Hot soup will also be useful.

Why: The virus is very sensitive to **Temperature**. It mainly enters through the **Nose** (WHO). Testing is done with swabs from the nasal cavity and the back of the **Mouth**.

Important: Only even Convector Room Heater and Warm Salt Water gargle, Hot Drinks can serve the main purpose.

b)

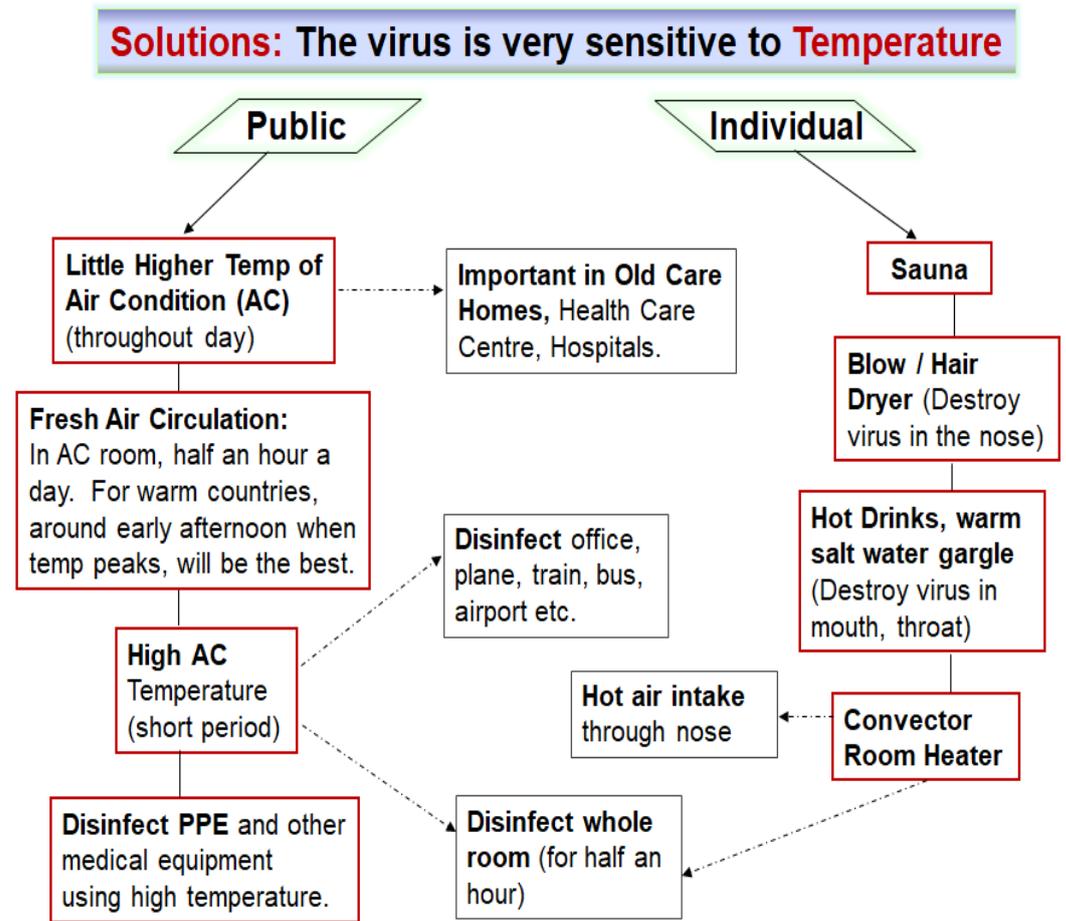


Fig. 1. Heat-based simple solutions to combat COVID-19: a) general measures at initial stages of the disease, b) an overview in a form of schematic, depicting actions towards solutions at individual level (right) and public level (left).

(Source: Roy, 2020 [14-16])

COVID-19 is an extremely contagious disease and invaded most of the globe in less than two months (WHO). Warm countries like SAARC, South East Asians countries (SEAC) and many countries of Africa were also affected though the scale of severity was much less in comparison, during the whole of 2020 [15,16]. Those indicated the importance of exploring the nature of contact transmission in addition to airborne transmission. Contact transmissions in variable temperatures were studied in Clinical Trial experiments with guinea pigs, that showed contact transmission is still possible at high temperatures, even at 30°C [20]. When guinea pigs were kept in separate cages at the temperature of 30°C for 1 week, no recipient guinea pigs were infected indicating an increase in temperature arrested airborne transmission. However, when those were kept in the same cage to simulate contact transmission, between 75% to 100% became infected indicating contact transmission plays role in all temperatures. No role of humidity was found in those experiments.

As temperature played such an important role in transmitting this/similar diseases, heat-based simple solutions are proposed. Fig. 1a shows general measures at the initial stages of the disease; whereas, Fig.1b suggests an overview in a form of a schematic, depicting useful actions towards solutions at the individual level (right) and public level (left). These measures in Fig.1a at the initial stages of the disease are proposed because the virus, which is very sensitive to temperature, mainly accumulates at high volume in the back of the mouth as well as in the nose. Testing is done with swabs from those places. The important point here is - **the high temperature (of course**

keeping comfort level) at early stages of the disease can reduce viral loads in the areas where the virus largely accumulates initially and hence the body can have time and strength to fight against the virus. [Caution: if people already developed major symptoms, then all these methods discussed will not be effective and proper medical advice need to be solicited [14-16]].

After receiving approval from the ethical committee, successful clinical trial experiments following heat-based solutions to fight against COVID-19 were also conducted and published [23]. Furthermore, a thorough literature review in support of heat-based solutions for COVID-19 was published in a peer-reviewed journal too [24]. The author being a medical doctor, discussed different mechanisms linked in the biological processes [24]. If at initial stages of the disease these heat-based simple solutions become popular [Fig. 1] then we do not need to worry about long COVID, further lockdown, mutated variants, losing immunity after six months etc. In this regard, a famous quote from Prof Feynman is worth mentioning “Education isn't about the ability to remember and repeat, in which people study to pass exams, and teach others to pass exams, but nobody knows anything. It is the ability to learn from experience, to think, solve problems, and use our knowledge to adapt to new situations” [Prof Richard Feynman].

In this study, further exploration is made on the exit strategy of COVID-19 via pathways of vaccination, (which is opted for by the policymakers as the only possible exit pathway). This analysis suggests critical evaluation of any strategy with useful timely insight and thorough monitoring is equally important so as the openness of vision and outlook. Pragmatic outlook, identifying problem areas beforehand has enormous potential not only to mitigate huge economic burden, but also to give directions to solve a prolonged crisis. Differentiating between optimism vs. pragmatism is another crucial aspect, which are very important for policy purposes in the current COVID-19 scenarios.

2. Results

Few important aspects of current COVID-19 situations from critical viewpoints are discussed pointwise as follows:

2.1. Some influence variables: Lockdown, Vaccination and Seasonality

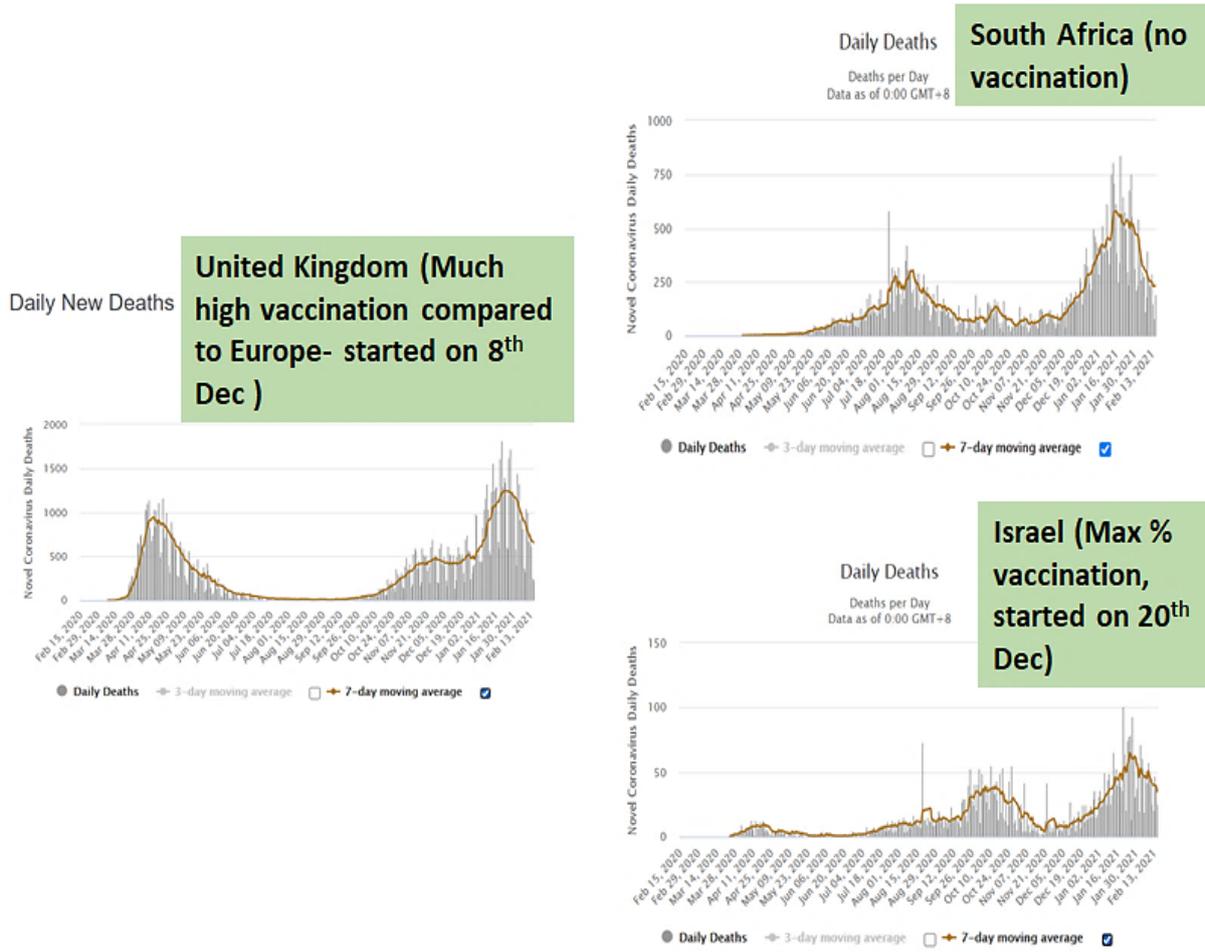
During the end of 2020 and beginning of winter, many countries showed a sudden surge in transmission. It indicated about the influence of seasonal temperature. After strict lockdown measures, surges decreased. Moreover, different countries also started vaccination at different points of winter; some started late winter e.g. South Africa (17th February, 2021 [25]); whereas, some started early winter e.g. UK (8th December 2020 [26]). It is beneficial to analyse effects of vaccination, lockdown and seasonality in different countries and we need to have critical judgement to understand apparent vaccine success.

For UK and Israel, the second peak occurred after vaccination started and the 2nd peak was much stronger than the first one (Fig. 2a). For South Africa, the 2nd wave peaked at the same time with the UK and Israel (around mid-January), but South Africa did not start vaccination till 17th February. Moreover, upto 17th February, 2021, the 2nd wave was falling much faster than UK and Israel [27] (Fig. 2a). Massive vaccination drives took place in Israel and UK and total deaths in the three months after vaccination (with strict lockdown), reached the overall death of the past 10 months of pre-vaccination period [25].

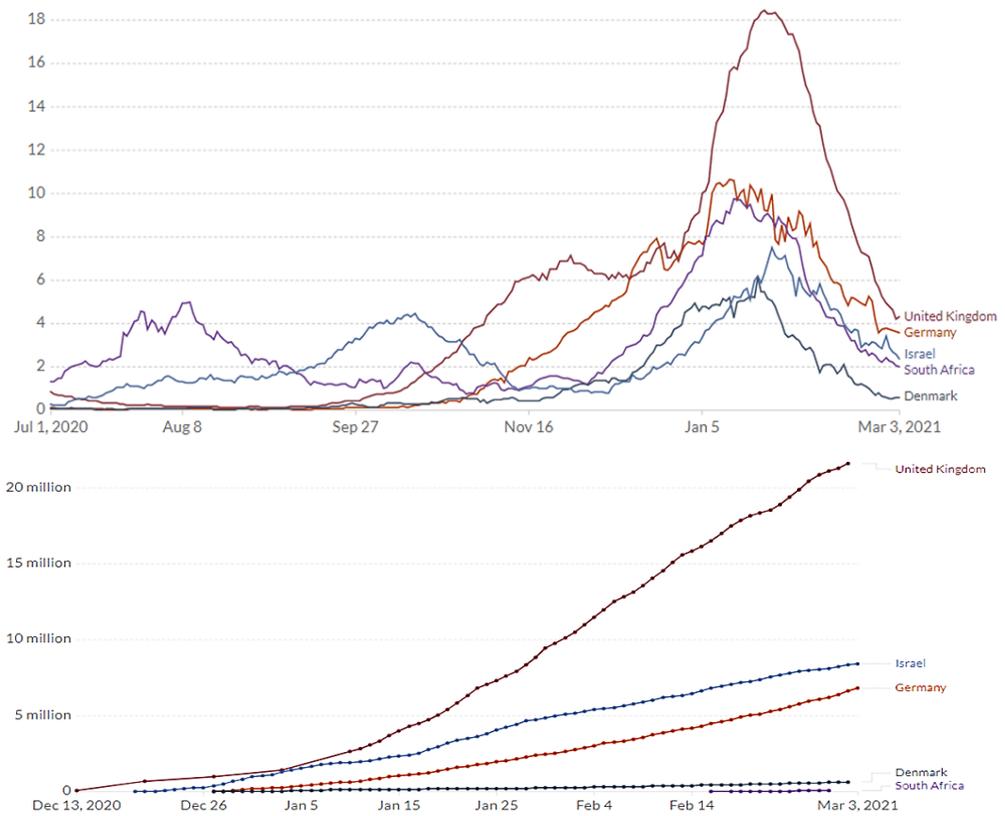
Focusing on initial stages of vaccination (upto the beginning of March, 2021), we note that UK not only had much higher vaccination than any other EU countries but also showed the highest daily deaths among other EU states [25, see till 28th February 2021, 7-day average]. Fig. 2b shows Israel and UK had the highest vaccination, though daily deaths were still higher at the beginning of March. South Africa did have practically nominal vaccination, but the daily death though peaked higher than in Israel but fell at a much faster pace and even lower than in Israel. Now the UK imposed strict lockdown in most of winter and death decreased in late winter (Fig. 2b), as expected. As initial vaccination success story in Israel attracted global attention [27a], so as the UK, it deserves critical analysis.

Interestingly, Israel, UK and South Africa all show a rise in transmission again during July 2021 (Fig. 2c, bottom). Israel and UK are among the topmost countries with very high vaccine coverage and a very high percentage of population received both the doses (much higher than the herd immunity 60% threshold [25]). For the UK and Israel, cases and deaths both are on the rise [25]. South Africa increased vaccination dose suddenly in the later period and a strong correlation with cases are noticed (Fig. 2c, top). For Israel and UK there is no lockdown in July 2021. It indicates we need to be vigilant about vaccine success and before acclaiming any vaccine accomplishment, we need to analyse data with a critical mindset.

a) Daily New Deaths



b) Daily new confirmed deaths per million, 7-day average (Top); cumulative vaccination dose (bottom).



c) Cases in UK, Israel and South Africa covering June 2021

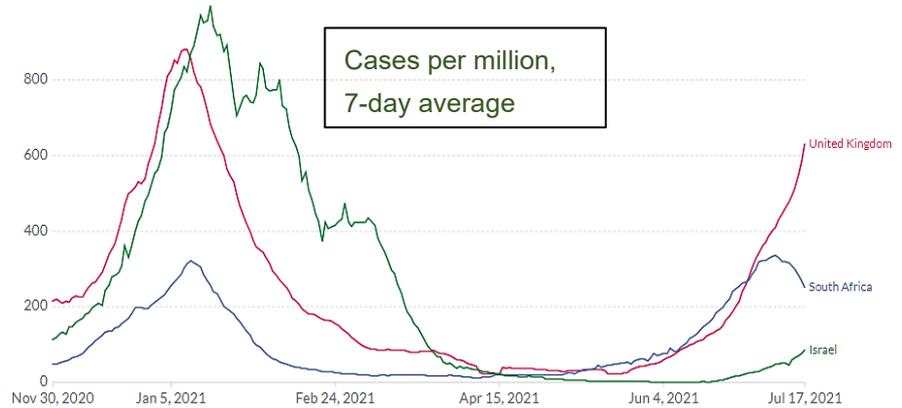
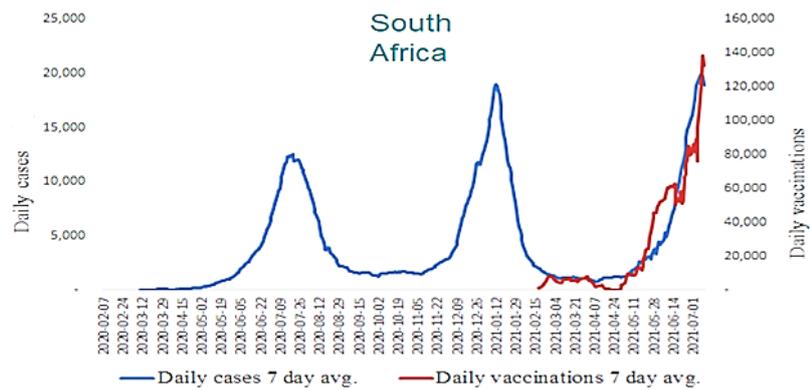


Fig.2. a) Daily new deaths for Israel, UK and South Africa before South Africa started vaccination (on 17/02/21). The seven-day moving average is shown by thick line (<https://www.worldometers.info/coronavirus/country/>, accessed on 17/02/2021, [27]). b) Deaths of Covid-19 and Vaccination data of few selective countries, where deaths peaked in winter: top) Daily new confirmed deaths per million in rolling 7-day average, bottom) cumulative COVID vaccination dose. (Source: <https://ourworldindata.org/coronavirus-data-explorer>, [25]). c) Cases (7-day average) in UK, Israel and South Africa covering June 2021. The top panel is for only South Africa and it also included vaccine dose (7-day average); whereas, the bottom panel shows cases per million (7-day average) of three countries [25]. a) and b) focuses first three months after vaccination, while c) covered even some days of July.

2.2. Short-term adverse effects reporting after vaccination

There were hardly any possibilities to test the long-term and medium-term adverse effects in the short time frame of COVID-19 vaccine clinical trials. Even in the short term, many complicated interactions among various underlying health issues are likely to be missed and could not be tested because of the small sample size. Only a few thousand people took part in trials among which half were given Placebo.

Questions were also raised for short-term adverse effects [28]. Till 26th February, a total of 1136 individuals died in the United States, after receiving mRNA vaccines for COVID-19, of which, 587 (51.7 %) died within a week. Among the dead 94 (8.3 %) died on the same day, 150 (13.2 %) died the day after, 105 died 2 days after, and 68 within 3 days [28, 29]. Upto 8th March the death reporting was 1637 and upto 5th April, 2021 it was 2,794 [30]. Thus, adverse reporting of deaths after vaccination seems consistent over periods of time. Anaphylaxis, temporary facial paralysis, blood clots and Bell's palsy were reported among the majority of critical patients, while Cardiac arrest was one of the main causes of deaths. Biological processes and physical scientific basis of such observations of adverse reactions are reported in a recent review [6a]. It could be wise to track vaccinated people afterward and to monitor if they were affected by any of **those diseases or related symptoms** in later stages. Though straight monitorization of patients is compulsory in all pharmacovigilance systems especially for severe drug adverse reactions [30a], monitorization of patients for medium and long-time scale and for moderate adverse reactions also deserve attention. The task is extremely difficult when crores of people are vaccinated on a regular basis. It is worth mentioning that for highly populated third world countries such tracking could be practically impossible. Also, a monitoring system could be proposed to check if deaths caused due to some of those specific symptoms/diseases or apparent unexplained reasons exceed normal count in the coming months or not. Such anomaly counts of death as well as adverse symptoms could give some ideas of medium and long-term side effects due to vaccination.

A comparison from VAERS reports between deaths after the COVID vaccine and Influenza (Flu) gives useful information. A total of 45 deaths occurred for Flu vaccine in 2019 influenza season, which is 0.0000265% of total vaccination. However, a total of 1136 deaths are reported for the COVID vaccine, as of Feb. 26. It is approximately a rate of .0024 %, which is 100 times high than reported deaths from Flu vaccines [29].

In India, around 180 people have died as of March 29 and 617 had serious adverse events following vaccination [reported by Immunisation (AEFI) committee, the main government reporting center [31]]. The majority of those deaths happened less than three days after the vaccine intake and major causes are noted as Acute Coronary Syndrome/ Myocardial Infarction. Authorities said deaths were not related to vaccines. In the UK, the Medicines and Healthcare products Regulatory Agency (MHRA), a govt organisation reported that up to March 31, there are 79 reports of blood clots accompanied by low blood platelet count. A total of 19 people died, of those three were under the age of 30 [32]. In the UK, as of 4 August 2021, 101,483 adverse reporting was made for the Pfizer/BioNTech vaccine, 226,959 for the vaccine AstraZeneca, 12,569 for the vaccine Moderna [32]. It is decided that clotting syndrome must be listed as a very rare side-effect in one of the vaccines, Oxford Astra Zeneca [33, 30]. Reports indicated a plausible causal relationship between the Johnson

and Johnson COVID-19 vaccine and a rare and serious adverse event, blood clots with low platelets, which has caused deaths [30].

2.2.1. Some disproportionate adverse reporting on the young and male population

In the US, vaccination above 12 years has been initiated quite early compared to rest other countries and even for short time span, adverse reporting in the CDC is available [34]. There is a likely link reported between rare heart inflammation (known as myocarditis) and vaccines, in adults under age 30, especially after the second dose [Table 1 and Fig. 3]. Males are worst affected after the 2nd dose compared to females in various age groups too. As the adverse reporting was disproportionate based on gender, dose and age, it got attention and such features need monitoring [reporting from CDC's COVID-19 Vaccine Safety Technical Work Group]

Table 1: Preliminary reports of Myocarditis/ Pericarditis to VAERS after mRNA COVID-19 vaccination by age and dose, upto June 11,2021. Females are performing better than male counterparts. Young males are worst affected, which are more prominent after the 2nd dose (Source, CDC,[34])

Age groups	Overall reporting rate per million doses			Reporting rate in females per million doses			Reporting rate in males per million doses		
	All doses	Dose 1	Dose 2	All doses	Dose 1	Dose 2	All doses	Dose 1	Dose 2
12-17 yrs	18.1	5.3	37.0	4.2	1.1	9.1	32.4	9.8	66.7
18-24 yrs	15.9	4.8	28.4	3.6	1.5	5.5	30.7	8.7	56.3
25-29 yrs	6.7	2.5	10.8	2.0	0.8	2.6	12.2	4.5	20.4
30-39 yrs	4.2	1.7	5.6	1.8	1.4	1.8	6.9	2.0	10.0
40-49 yrs	2.7	0.9	3.8	2.0	0.9	2.8	3.5	1.0	5.1
50-64 yrs	1.7	1.0	2.0	1.6	1.0	1.8	1.9	1.0	2.3
65+ yrs	1.1	0.7	1.3	1.1	0.6	1.2	1.2	0.7	1.4

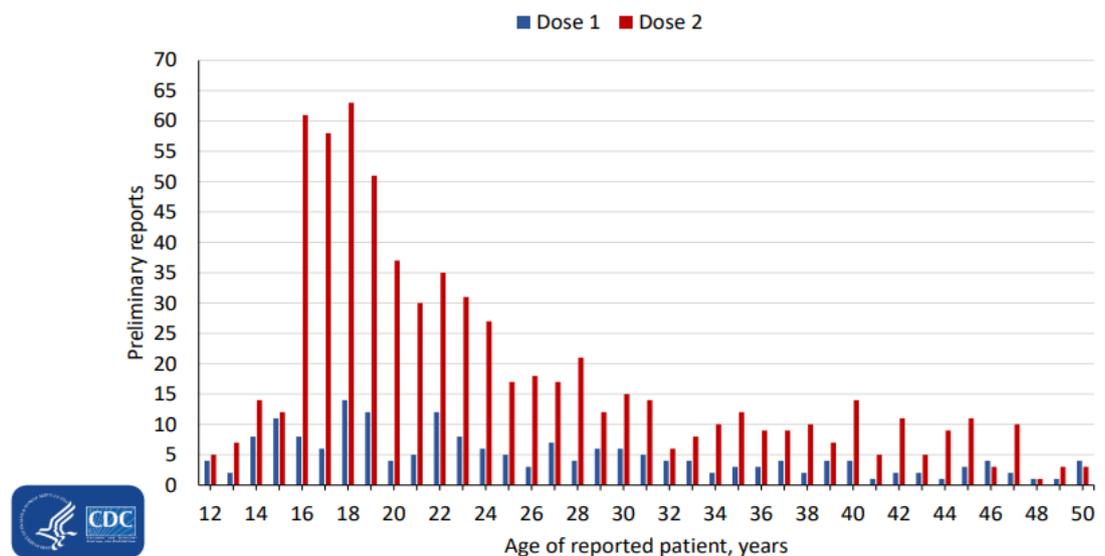


Fig. 3. Reporting to VAERS of myocarditis/ pericarditis after mRNA COVID-19 vaccination by age and dose number, upto June 11, 2021 in a form of a schematic. Age groups from 12 years to 50 years are shown to emphasize the younger age groups. Adverse reporting is higher after the 2nd dose, which is more prominent in younger groups (16-28 years). (Source: CDC, [34])

2.3. Indirect effect of Mass-Vaccination.

Many indirect consequences of mass vaccination were not properly apprehended before the start of mass vaccination, neither are those monitored globally, country-level or at regional level. Following observed data, concerns were raised as early as 11th March 2021 in scholarly platforms and on 22nd March in BMJ [7].

Globally cases and deaths started increasing after 5 weeks of a steady decline [27] and coincidentally, the period of rising matched when major vaccination programme was initiated worldwide. A distinct difference is noticed between number of deaths in the pre-vaccination and post-vaccination stages and it is true for cases too (Fig 4). The two highest peaks in Fig. 4 occurred after the start of Mass Vaccination. A peak in the winter just after the start of mass vaccination was the highest peak of all. It did not return to the pre-vaccination stage yet (till 13/12/2021), neither for cases nor deaths, even after much vaccination doses were administered. More than 8.59 billion vaccine doses were administered all over the globe till mid-December, 2021; while 56.5% world population received at least one dose [25].

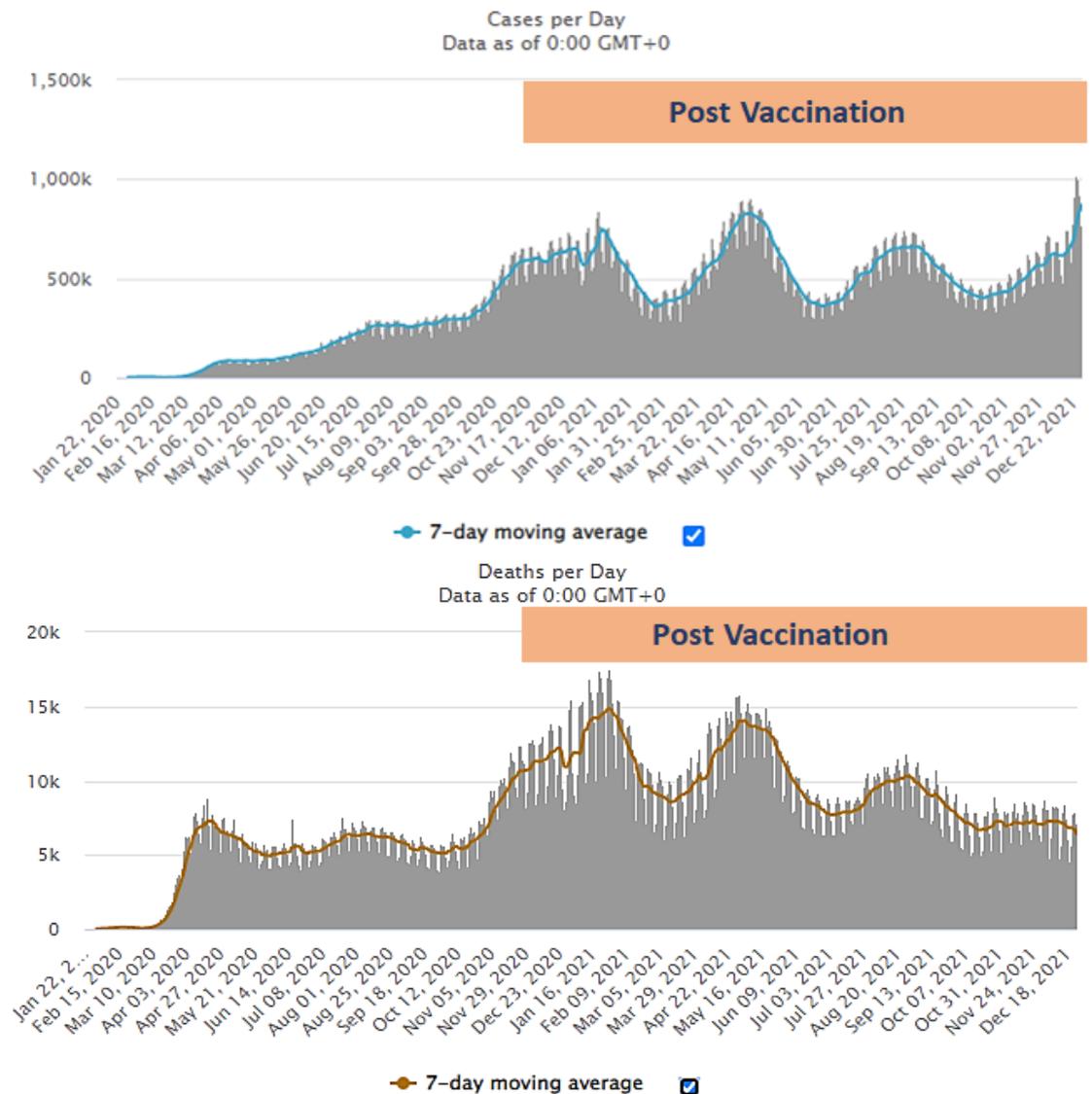


Fig. 4. Daily Cases (top) and Deaths (bottom) in the world for COVID-19. Seven-day moving averages are marked by coloured thick line. The vaccination programme started at December, 2020 (2nd week), but till upto 3rd week of December 2021, it did not reach the pre-vaccination stage. [1]

A highly populated country India was having a steady decrease for five months before the vaccination drive. Though neighbouring countries Pakistan and Bangladesh experienced the 2nd wave in winter (end of 2020) but India did not. India passed major festive seasons where social distancing was very difficult to be maintained, surprisingly, still cases and deaths continued to decline. There is a sudden reversal in the trend of cases and deaths in India, from declining to rising, within a month after the start of vaccination. As the vaccine dose was suddenly increased in April, 2020, the surge became nearly uncontrollable soon afterwards. Such a steep rise in deaths and cases for India never happened in the entire period of the pandemic [25]. Another highly populated country Brazil also showed a similar pattern after the start of mass vaccination.

2.3.1. Synchronization of cases with Vaccine doses

Many countries showed synchronized patterns between new cases and new vaccination doses as shown in Fig. 5. Few are presented here but there are many more countries showing a similar pattern [25]. Before the onset of mass vaccinations, all those countries are seen had low cases as well as deaths, though such features suddenly increased after the onset of vaccinations. For India, the rise and fall in the 2nd peak were unusually steep. Cases however maintained a certain lag with vaccine doses, probably due to the very high population. Like India, another example of a steepest fall in cases happened for Bahrain and that fall matched with the same time frame of vaccine doses [Fig 5]. However, we must note that such pattern was noticed at the initial period of mass vaccination. In the later period, whether herd immunity for highly populated countries are overtaking such effects need to be checked further.

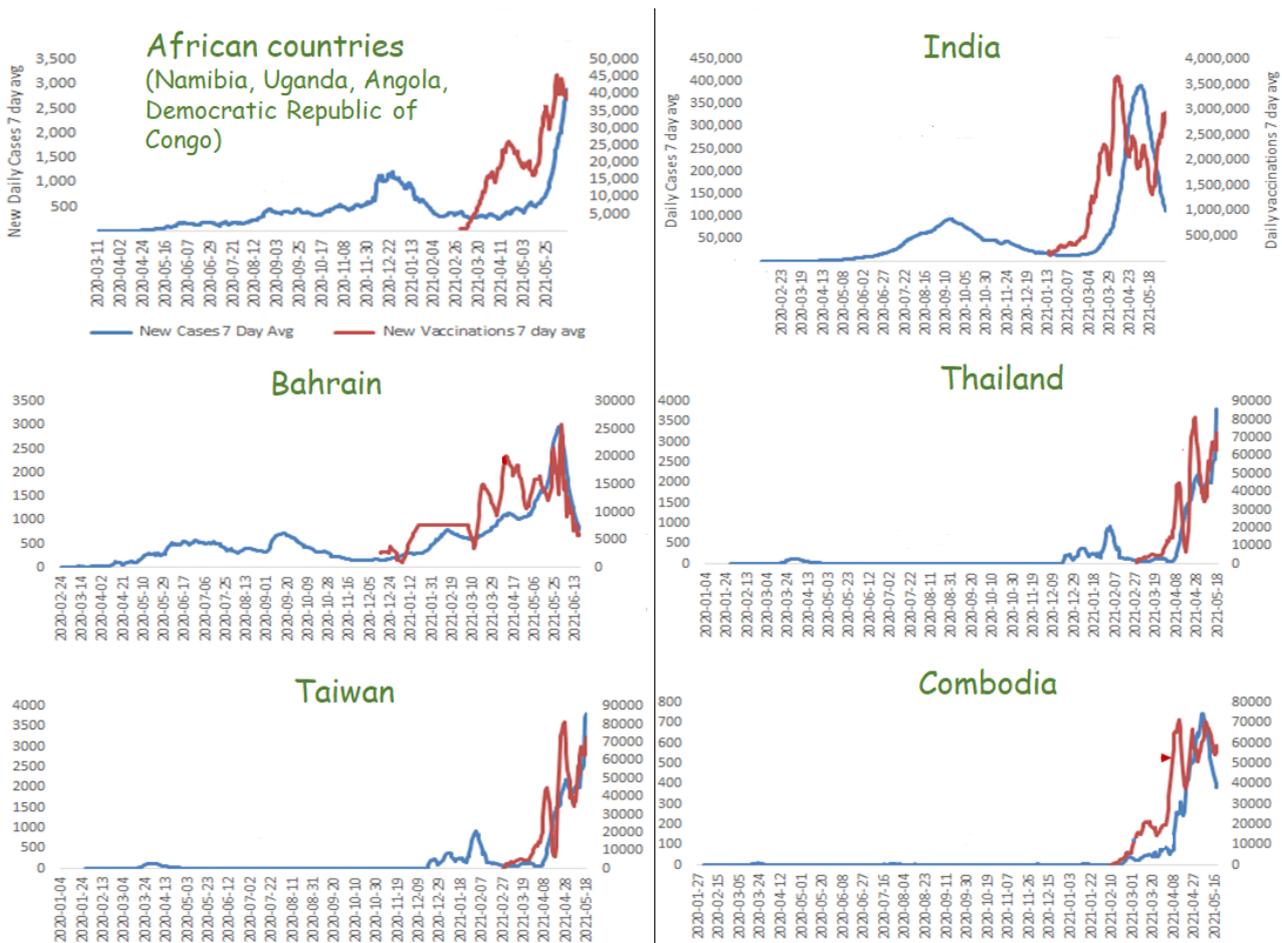
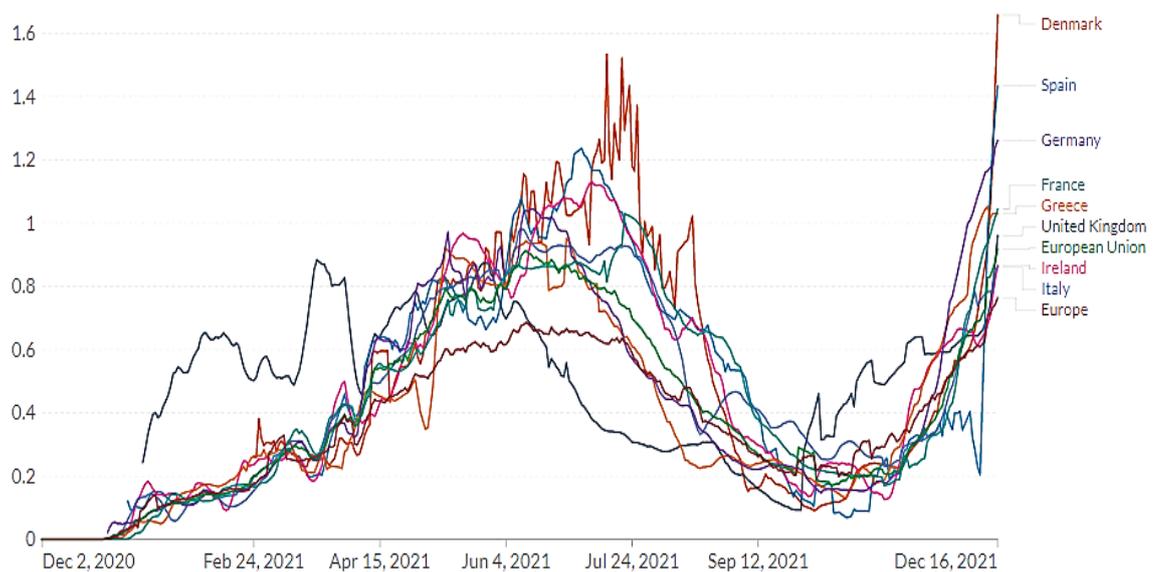


Fig. 5. Countries showing synchronized patterns between new cases (blue, left axis) and vaccination doses (red, right axis) are shown in a form of 7-day average; data used from [25]. Initial period of vaccination drive was the focus. Few countries are presented here but many countries show similar patterns.

The situation turned again uncontrollable mainly in Europe and US since the middle of December, 2021. However, that is the first time since the start of vaccination, the death curve attained that low and near flat peak (Fig. 4, bottom). Interestingly, around the similar time there was a sudden increase in vaccine dose in most European countries [see Fig. 6a] and the rising trend of vaccine dose was the steepest for the whole of the pandemic. A major surge in cases was observed in highly populated European countries [Fig. 6b]. Many European countries attained the highest number of cases and the peak till date (December end, 2021) either became the highest peak, or near highest of respective countries. Moreover, as the timing further matched with the beginning of winter season (knowing seasonality plays an important role for COVID-19, like Flu), it is likely to fuel the fire and caused such an unusual surge in cases and needs exploring. Global cases reached all time high near the end of December 2021 (Fig. 4a) and case numbers were mainly dominated by US and highly populated European countries.

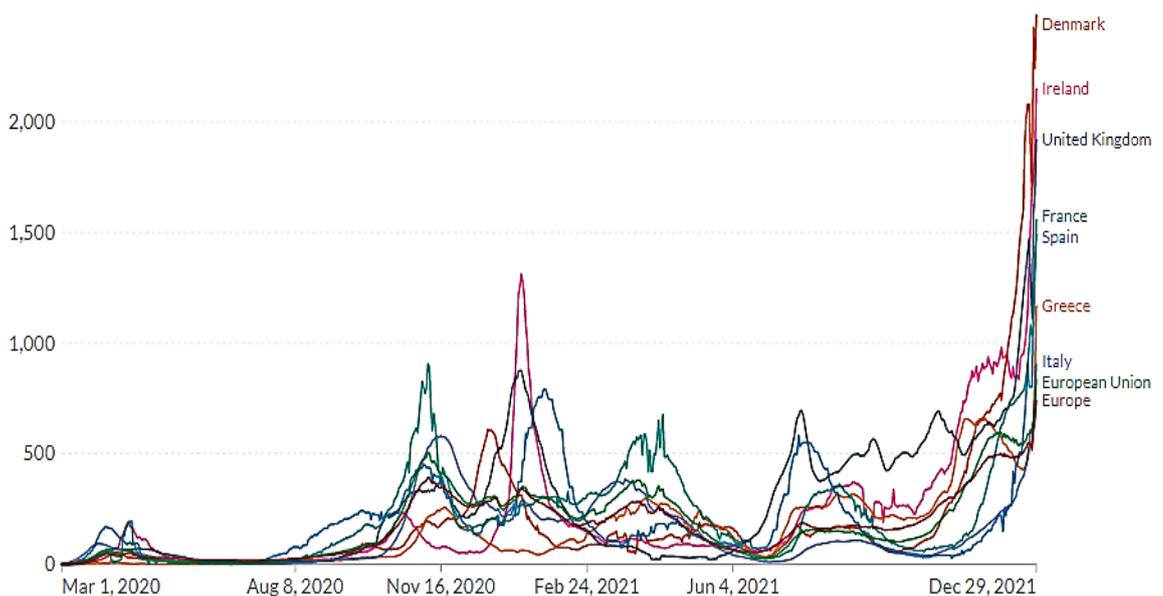
a) Vaccine Doses



Source: Official data collated by Our World in Data

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b) Daily Cases



Source: Johns Hopkins University CSSE COVID-19 Data

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Fig. 6. Vaccine doses and cases (7-day rolling average) [25]. a) Number of daily COVID-19 vaccine doses administered, divided by the total population of the country. All doses, are counted individually, including boosters. b) Daily new COVID-19 cases per million people. Most of those countries showed an unprecedented steep rise in vaccine doses from 15th November upto 15 th December, 2021. Cases upto 29th December sored all time high. For the vaccine dose as well as cases, the rise in trend was unprecedented.

2.3.2. Vaccine Equity and Increase in Doses

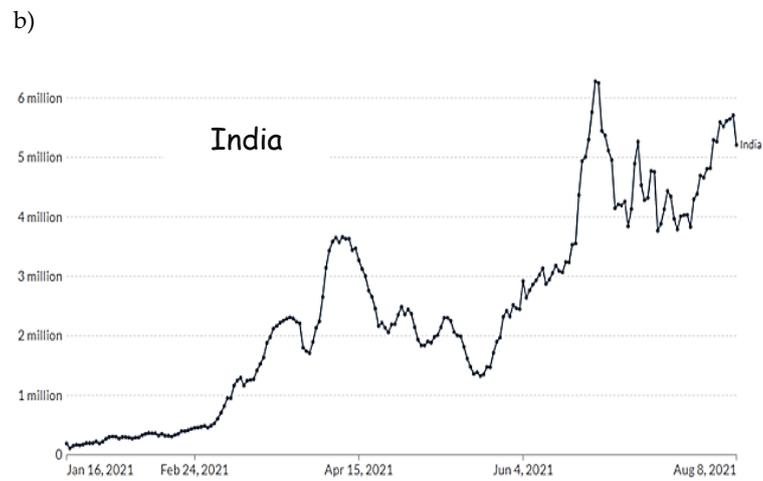
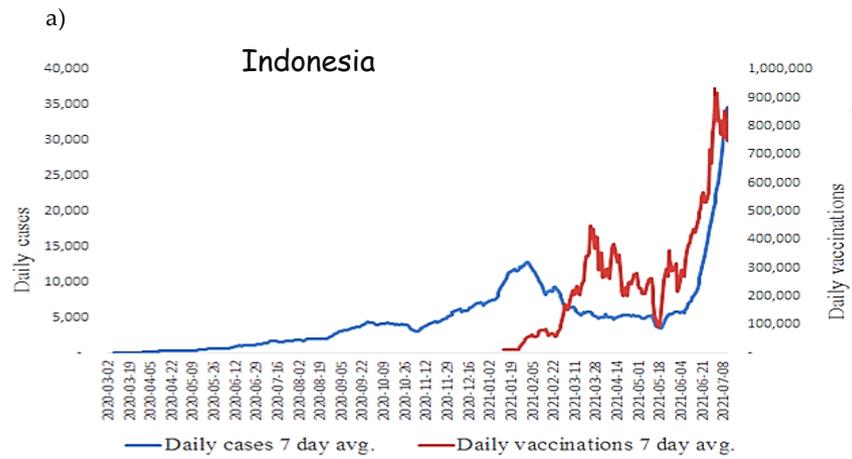
Interestingly, most of the third world countries were least affected by the disease before the vaccination drive, whereas, western world was the most hit [25]. After the launch of mass vaccination programme there was a huge cry about 'Vaccine Equity'. Like Flu, other tropical warm countries e.g., SAARC, South East Asian countries (SEAC), most African countries were least affected due to COVID before the start of mass vaccination. Arguments could also be raised/debated on vaccine equity stating that whether distribution of vaccination (countrywise) would be based on death rate of COVID-19 or not.

After the vaccine doses were initiated and increased, those countries with a low prevalence of diseases started showing a massive surge. The situation for one of the countries, Indonesia is shown in Fig. 7a. For some consecutive days, it experienced the **highest daily deaths in the whole world**. Reported deaths were 1093 and 1338 respectively on 18/07/21 and 19/07/21 respectively. In addition to that, it also reported the 2nd highest cases in the world on 18/07/21 which was 44,721 [27].

After the alert was triggered in 11th March and thereafter on 22nd March 2021 (<https://www.bmj.com/content/371/bmj.m4037/rr-20 dt 21.03.21>) some action seems to have reflected relating to vaccine doses by some countries those were most proactive at initial stages e.g., Israel, US and UK (Fig. 7c). Israel decreased vaccine dose since 11th March; whereas the US decreased the dose from mid-April. Since mid-April, 2021 US maintained that decreasing trend. For the UK, vaccine dose had never increased the limit that was reached on 22nd March, and showed a steady decline in later periods upto September, 2021. However, after September, UK started increasing vaccine doses.

The situation was mixed for India (Fig 7b) with a combination of sharp fall and rise in vaccine doses. Since Mid-April 2021, cases and deaths went out of control and India decreased vaccine doses. With a certain lag, there was a very steep fall in cases and deaths happened (can be seen in Fig 5). The lag between vaccine doses with cases and deaths probably occurred due to the very high population in India. In later stages, India though increased vaccine doses but cases/deaths became stagnant and it seems India may have achieved herd immunity and need further observation.

At the beginning of winter 2021, UK and most European countries suddenly increased vaccine dose [25] and cases skyrocketed (Fig.8). Cases around the world showed a surge (Fig. 4, top). All the highly populated European countries however started decreasing vaccine doses since 15th December onwards. The recent rise and fall of vaccine doses in highly populated European countries are steepest of the entire pandemic (Fig. 8). Even though vaccine doses are decreased abruptly, it is worth following how the situation evolves in the presence of winter seasonal cycle in US and Europe. A new variant Omicron is detected which seems highly transmissible [WHO] but as the deaths globally are still showing a decrease as oppose to cases [Fig. 4], it indicates optimism.



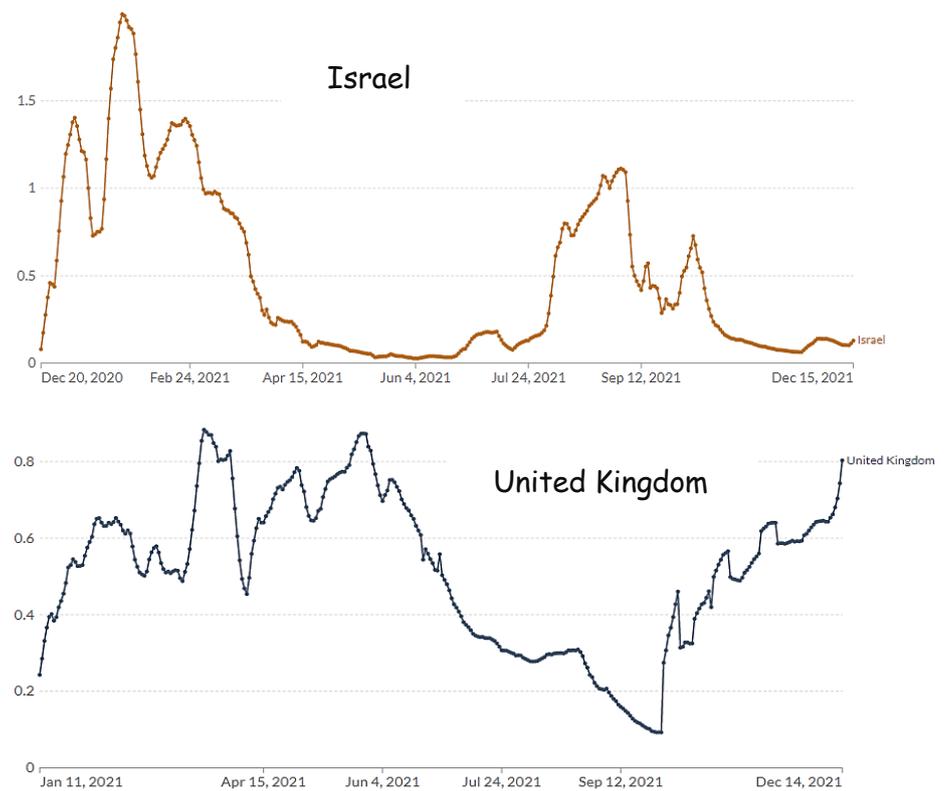
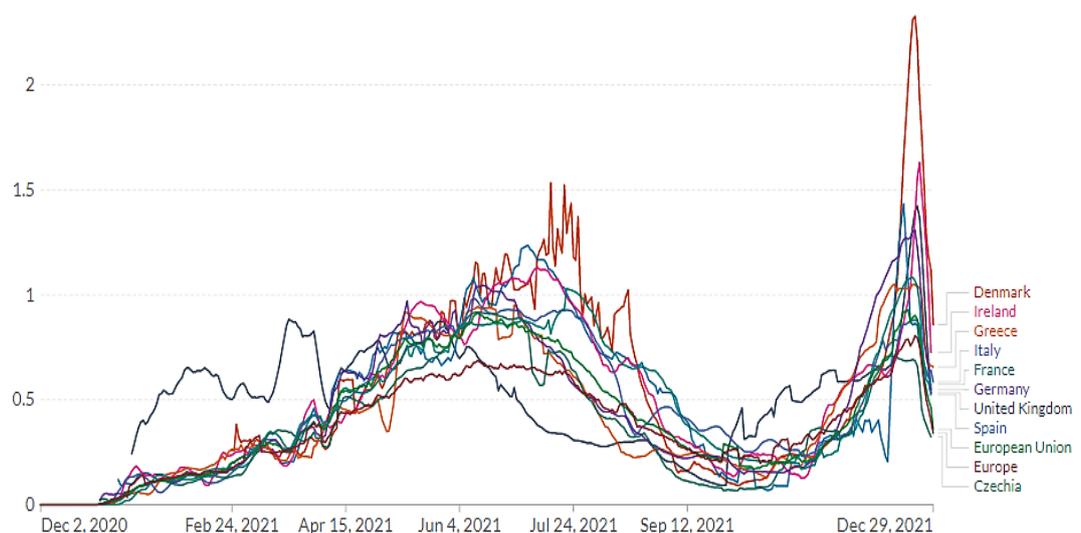


Fig. 7. Control of vaccine dose and discussion for few countries (data for 7-day rolling mean) [25]. a) Indonesia showed an abrupt increase in vaccine doses around May-June and cases skyrocketed. b) India increased vaccine dose from March, cases/deaths suddenly escalated. India decreased vaccine doses since mid-April, cases and deaths which were uncontrollable showed a steep fall. India increased the vaccine dose again and the steep fall became stagnant in the later period. c) For the US and Israel, the current vaccine dose (17/12/21) is much lower than the first peak. Both are in a decline state of vaccine dose. On the other hand, UK showed a rise in doses after September. Cases of transmission for all those three countries are on the rise at the end of December. c) shows number of daily doses administered, divided by the total population of the country and all doses including boosters, are counted individually.



Source: Official data collated by Our World in Data

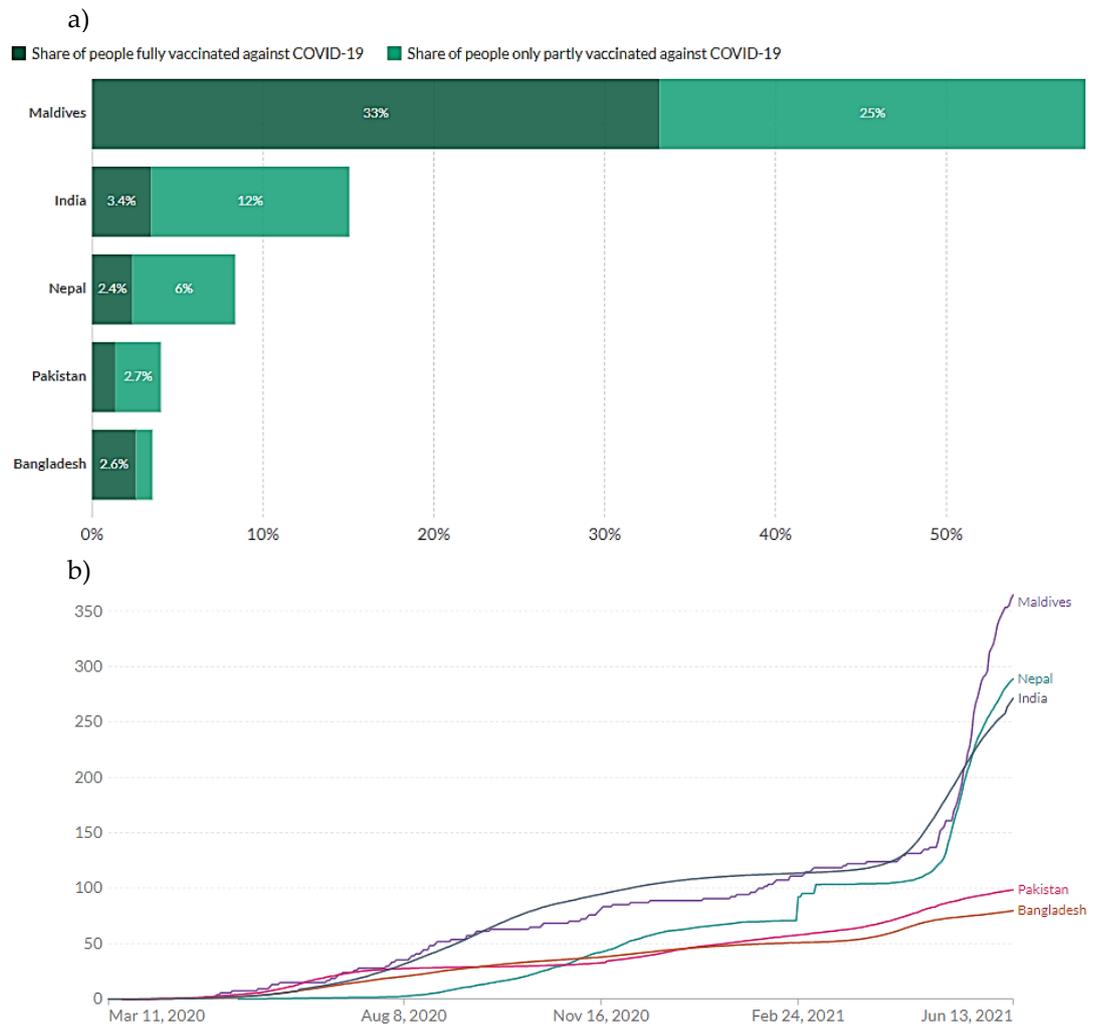
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Fig. 8. Number of daily COVID-19 vaccine doses administered (7-day rolling average), divided by the total population of the country. All doses, are counted individually (including boosters). All countries those showed steepest rise in vaccine doses, abruptly reduced the dose after 15th December [25].

2.3.3. Whether Vaccine dose matters

An obvious question arises whether vaccine dose matters. Many countries already exceeded much higher vaccine doses than herd immunity threshold e.g., UK, Israel. Interestingly, UK and Israel showed another surge in later period. In Israel, the third dose of vaccination drive is nearly complete; whereas, for the UK it is now in a very high percentage.

Results of vaccination and deaths for five neighboring countries from the Indian subcontinent are presented in Fig. 9. The Maldives ranked topmost in terms of share of people vaccinated (Fig 9a); whereas, Pakistan and Bangladesh ranked in bottom two, with India and Nepal in the middle. The ranking of those five countries was still maintained in terms of cumulative deaths per million and vaccine doses. A sharp rise in deaths for the Maldives was noticed in later periods in spite of maximum vaccine doses were administered. Deaths/million were lowest in Pakistan and Bangladesh those administered the lowest vaccine doses. India and Nepal ranked in the middle in terms of deaths per million and followed the ranking of countries for vaccine doses of Fig 9a and 9c. Here I showed a particular feature and covered only upto 13th June 2021. Similar observations can be noticed for many other neighbouring countries, even covering upto latest record.



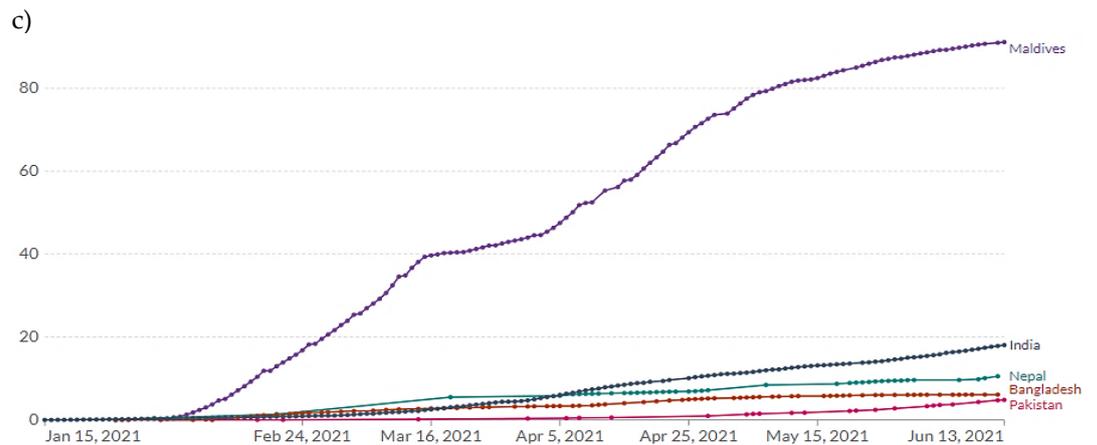


Fig. 9. Comparison of vaccine doses and deaths for five neighboring countries from the Indian sub-continent: a) share of people vaccinated relative to population; b) cumulative deaths per million; c) Vaccine doses per 100 people, upto June 13, 2021. [25]

2.4. Transparency, healthy Peer-review and services to Humanity

Healthy peer-review and constructive criticism, are always the pillars of good science, which became more important when the lives of billions of people are involved. Transparent healthy peer-review from experts and qualified scientists from various disciplines are likely to dismantle many unsorted puzzles and urgently needed. Enough scrutiny in every step was indeed expected with the mass vaccination as it was an extremely crucial endeavor.

Scientists and experts raised many sensible questions on numerous platforms e.g., the trial process for understanding medium and long-term effects, questions on mRNA technique etc. among others [6a]. Those need to have complied and are very important steps when millions of people are vaccinated on a regular basis. Relating to COVID-19 vaccine trials, it was pointed out in one topmost medical journal BMJ that ‘studies seem designed to answer the easiest question in the least amount of time, not the most clinically relevant questions’ [35,36]. Studies further discussed that current trials aren’t designed to say whether these vaccines can save lives [36]. The frail elderly were insufficiently recruited in the randomized trials though they are disproportionately contributing to the serious cases of the disease [37]. A very valuable comment in this regard was made by Prof Fiona Godlee, editor in chief, BMJ, “‘Science by press release’ is just one of many flaws in the way new treatments are evaluated, brought into stark relief by the pandemic’ [38].

A recent record unveiled a list of 40 new billionaires who joined the billionaires list benefitting from COVID-19 [39]. Many vaccine groups are earning billions from the COVID-19 vaccine [40]. As there are huge vested interests involved for vaccine and allied industries, long chains of beneficiaries are linked, additional precaution and surveillance/monitoring transparency must have been in place throughout. Some obvious questions could be: i) whether any important research and solutions other than vaccines are sidelined or suppressed and what measures are in place to stop that? ii) Whether fabricated analyses and biased results promoting vaccines and certain narratives are on the headline in everyday news and media or not? How open the critical evaluation process is taking place? Transparent open debates involving scientists with varied views (not the same scientists, same institutes, same viewpoints) need to be covered by media from time to time. iii) So far 140 COVID papers are retracted till mid-August, 2021. Whether the mechanism of retraction is serving the goal of particular interest groups or not, a secret vigilance operation needs stepping up to safeguard the peer-review publication system. Few questions could be: Is there a single paper retracted that was in favour of vaccines? Why there is unequal distribution, as numbers of retraction for both sides of narratives are likely to be equal. Those could be some constructive approaches to eradicate biases and improve transparency.

Ethics and integrity should not be compromised in that novel goal of saving humanity. Surveillance on excessive economic profit, wealth equity are certain areas those also need addressing.

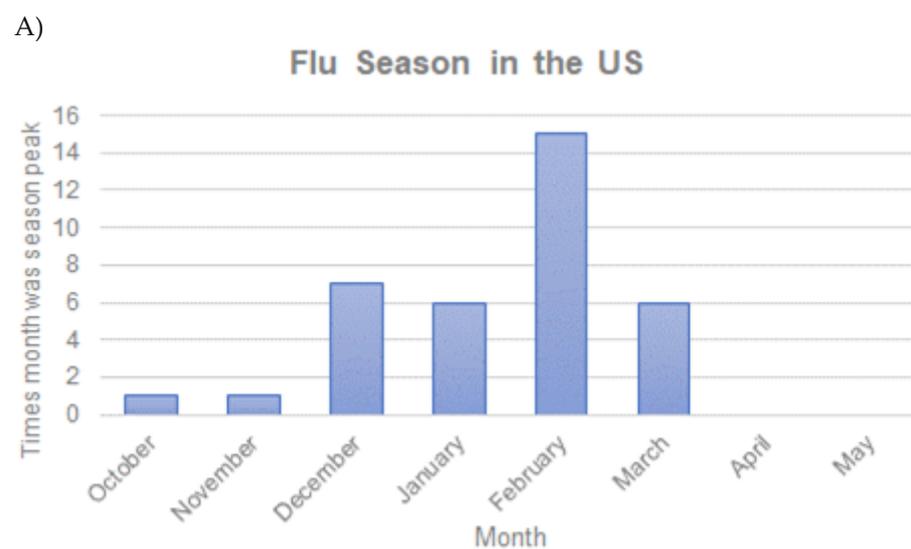
Few safeguarding mechanisms in this regard are suggested too. One proposition in that direction could have been producing and distributing vaccines on a not-for-profit basis by all vaccine groups. As that proposition is not yet implemented by all vaccine groups, an alternative idea can also be proposed that can act towards safeguarding the interest of general public. Imposing huge tax to vaccine and allied groups (**vaccine or COVID specialty tax/ 'COVID wealth equity' tax**) who are making tremendous financial benefit out of this crisis is an important step forward. It could be another way out to mitigate the worldwide economic crisis too. All the profit so far accumulated by vaccines and related business could be under that specific tax scheme say 'COVID wealth equity' tax. Another proposition could be open public auditing of finances for vested interest groups to check various aspects especially, **how much funding (direct and indirect) are spent on media, promotion and related activities**. Otherwise, there are huge risks that the interests of general people are overlooked or disregarded.

Those could have been very welcoming initiatives from government and policymakers involving all vaccine groups and allied sectors and would be highly appreciated and valued by general public.

2.5. The resemblance with Flu and useful timely insight

Tens of thousands of people die in the UK, Europe and northern America every winter, from a virus-borne respiratory disease, Influenza (Flu). The CDC (Centers for Disease Control and Prevention) estimated 61,000 deaths in the US from influenza during 2017–2018, which was higher than any season since 2009 [41].

Fig. 10A shows peak flu activity during flu seasons in the US by month from 1982-1983 through 2017-2018. During this 36-year period, Flu activity most often peaked in February. For COVID-19 also, countries those are Flu prone, peaked in cases and deaths in February 2021. The spatial pattern of Flu activity level is shown in Fig 10B. Brown and dark brown indicates a high prevalence of Flu which dominates later periods (2017-18 and 2016-17); whereas the green and light green suggests a low prevalence of Flu as seen for the earlier period (2009-10 and 2008-2009). It is clear Flu deaths in the northern US increased in later periods compared to previous years (Fig. 10B). In spite of many new vaccines over time, it is not yet been possible to eradicate Flu. On the contrary, it became more destructive in later years in spite of many new vaccines. The main reason is that the virus is mutating over time and space.



B)

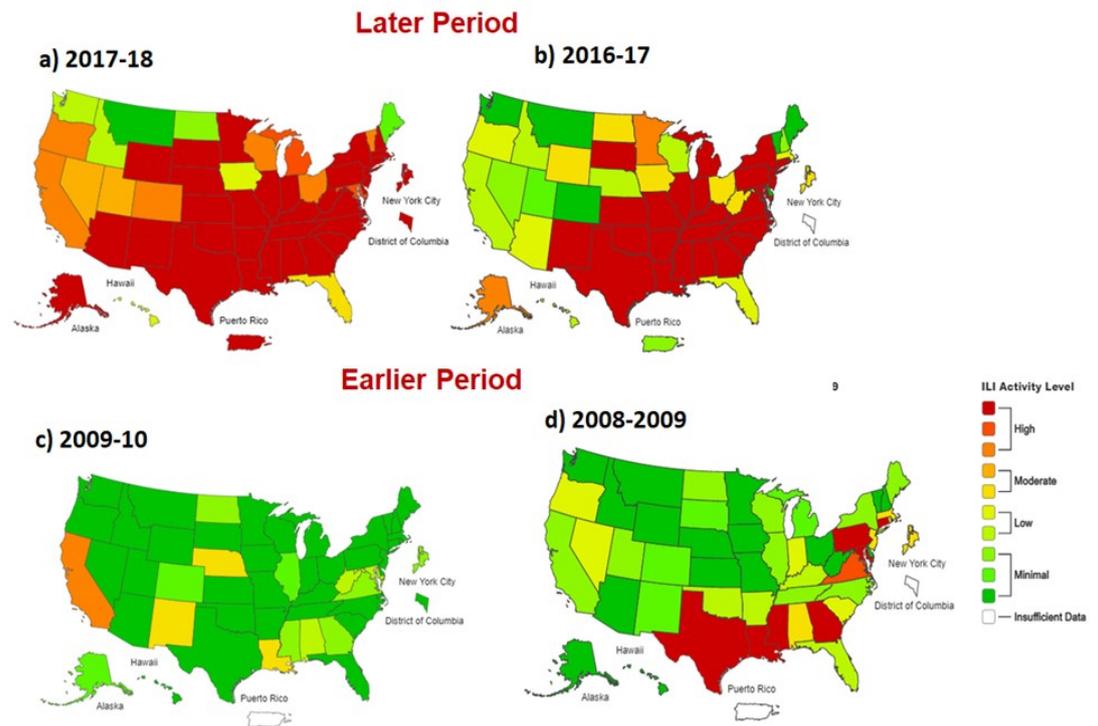


Fig. 10. A) Peak Flu activity during Flu seasons in the US by month from 1982-1983 through 2017-2018. During this 36-year period, Flu activity most often peaked in February [<https://www.cdc.gov/flu/about/season/flu-season.htm> accessed 21st July 2021]. The spatial pattern of Flu activity level in the middle of February is shown in (B). Top plot (a, b) for later periods (2017-18 and 2016-17) and bottom (c, d) for the earlier period (2009-10 and 2008-2009). [Source: <https://www.cdc.gov/flu/weekly/usmap.htm>, accessed 21st July 2021]

Other pertinent observations and similarities between Flu and COVID-19 as follows. i) Both viruses mutate over space and time. Since the first vaccine of COVID-19 came up only in December 2020, many new variants are already detected [42] and many are ineffective to the vaccine [5, 43]. ii) During summer the situation improved in Europe and North America as it happens for Flu. Last summer, **deaths from COVID-19 in Europe, were practically nil without any vaccination.** Before the coming winter, people vaccinated in March 2021 for COVID-19, need to be vaccinated again. This is because after six months the immunity to the disease is expected to wane [44]. Whether the same vaccine will be effective, whether the third dose of vaccine will be administered without any trial, how adverse effects (direct and indirect) will be evaluated for the third dose etc. complicates the matter further. In this winter, 2021 a new variant, named Omicron emerged (WHO) and even though millions of people already got the third dose of vaccines, many among those already got infected.

There could be relevant to this discussion that **Flu vaccine ineffectiveness was one responsible factor for excess of 50,100 deaths in the EU and UK in 2017-18** [45]. Though many vaccines were evolved and modified during the last 40 years, deaths were highest in more than 40 years. 'The Office for National Statistics said **flu and the ineffectiveness of the flu vaccine were key reasons for the rise of excess winter deaths in 2017-18**' [45]. The government's public health agency admitted that even for 2016, the rise in deaths in Wales and England for the previous 12 years, was ascribed to the failure to offer an effective Flu vaccine [46]. Those records indicated compared to the past how poorly Flu vaccines performed in later periods. Following our past experience with the Flu vaccine, the situation can also be speculated easily beforehand for the COVID-19 vaccine too.

We need to analyse the whole situation to take a timely intervention and need to question whether the intervention with the vaccine is making situations better or worse. We need to judge whether we have more and more liberty to accept excuses when the solution does not work. The proposition of vaccinating billions and billions of people every six months times for COVID-19, with the constraints of fixed world resources, raises a very obvious question, whether such an effort is

essential and worth it. The indirect and direct costs of that strategy deserve attention so as the usefulness of such a strategy.

Interestingly, Flu deaths reduced dramatically from Europe and the northern US when COVID-19 took a stronghold. During the last winter Flu deaths in the US were practically nil (Fig. 11, attached Figure from CDC, <https://www.cdc.gov/flu/weekly/>). The number of Influenza coded deaths (yellow) were missing last winter (Fig. 11). This winter also deaths from Flu so far is practically nil like last winter. Among the 3,330 Pneumonia, Influenza and Covid-19 (PIC) related deaths reported for the week ending December 11, 2021, (week 49), 2,569 had COVID-19 listed as contributing cause of death or an underlying cause on the death certificate. Only eight are listed for Flu, indicating that current mortality among COVID-19 and Flu, is primarily due to COVID-19, the most prevalent circulating virus among those two. Hence it is interesting to watch whether deaths due to Flu diminishes with the prevalence of COVID-19 or not in this winter and subsequent winters.

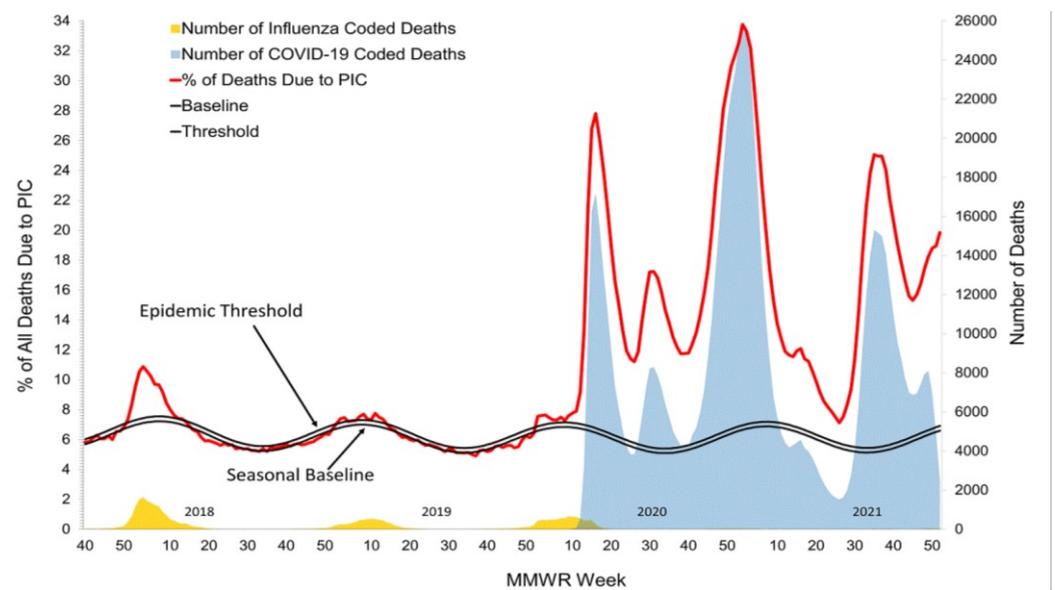


Fig. 11. Pneumonia, Influenza (Flu) and Covid-19 (PIC) mortality from the National Centre for Health Statistics Mortality Surveillance System, Data as of 6th January, 2022. Flu deaths (by yellow) were seen in fact negligible since the last winter till after the first week of January, 2022. (Source: <https://www.cdc.gov/flu/weekly/> dt 09/01/22)

2.6. Fast Mutation and New Variants

To monitor the progression of mutated variants of COVID-19 virus, an inspiring initiative was taken to develop a virus mutation tracker [42, 47] which is immensely beneficial. How rapidly it can mutate over spatial and temporal scales can be monitored [Fig. 12]. The fingerprints reveal the virus transmission route so as timelines of different mutations. For UK, the number of unique variants till 03/03/21 was identified as 11,098, of which foreign variants were 3,066 and local variants 10,7038 [42]. Interestingly, the timeline suggests a sudden increase in new mutations since December 2020 [42] (Fig. 12b). That is the period when the major vaccination programme started. Prior to that, upto November 2020, (during the initial 11 months of the pandemic), the progression was really slow (see the numbers in Fig.12b, bottom) in comparison.

COVID-19 vaccines can add fuel to the evolution of mutation of Coronavirus as vaccines themselves can drive viral mutations, suggested by Professor Bieniasz from Rockefeller University, USA [48]. According to him, the time between the initial vaccine dose and the second shot to boost the immune response might play as a kind of breeding ground to acquire new mutations of the virus. It may give one possible explanation why there is a surge in mutated variants after the start of mass vaccination, so as the rise in cases of transmission globally.

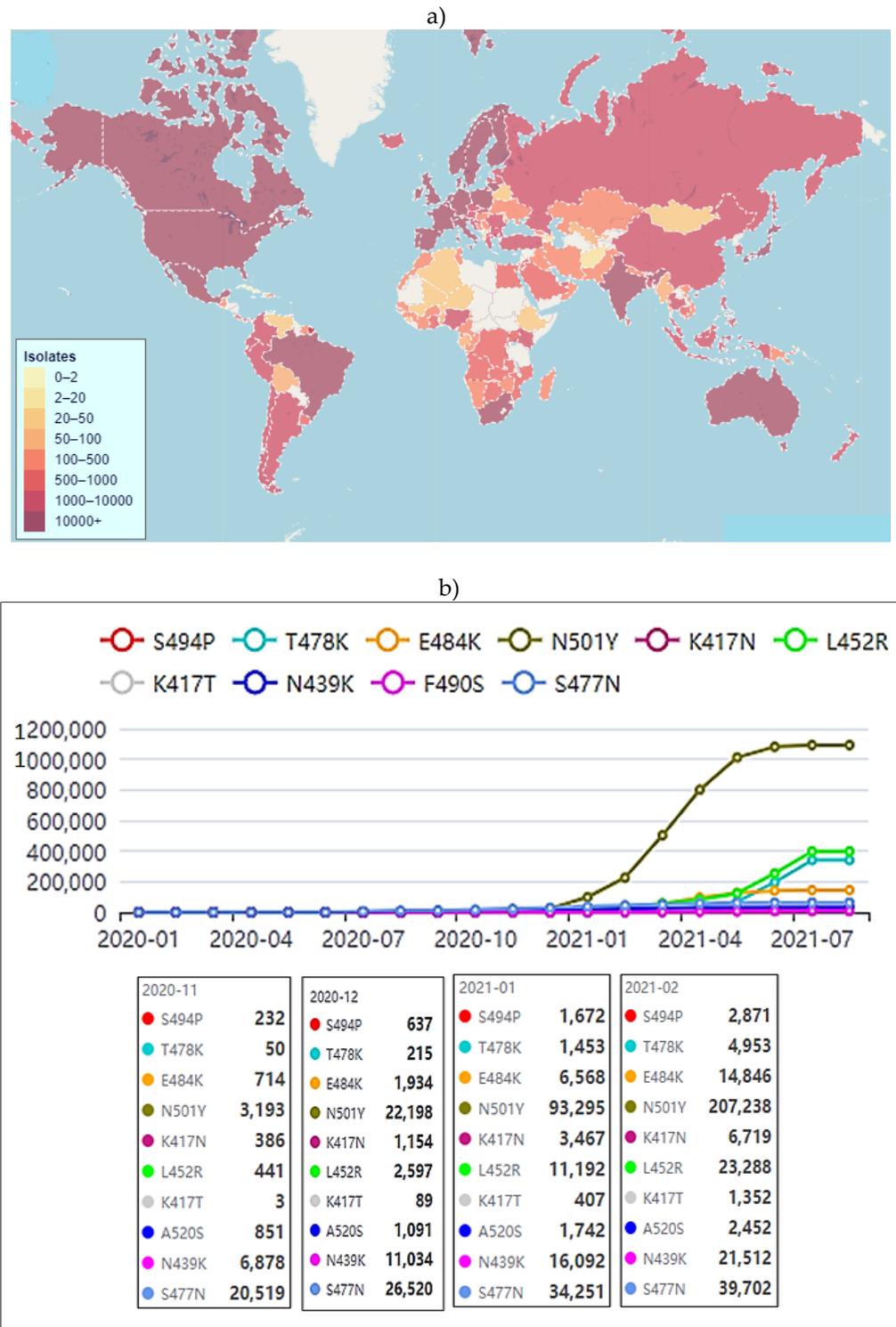


Fig. 12. COVID-19 virus genome isolates from patients are being regularly sequenced world-wide and continuously updated; for each sample, there is an accession number. The spatial distribution patterns (a) and temporal patterns (b) are shown. b) presents timelines of the top 10 major virus mutations those are progressing at a very rapid rate since December 2020. Numbers in each month from November to February are shown at the bottom of (b). It depicts how slow was the pace, in comparison, upto November 2021.

To check whether vaccine generated variants, a study analysed the countries where the first trial of each vaccine took place [48a]. Figure 13 shows a gnat chart marking the timing and locations where major vaccine trials took place, and maps it to the date the different variants were identified in those places [48a]. It is noticed major variants were identified in the countries where vaccine trials were taking place. Some variants were identified at the beginning of the trial, while some at the end [Fig. 13]. Various biological processes and physical mechanisms involved in how vaccines can accelerate mutation and how vaccines can also increase mass transmission is nicely discussed in a recent review [6a].

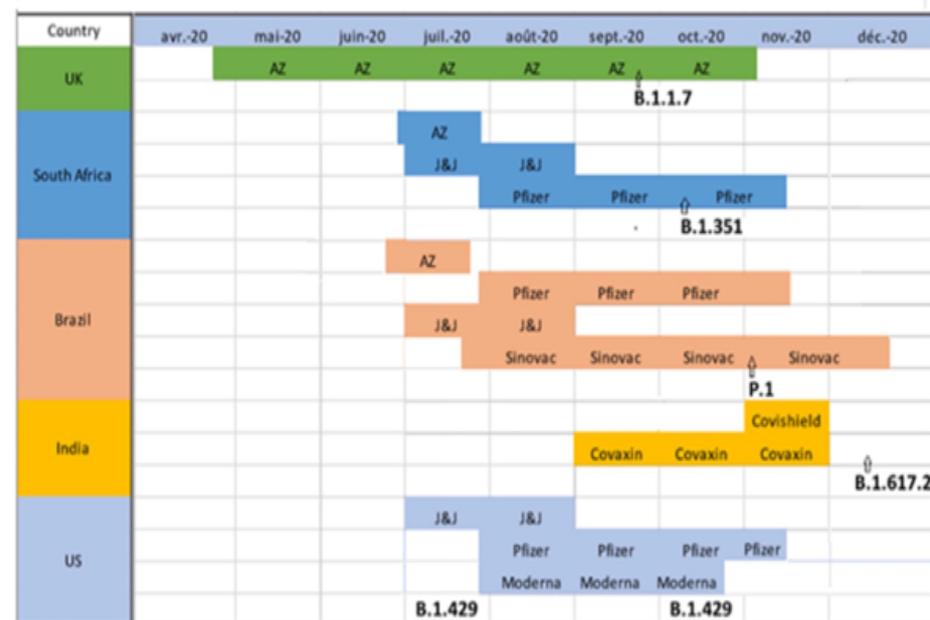


Fig. 13. Gnat chart showing the timing and locations where major vaccine trials took place, and maps it to the date the different variants were first identified in those places. [Tan et al., 2021 [48a]]

2.7. Trial experiments/Observation: Mass vaccination and transmission

Trial protocols and experiments assigned for COVID-19 vaccination did not take into account many indirect and direct effects of mass vaccination. After vaccination, apart from looking into details of direct side effects, the secondary effect that might be triggered after mass vaccination also needs attention. A trial experiment was conducted in the US, California at the very early stages of vaccination (m-RNA vaccine) and participants were chosen among vaccinated health care workers (being exposed to patients and hence more likely to catch the disease) and discussed underneath. It showed even after 15 days of 2nd dose, vaccinated people can be a carrier and spread the disease.

In the transmission and spread of SARS-CoV2 infections, asymptomatic cases also have roles [49]. That clinical trial experiments conducted among vaccinated healthcare workers also allowed for increased detection of asymptomatic infections [50]. The period considered was as early as December 16, 2020, through February 9, 2021. A total of 14,604 were monitored among vaccinated people, out of those 379 tested positive at least 1 day after vaccination. Within the first 2 weeks after the first vaccination, the majority of infections took place (71%). Whereas, after receiving both doses, 37 health care workers were tested

positive. Even after 15 or more days of the second dose, 7 tested positive. Note, the time period is less to have enough samples after 15 days of the 2nd dose [Table 2, 50].

Table 2. New SARS-CoV-2 Infections among Vaccinated Health Care Workers from December 16, 2020, through February 9, 2021.

Days after Vaccination	Vaccinated Persons		
	With New Infection (N=379) Number	Tested (N=14,604)* Number	Eligible for Testing (N=36,659)+ Number (percent)
Dose 1			
Days 1-7	145	5794	35,673 (97.3)
Days 8-14	125	7844	34,404 (93.8)
Days 15-21	57	7958	32,667 (89.1)
Day 22 or later, Before dose 2	15	4286	32,327 (88.2)
Dose 2			
Days 1-7	22	5546	23,100 (63.0)
Days 8-14	8	4909	16,082 (43.9)
Days 15 or later	7	4167	14,990 (40.9)

[after, Keehner et al., 2021 [50], see details there]

To gain useful insight, one interesting point could be to check whether the rate of infection (379 out of 14,604) within two months is comparable with the general infection rate among the unvaccinated adult (not old, frail or retired). This study indicates that after vaccination, the absolute risks of testing positive for SARS-CoV-2 are higher than the risks noted in original phase III trial experiments. Moreover, over-confident, vaccinated people, if develop mild symptoms or remain asymptomatic can be super-spreaders.

Such analyses raise obvious questions, as mentioned underneath, which require in-depth investigation and could have been explored at the start of a rapid **mass vaccination** program. i) Do vaccines have any role to cause more mutation of virus? ii) If right, can more forms of mutations be linked to different types of vaccines? iii) For viral mutation, if vaccines have any roles, is it dependent on climate, ethnic groups, past health conditions of individuals, various genetic groups of people, etc.? iv) Patients who are immunocompromised are they playing major parts in viral mutations after vaccination? v) Did mutation originated and progressed first in countries where vaccine trials started. vi) If vaccines can cause mutation, it is not only traveling that can spread the mutated virus country-wise or region wise; it can equally happen within any community sooner or later, even with strict lockdown or travel ban. vii) some countries by reducing vaccine dose and lockdown measures, could subside transmission which became uncontrollable otherwise (e.g., India in April/May 2021, Bahrain in May/June 2021 [3], also see Fig. 5). Such intervention on time showed that policymakers and government can be controllers of the rate of viral transmission by regulating the number of vaccine doses, spatially as well as temporally.

viii) Following patterns of Flu, another surge was predicted to happen in the northern US and Europe, at the beginning of winter 2021 (<https://easychair.org/smart-slide/slide/S39n>, presentation on July 2021, [51], [52]). Here are some relevant important quotes [51], [52]: “At the beginning of winter 2021, like Flu, there is another surge likely to happen in Europe and northern US. It is very likely that we are going to blame on new mutant variants and another lockdown will be impending”; “**Can the timing and severity of global future waves (third/fourth etc.) in the future be controlled by regulating vaccine doses?**” Thus, we need to be **Pragmatic** and not simply optimistic or pessimistic. We need to explore alternate pathways and be well-prepared side by side with substitute solutions beforehand [14, 15, 16]. If there is a possible solution without any vested interest and which is easy to practice, that could be worth an explore.

Moreover, it is worth mentioning that without proper examination of all indirect and direct consequences of mass vaccination, any hasty actions **can cause more harm than good**. It can lead to severe consequences to high populated countries that we already eyewitnessed. Those areas need urgent attention and thorough investigation on time to arrest further escalation of the deteriorating situation.

2.8: Some comparison of vaccinated vs. unvaccinated.

In December 2021 we already completed one year after the start of vaccination in the UK and hence there are enough data to do some comparison between vaccinated and unvaccinated groups. Main findings among those two groups are likely to be similar in other countries too.

2.8.1. Some Observations on Dominant variants and claims on vaccine success.

Cases and deaths in England due to two dominant variants, Alpha and Delta, from 1 February 2021 to 2 August 2021 are shown in Table 3 [10]. Other variants viz. Beta, Eta, Gamma, Kappa,

Table 3. Cases and deaths in England due to dominant two variants (1 February 2021 to 2 August 2021, [10])

Variant	Age Group (Years)	Cases since 1 st Feb	Deaths number (%)	Post dose1	Received 2 dose	Unvaccinated
Alpha	< 50	118,178	66 (0.1%)			
	≥ 50	32,274	1,548 (4.8%)		Not available	
	Total	150,541	1,614 (1.1%)			
Delta	< 50	265,749	71 (0.0%)	8	13	48
	≥ 50	33,736	670 (2.0%)	71	389	205
	Total	300,010	742 (0.2%)	79	402	253

Lambda, Theta, Zeta etc. were also identified earlier, however, those were nominal compared to Alpha and Delta. The fatality rate for Alpha was much higher than Delta so far; as deaths/ cases were 1.1% and 0.2% respectively (Table 3). Death statistics between the vaccinated and unvaccinated categories for Delta indicate that those statistics are comparable [Table 3]. It does not reflect vaccinated groups are performing better than unvaccinated. It is also noteworthy that under 50 groups also consist of less than 18-year group and they are unvaccinated during that period (as

vaccination did not start). Many of those under 18 years also have comorbidities. For the UK and England, Delta is the most prevalent variant in the last few months upto November (~ 99%, [10], [25]). As percentage of deaths from Delta was also less among the unvaccinated group, it indicates Delta was less deadly than Alpha so far irrespective of vaccination category. Thus the claim for UK, which is one of the topmost vaccinated countries, that vaccine is reducing deaths inspite of high cases can not be substantiated by observed data. With the recent emergence of another new variant Omicron [WHO], the initial data suggests it is less deadly than Delta, though more transmissible [BBC]. It is in line with the recent observed record of global cases and deaths statistics (Fig. 4), though need to monitor closely.

2.8.2. Progression of Deaths for vaccinated vs Unvaccinated.

Vaccine efficacy is heavily reduced though proclaimed very high (above 90%) initially. For England, further analyses were conducted to study the progression of deaths weekly/biweekly basis due to Delta variants (Public Health England Technical Briefing various issues, [10]). It indicates that deaths among fully vaccinated are rising at a much higher rate than the rest two groups (unvaccinated as well as people having one dose) [Fig.14] and it is clearer when we focus on the trend lines. The last biweekly counts of death upto mid-August also indicated consistent results; a total of 277 died from the fully vaccinated group while 137 were from the unvaccinated group [Fig. 14]. For Scotland upto 21st of June 2021 a total of 2247 fully vaccinated (28 days after the 2nd dose) people died [12]. In Israel, it is noted that most hospitalised severe patients are fully vaccinated [11]. As the effectiveness of vaccines is waning, Israel first initiated 3rd booster dose at the beginning of winter followed by many other countries [25]. Now forth doses are underway and already granted in Israel (BBC). Further worrying news is that immunity via vaccine is now shown fading much faster than proposed earlier, which was earlier six months [BBC]. Portugal with very high vaccine rate was portrayed earlier as a vaccine success story. Similar like Israel and Gibraltar and all three are now showing a rise in case numbers [1, 25]. For Gibraltar (a small country), they vaccinated more than 100%, (this is because non-resident employees are also fully vaccinated) [25].

Another important point to note is that people within 2 weeks of 1st vaccination dose is considered as 'unvaccinated' group in England, whereas it is within 3 weeks for Scotland. Interestingly infected cases within 2 weeks of vaccination are exceptionally high compared to the whole infected cases (see Table 3). Thus, the high case number among unvaccinated group is misleading and will give bias results for that group. If such definition of threshold is followed, cases among vaccinated and unvaccinated group also favours vaccinated category. Such biased results are often portrayed as another vaccine success story.

If there are records of percentage cases separating within 14 days of 1st dose vs not received any vaccination at all, but infected, that may give rise to some interesting picture. It might give some explanation why there are rise in cases for almost all countries after the start of mass vaccination. Scientific basis in this regard are also analysed in a recent review [6a]. Our discussion indicates that claimed success stories of vaccination need thorough investigation with critical

viewpoint and it is crucial to figure out the actual success stories of vaccine and to do risk vs benefit analyses.

Time progression of deaths from Delta variants in England, indicates that the rise in deaths among vaccinated with double dose are rising much faster to that from the unvaccinated group. Data though shown here upto mid-August but such pattern is still consistent. Though more population are getting double vaccinated as time progresses, but such observation clearly raises doubts of proclaimed vaccine success stories.

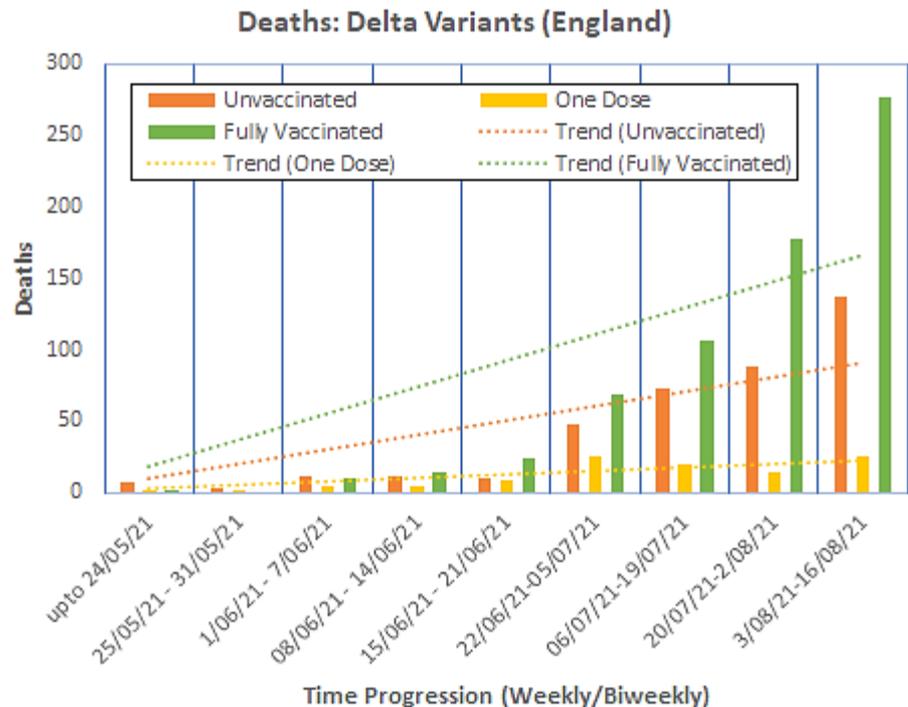


Fig. 14. Time progression of deaths from Delta variants in England, using data from [10] among unvaccinated, fully vaccinated and people with one dose. Trends (with no intercept) are shown by same-colored dotted lines.

2.8.3. Covid Deaths absolute numbers (agewise): Most unvaccinated or vaccinated?

Data from UK hospitals were also analysed upto week 46, 2021 (3rd week of November) since August and explored agewise variation too. Here are some records of UK government statistics and results are consistent over time. Attention is on people aged 50 years and above as they are the most vulnerable categories.

- *Date till 12th September in England:*
 - a. Cases: double vaccinated 71,991 (14 days after 2nd dose); whereas it is 8551 for the Unvaccinated group.
 - b. Serious hospital admission: 3,913 who are double vaccinated; whereas it is 1,786 for the Unvaccinated group.
 - c. Deaths: 1565 who are double vaccinated; whereas it is 590 for the Unvaccinated group.

[https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1018547/Technical_Briefing_23_21_09_16.pdf, their Table 5]

- *Date: week 40-43, 2021 in the UK*

COVID-19 deaths within 60 days of a positive specimen or with COVID-19 reported on death certificate, by vaccination status between week 40 and week 43, 2021 in the UK: Death 2951 for fully vaccinated, while 573 for unvaccinated.

[https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1032671/Vaccine_surveillance_report_-_week_44.pdf, their Table 4b]

- *Date: week 43-46, 2021 in the UK*

Deaths among the unvaccinated group in both attached Table 4a and b are less than 700 hundred (shown by green); whereas it is 2844 to 3393 among double vaccinate people (14 days after 2nd dose, shown by red).

[https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1036047/Vaccine_surveillance_report_-_week_47.pdf, their Table 10a]

Table 4: COVID-19 deaths (a) within 28 days (b) within 60 days of positive specimen or with COVID-19 reported on death certificate, by vaccination status between week 43 and 46, 2021.

(a)

Death within 28 days of positive COVID-19 test by date of death between week 43 and week 46 2021	Total**	Unlinked*	Not vaccinated	Received one dose (1-20 days before specimen date)	Received one dose, ≥21 days before specimen date	Second dose ≥14 days before specimen date ¹
[These data should be interpreted with caution. See information below in footnote about the correct interpretation of these figures]						
Under 18	9	1	8	0	0	0
18-29	13	0	9	0	2	2
30-39	44	1	28	0	4	11
40-49	104	3	51	0	4	46
50-59	250	5	108	0	11	126
60-69	555	3	154	0	18	380
70-79	1025	6	163	1	9	846
≥80	1,726	7	187	5	35	1,492

(b)

Death within 60 days of positive COVID-19 test by date of death between week 43 and week 46 2021	Total**	Unlinked*	Not vaccinated	Received one dose (1-20 days before specimen date)	Received one dose, ≥21 days before specimen date	Second dose ≥14 days before specimen date ¹
[These data should be interpreted with caution. See information below in footnote about the correct interpretation of these figures]						
Under 18	12	1	10	0	1	0
18-29	16	0	9	0	2	5
30-39	52	1	32	0	4	15
40-49	132	4	62	0	5	61
50-59	312	6	134	0	14	158
60-69	658	5	181	0	20	452
70-79	1,195	7	175	1	16	996
≥80	2,054	7	207	6	47	1,787

[Source: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1036047/Vaccine_surveillance_report_-_week_47.pdf, their Table 10a and b]

Table 4a shows there are 3456 deaths among which 612 unvaccinated people; whereas 2844 died who are fully vaccinated (double dose >14 days). That means approximately for **every 6 deaths from Delta, 5 persons are fully vaccinated, while 1 is unvaccinated**. Proportions could be a little less if total numbers of vaccinated and unvaccinated populations are considered. However, considering the absolute numbers (Table 4) a question definitely arises on how effective the vaccines are and whether it matches with high vaccine effectiveness as claimed initially before the start of mass vaccination. Those statistics for unvaccinated and vaccinated are shown similarly for the earlier period too.

Honest journalism is also important to disseminate transparency and reality to common people. An article published in the top-level newspaper 'The Guardian' with headline, 'Covid patients in ICU now almost all unvaccinated'.

<https://www.theguardian.com/world/2021/nov/23/covid-patients-in-icu-now-almost-all-unvaccinated-says-oxford-scientist>

Following previous data, as presented, how anyone interprets and presents any result is another area that needs attention. Honesty and transparency in journalism are other important areas that deserve improvements.

2.9. COVID-19 and Seasonal temperature

Seasonal effects especially the temperature should be considered a crucial factor for the transmission of COVID-19 in many countries [14,15,16,17]. COVID-19 transmission becomes high in wintertime of respective hemispheres [14,15] and months of winter in the Northern hemisphere coincides with the summer in the southern hemisphere and vice versa. By around mid-April 2020, almost all European countries and countries from the northern USA showed a decrease in transmission and that happened without any involvement of vaccines. Reporting of cases is likely to be influenced by various reasons e.g., testing facility, location (remote or urban), some countries had very high testing while some very less. As death reporting is usually authentic, this study considered 'deaths' as a better and useful metric to analyze results.

Figure 15 shows COVID-19 deaths in 20 European countries upto 7th August 2021. As it happens for Flu in every year, the transmission of COVID-19 in those countries, in fact, was nominal during mid-June to September 2020, compared to the severity of other months. Here 20 countries are presented and there are varied characteristics of those countries e.g., some are international business hubs with more foreign travellers, while some are popular tourist spots, countries also have different levels of testing, moreover infrastructural and medical facility could also be different. Population density as well as different degrees of lockdown restrictions also affects results. Interestingly, in spite of all dissimilarities still, there is one common factor which is deaths (shown as 7-day average) for all those 20 neighbouring countries were practically nominal from July 15 to Sept 15, 2020 (Fig. 15a) Whereas, high deaths were noticed during 15th October '20 till 15th May '21. Now as the absolute number of deaths vary based on population, to analyse the degree of vulnerability, death/million population of a country is also considered in Fig. 15b. Results are plotted as cumulative measures to understand the seasonal transition better. It shows considering the whole period of pandemics, the trend was nominal in most countries between 15th May to 15th October 2020. Such nominal trend is again noticed since 15th May 2021 (Fig. 15b, horizontal lines are distinct after dotted black lines).

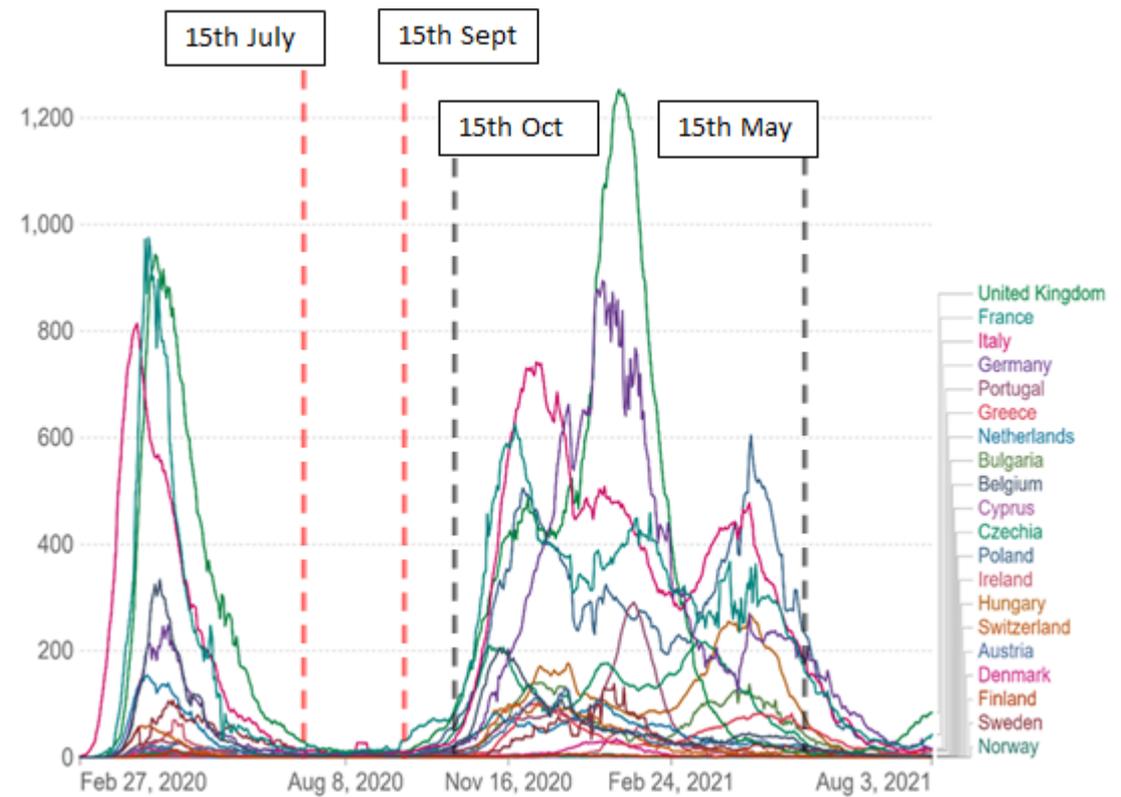
If vaccines were not in place, it would have been also expected **likewise from mid-April this year**. After major vaccination started there were surges in transmission in almost all countries and most countries had to impose strict lockdown conditions. Monitoring the situation of the last summer, 2020 with the current summer, 2021 may give ideas on how the effect of vaccines, (including the proportion of vaccinated percentage, time of major vaccination programme) may override the effect of seasonality in countries of northern US and in various European countries.

To study the effects of global temperature some analyses were done with global 2m air temperature using NCEP reanalyses data (Fig. 16). Using different data sources and other temperature parameters (say, 1000 mb air temperature) also suggested similarly. Spatial plots of 2 meter mean air temperature in different periods of the pandemic are shown. During mid-July to mid-September 2020, when COVID-19 deaths and transmission were lowest in Europe among the whole pandemic (Fig. 15a, between red dotted line) is shown in Fig 16a. Whereas, during mid-October 2020 to mid-May 2021 when deaths in Europe were very high is shown in Fig 16b (between black dotted lines, Fig 15b). Interestingly, the temperature upper and lower bound changed even 20 degrees in Fig. 16a to Fig. 16b; maximum temperature decreased from 310K to 290K, whereas, minimum temperature from 280K to 255K. Knowing that this virus and similar generic viruses are very sensitive to temperature [14-17, 18-24], such a huge change of air temperature around Europe in a few months' time could be playing an important role. This is true for Flu as well as COVID-19. Temperature spatial plots in two transition periods when the trend of deaths was very steep (Fig 15) are also shown (Fig. 16c and Fig. 16d). Figure 16c is for mid-April to mid-May, 2020 and Fig. 16d for mid-October to mid-November, 2020. The minimum temperature limit reduced from 280K in Fig 16a to 265K and 255K respectively in Fig. 16c and Fig. 16d. Not only minimum temperature bound reduced 15K and more, but a sudden decrease for the maximum temperature bound is also noticed. Maximum temperature also reduced 10K or more in Fig. 16c and Fig. 16d with respect to Fig. 16a. Such a sudden decrease in temperature for minimum and maximum bound happened in only a few months' time.

One of the main dominant factors, seasonal temperature, for COVID-19 transmission is undermined by the scientific community and in all important publications. Thus, the concept of avoidable deaths as speculated by models which did not take proper consideration of seasonality could be pure speculation rather than a reality. Moreover, there are many other unknowns and confounding factors too for the spread of COVID-19 transmission which makes modelling of its spread and estimated death counts far from reality.

A systematic review work [53] studied the effect of seasonal temperature by selecting sixteen relevant articles and all unanimously stated that cool and dry conditions were potential factors for the spread of COVID-19, with the spread being largely absent under very hot and extremely cold conditions. The Authors found there was great homogeneity in the results of the effect of temperature in the seasonal variability and spread of the virus. However, based on their Table 3 [53], the authors finally concluded that certainty of the evidence was graded as low. A careful observation suggests that 'low' grading is not supported by their Table 3 from [53]. On the contrary, it is completely the other way round.

a)



b)

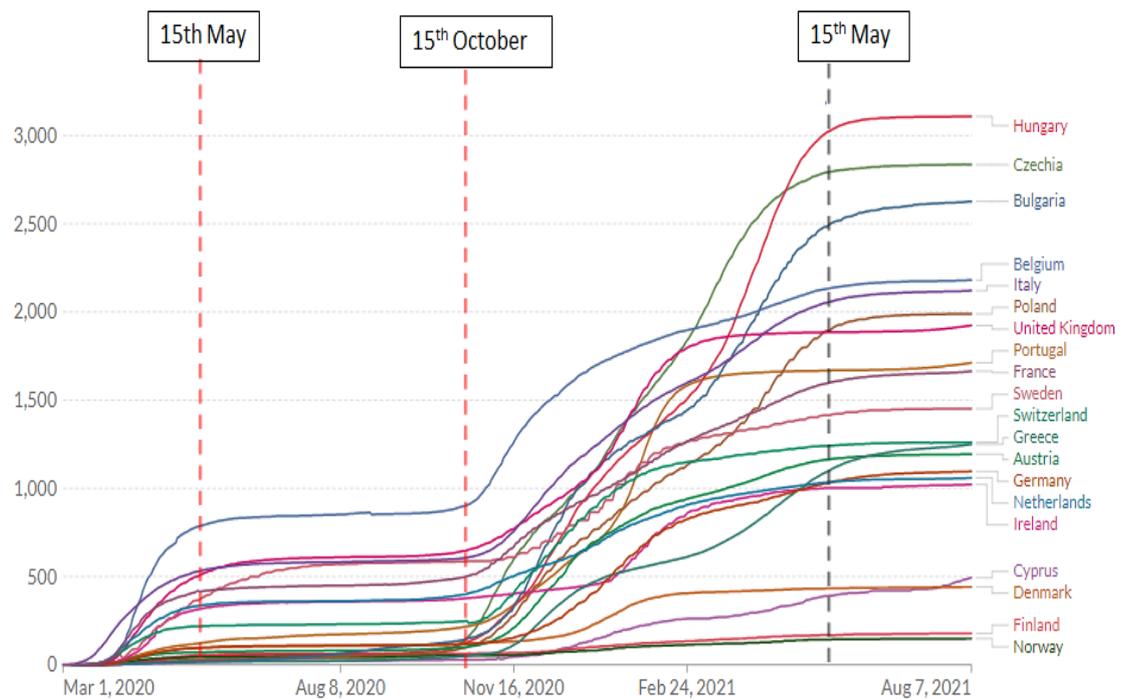


Fig.15 COVID-19 deaths in 20 European countries upto 7th August 2021. a) Daily new deaths 7-day average; b) Cumulative deaths per million people. a) shows deaths are practically nil between 15th July to 15th September for all those countries (periods shown between red dotted lines). High deaths are noticed from 15th May '20 to 15th October '20 (shown between black dotted lines). b) shows considering the whole period of a pandemic, the trend was nominal in most countries between 15th May to 15th October 2020 (marked by dotted red, the horizontal part between those lines is quite distinct). Such

nominal trend is again noticed since 15th May 2021 (horizontal lines are distinct after dotted black lines).

(Source: <https://ourworldindata.org/coronavirus-data-explorer> accessed on 07/08/2021, [25])

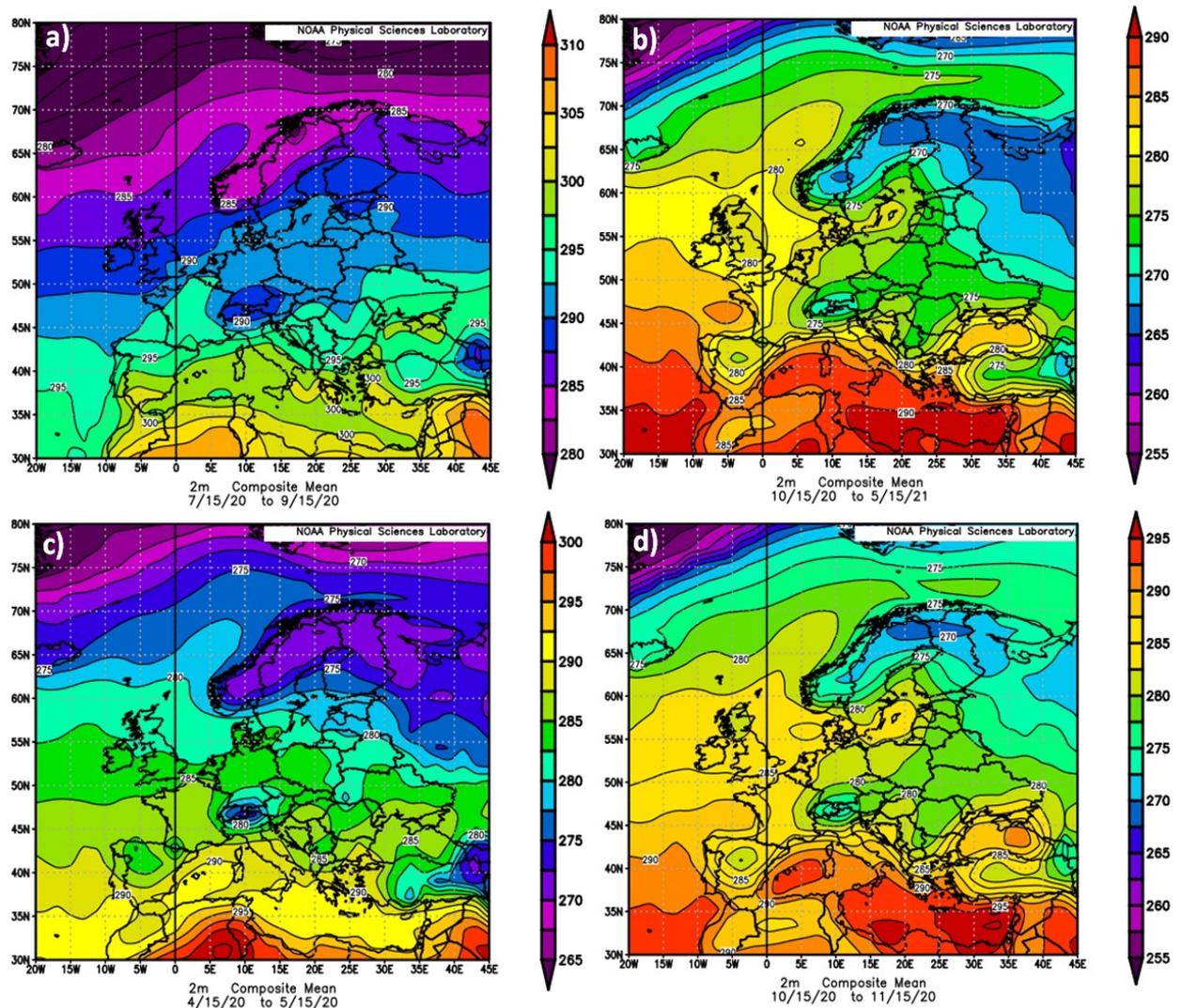


Fig. 16. The spatial plot of 2 meters mean air temperature in different periods of the pandemic from NCEP Reanalysis data. a) mid-July to mid-September 2020 when COVID-19 deaths and transmission were lowest in Europe among the whole pandemic. b) mid-October 2020 to mid-May 2021 where deaths in Europe were very high. c) mid-April to mid-May, 2020 and d) mid-October to mid-November, 2020 the two transition periods when deaths suddenly increased. Plots generated using site <https://www.esrl.noaa.gov/psd/data/composites/day/>.

Very few limited studies are there that disregarded the effect of temperature on transmission of the disease [53, 54]. Some studies were already excluded from the final analyses of systematic review[53] stating obvious biases in those analyses while the other study [54] used a technique that is not suitable to explore effects of seasonal temperature. The latter study [54] also mixed data of lockdown and non-lockdown periods. Moreover, it used the non-linear least-squares method to study the relationship between COVID-19 transmission and temperature where many confounding factors play roles. They

separated countries into three groups based on first reporting cases of the disease as January, February and March respectively. To study the effect of seasonal temperature to categorise countries based on criteria, which is heavily linked with foreign travel, is not at all appropriate. On the contrary most of the studies that detected the effect of seasonal temperature categorised countries based on temperature viz. very cold, moderately cold and warm [14-17 among others]. The relationship between temperature and transmission is also not linear; e.g., very cold and warm countries showed less transmission while moderate cold countries showed maximum transmissibility and death counts. Hence the transition from one state to another to any country based on temperature makes a huge difference to the risk and vulnerability of any country [14-16].

Though the dependency of seasonal temperature was very apparent throughout, till vaccination started, but surprisingly undermined by the science community and in many important publications. Could it be because of the earlier experiences with the seasonal Flu Vaccine?

3. Conclusions

A strong coordinated effort is in place from vaccination groups to put an end to the current COVID-19 crisis. The mass vaccination programme was initiated in early December 2020 and countries all over the globe are part of it. We now have enough data to compare results to study the effectiveness, shortcomings and aftereffects of mass vaccination. This study explores exit strategies of the COVID-19 crisis using pathways of vaccination. It is a pragmatic approach to address various aspects of the strategy with an open and critical mindset.

Some influence variables on transmission of the disease are discussed e.g., lockdown, seasonality and mass vaccination. Seasonality played an important role in the global transmission of the disease before mass vaccination and some contrary findings/ publications in that respect were attended. In spite of strong effect of seasonality, though present like Flu, why it was undermined by many important publications were discussed. To address seasonality, many similarities between seasonal Flu and COVID-19 received attention to gain useful insight. In spite of many differences, striking similarities between these two diseases are noted. Seasonal Flu kills tens of thousands of people in Europe and the northern USA every winter which became more vulnerable in later years compared to the past. In spite of modern and evolving vaccines, it is not yet been possible to eradicate Flu. On the contrary, it became more powerful and destructive in later years. The main reason is that the Flu virus is mutating over time and space. From the experience of the last few months, we are observing a similar pattern in relation to mutation of the COVID virus too. Hence this study questioned whether, like Flu, it could be similar for COVID-19 in the long run or not. Moreover, we are reminded that there are yet not any successful vaccine developed/ passed trial phase for some virus borne diseases too (e.g., AIDES etc.). Thus, question arises that are we prepared for the coming northern winter with any alternate strategies? Some published research, clinical trial experiment and supported analyses suggested heat-based simple solutions at initial stages of the disease could be a useful strategy that deserves attention. It does not have any vested interest.

Trial protocols and experiments designed for COVID-19 vaccination did not take into account many direct and indirect consequences of mass vaccination. Adverse reporting of data raised questions for short-term direct effects, which is compared with adverse report data of other vaccines. Some disproportionate adverse reporting on the young and male populations were also discussed. Furthermore, when attention is on indirect consequences, we notice, almost all countries experienced a sudden surge of transmission after the initiation of vaccine programmes, and most countries had to impose strict lockdown measures. Even for the Israel and UK, where massive vaccination took place, the total deaths in the next three months after the start of vaccination reached the overall death of 10 months prior to vaccination; moreover, they also had strict lockdowns. Brazil started vaccination at around mid-February and just after a month a very steep rise in deaths is noticed. A

highly populated country India was about to control the disease without any vaccine or lockdown, but since the middle of February, just after a month of the start of vaccination, it reversed the trend of deaths and cases from decreasing to increasing. Such a steep rise in deaths/cases for India never happened in the entire period of pandemics. The dose of vaccine was again varied abruptly in European countries at the start of winter 2021. From around middle of November 2021, UK and most European countries suddenly increased vaccine dose, which again matched with the winter seasonal cycle and cases skyrocketed. Cases around the world showed an unprecedented surge. Following that unusual surge, most European countries however started decreasing vaccine doses since 15th December onwards. The recent rise and fall of vaccine doses in highly populated European countries are steepest of the entire pandemic. In that context, new variants and fast mutation of the virus with relevance to mass vaccination were addressed with a critical mindset.

Many countries also showed synchronized patterns between new cases and vaccine doses. Countries with a low prevalence of diseases in the earlier period of pandemic (e.g., many countries from African continents, SAARC, and South East Asian countries etc.) showed a massive surge when vaccine dose was suddenly increased. Such observation has relevance to vaccine equity. In this regard, the country Indonesia was the latest addition when a sudden rise in vaccine dose caused the highest daily deaths among the world during July-August, 2021.

This study further discussed whether vaccine dose matters and whether countries those vaccinated a high percentage of the population perform better or not than those who did not. I showed it is not the case as is clearly reflected from the recent surge in UK and Israel during August 2021 (those are among the top-ranking vaccinated countries). Results of vaccination and deaths for five neighboring countries from the Indian subcontinent are presented where the Maldives ranked top-most in terms of share of people vaccinated; whereas, Pakistan and Bangladesh ranked in bottom two, with India and Nepal in the middle. Interestingly, the rankings of those five countries were still maintained in terms of cumulative deaths per million. The Maldives had the highest deaths, followed by India and Nepal. Pakistan and Bangladesh who received the lowest vaccination even showed lowest deaths among the five. The recent record further triggered doubts as Israel initiated the 4th dose. Portugal with very high vaccine rate was portrayed earlier as a vaccine success story. Similar like Israel and Gibraltar and all three are now showing a rise in case numbers. For Gibraltar (a small country), they vaccinated more than 100%, (this is because non-resident employees are also fully vaccinated), but cases are still on the rise. Such observations raise many obvious questions on the future direction of the mass vaccination program and its aim and achievable proposed objectives.

Many people were infected not only after the first dose but even after 14 days of the 2nd dose (breakthrough cases), though the infection rate among the vaccinated group is unusually high within 14 days of the first dose. Vaccinated, over-confident people, if asymptomatic or develop mild symptoms, can also act as super-spreaders. Further analyses on England suggested that the high prevalence of Delta variants though caused high case numbers in July, August but death rates are low compared to Alpha variants. In England, Alpha and Delta variants were dominant variants so far in 2021. Interestingly, deaths among vaccinated and unvaccinated are comparable among Delta variants, which suggests it is not the effect of vaccine that caused a lesser percentage of deaths. On the contrary, it is due to the high prevalence of Delta variants (99%) which were less deadly than Alpha till August, 2021. Time progression of deaths in the England indicates that death counts are rising faster among the vaccinated group (with two doses) than the other two groups, unvaccinated or with group of one dose. A trial experiment with vaccinated healthcare workers from US suggested that infected cases within 2 weeks of 1st vaccination were exceptionally high compared to the whole infected cases of the sample group. However, people within 2 weeks of 1st vaccination dose are considered as 'unvaccinated' group in England, and most countries. It might give bias results and in this context, some success stories of vaccines, as claimed, are evaluated critically.

In December 2021, as UK completed one year after the start of vaccination there are enough data to do some comparison between vaccinated and unvaccinated groups. Analyses using government data show approximately for every 6 deaths from Delta, 5 persons are fully vaccinated, while 1 is unvaccinated. Considering the absolute number of deaths, a question definitely arises on how effective the vaccines are and whether it matches with the proclaimed high vaccine effectiveness or not. Honesty and transparency in journalism are other important areas that deserve improvements too.

As there are huge vested interests involved for vaccine and allied businesses, few safeguarding mechanisms to protect interest of general public are suggested too. One proposition could be imposing huge tax to vaccine and allied groups (**vaccine or COVID specialty tax/ 'COVID wealth equity' tax**) who made tremendous financial benefit out of this humanitarian crisis. It could be

another way out to mitigate the worldwide economic crisis too. Another proposition could be open public auditing of finances for vested interest groups to check various aspects especially, **how much funding (direct and indirect) are spent on media, promotion and related activities**. Otherwise, there are huge risks that the interests of general people are overlooked or disregarded.

Balanced discussion, healthy peer review, critical and open analyses, in the current crucial state are desperately needed, so as to monitor the progress of any adopted strategy on a regular basis. With that objective in mind, it is an effort to explore pragmatically, areas relating to the effectiveness of COVID-19 vaccine and the current exit strategy. This study will greatly benefit policy-makers, academics, patients, and common people.

Acknowledgement:

Two preprint versions available; the first version dt 20th March, 2021 <https://doi.org/10.22541/au.161642232.28976638/v1> [51] and 2nd version dt 8th July, 2021

<https://doi.org/10.22541/au.162584191.11801390/v1> [52]. Presentation <https://t.co/M7nu0JUAu1> and video

<https://t.co/k09eajW9iu>

Competing Interest Statement: This study did not receive any funding and there is no financial interest.

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