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Original article

Modelling the impact of perfect and imperfect vaccination strategy against SARS CoV-2 by assuming varied vaccine efficacy over India

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ABSTRACT

Background: The outbreak of Coronavirus disease (COVID-19) has swiftly spread globally and caused public health and socio-economic disruption in many countries. An epidemiological modelling studies in the susceptible-infectious-removed (SIR) has played an important role for making effective public health policy to mitigate the spread of COVID-19. The aim of the present study is to investigate the optimal vaccination strategy to control the COVID-19 pandemic in India.

Methods: We have applied compartment mathematical model susceptible-vaccination-infectious-removed (SVIR) with different range of vaccine efficacy scenarios and predicted the population to be covered for vaccination per day in India as well as state level was performed.

Results: The model assumed that a vaccine has 100% efficacy, predicted that >5 million populace to be vaccinated per day to flatten the epidemic curve in India. Similarly, different vaccination mechanisms such as 'all-or-nothing' (AoN) and leaky vaccines does not have potential discordance in their effectiveness at higher efficacies (>70%). However, AoN vaccine was found to be marginally effective than leaky at lower efficacies (<70%) when administered at the higher coverage strategies. Further state level analyses were performed and it was found that 0.3, 0.3, 0.2 and 1 million vaccinations required per day in Andhra Pradesh, Gujarat, Kerala and Maharashtra as it assumes that the vaccine efficacy is 70%.

Conclusion: The proposed modelling approach shows a range of assumptions on the efficacy of vaccine which helps the health authorities to prioritize the vaccination strategies to prevent the transmission as well as disease.

1. Introduction

Coronavirus disease (COVID-19) is an infectious disease caused by a newly discovered severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has spread rapidly throughout the world and established local transmission in many countries including the Americas, Europe, Africa, and Asia.[1,2] The World Health Organization declared SARS-CoV2 infection as a pandemic on March 11, 2020.[3] Followed by many countries and has imposed lockdown, ban on international travel, and other non-pharmaceutical interventions such as social distancing, wearing masks was implemented to curtail the disease transmission. Globally, as of June 15, 2021, there have been 175,987,176 confirmed cases of COVID-19, and 3,811,561 deaths, reported.[4]

The first laboratory confirmed COVID-19 case was reported on January 30, 2021 in Kerala, a Southern state of India and it was imported from Wuhan, China. In the following weeks several travel associated COVID-19 cases were reported throughout the country.[5] To reduce the spread of coronavirus Government of India has implemented countrywide lockdown (1st phase lockdown: 24 March-14 April 2019, 2nd phase lockdown: 15 April-3 May, 3rd phase lockdown: 4 May-17 May and 4th phase lockdown: 18 May-31st May 2020).[6] The high transmission of coronavirus was established in many states and union territories of India and most of the country have implemented COVID-19 protocols such as facemask, social distancing and other non-pharmaceutical interventions owing to the lack of proper treatment. Besides these control measures the cases are sharply increasing as of March 28, 2019 India had 909 confirmed cases of COVID-19, by April 28, 2019 the figure of 29,974, which is almost 33 times higher. Similarly, by July 16, 2019 the number of COVID-19 confirmed cases had gone up almost another 33 times.[7] As of June 15, 2021, India has reported 29,633,105 confirmed cases of COVID-19 with 377, 031 deaths, 38,33,06,971 samples tested for COVID-19. Among all the states the

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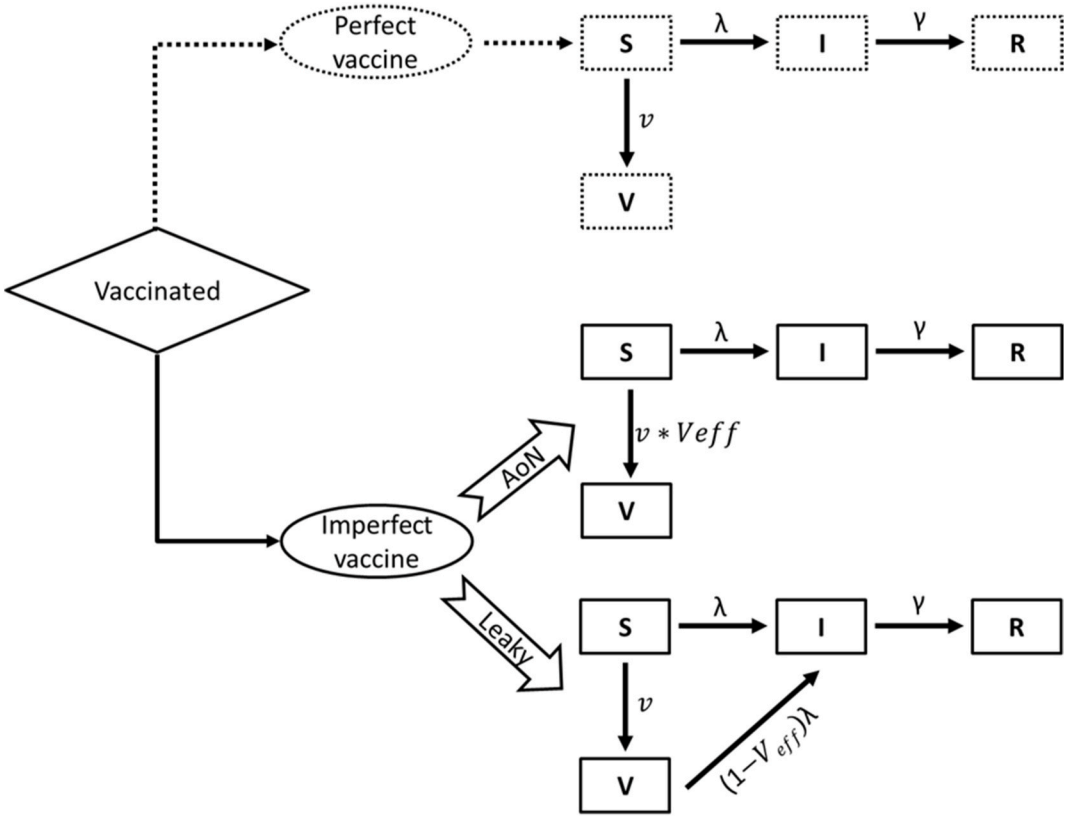

Figure-1. Schematic model for COVID-19 transmission dynamics. The rectangular boxes represent the different compartments in which the population is structured and are represented by the dotted and continuous lines in the perfect and imperfect vaccine types respectively. The thick black arrows represent the transitions that occur between the different compartments.

state of Maharashtra, Kerala, Karnataka, Andhra Pradesh, Tamil Nadu, Delhi, Uttar Pradesh and West Bengal were affected severely and reported high prevalence of COVID-19 cases.[8] To flatten the epidemic curve the Government of India has initiated COVID-19 vaccination program, till June 15, 2021 the country has administered a total of 26, 19,72,104 COVID-19 vaccine doses in various states and union territories of the country.[9]

Due to continuous mutation of SARS-CoV-2 resulted in evolution of multiple new variants and most of the variants having similar main characteristics, however with significant differences observed in their transmission pattern and mortality rates. The United Kingdom (UK) has reported a new SARS-CoV-2 variant on 14th December 2020, which is referred to as VOC 202012/01(VOC: Variant of Concern) and labelled as Alpha. The Alpha variant has been reported in 60 countries and transmissibility of Alpha variant is assessed to be 70% higher than the previous SARS-CoV-2 variants. The government of South Africa declared the emergence of a new variant on 18th December 2020 which is designated as Beta variant. The Beta variant is associated with high viral load and rapid spreading which is later reported from 23 countries across four WHO regions. Subsequently a new variant named P.1 with WHO labelled as Gamma has been reported from Brazil on 11th January 2021 and is currently considered as a Variant Being Monitored (VBM). Similarly, a potentially dangerous novel coronavirus variant named Delta strain has been reported in India on 4th April 2021 and this variant is characterized by rapid transmission, and strong infectivity. Another SARS-CoV-2 B.1.1.529 variant was detected in South Africa on 26th November 2021 and named as OMICRON variant of concern. This variant is characterized by less severity, and rapid transmission. Other variants named Epsilon, Zeta, Eta, Theta, Lota, Kappa, Lambda, and Mu are also been reported as Variants of Interest (VOI).[10]

There are a wide range of COVID-19 vaccines being developed globally with the goal of prevention of COVID-19 infection. There are more than 80 vaccine candidates in 212 clinical trials and 11 vaccines approved by various countries.[11] In India, two vaccines Covishield (by Oxford-Astra Zeneca, Serum Institute of India) and Covaxin (by Bharat Biotech) completed phase-3 trials and approved for immunization in India by Drug Controller General of India (DCGI) on January 03, 2021.[12]

In the present study, we have investigated the impact of providing different values of vaccination rate consist of different vaccine efficacy to the progression of active cases of COVID-19. The basic SIR model is used by adding another compartment of vaccination (perfect and imperfect vaccination) to the SIR model coupled with non-linear equations. The traditional Susceptible-Infected and Removed (SIR) models were extensively used for modelling infectious diseases.[13] SIR models are widely applied for modelling the various infectious disease such as Influenza,[14] Tuberculosis,[15] Malaria,[16] Measles,[17] Lyme disease,[18] Dengue[19] and Ebola[20] to understand and predict the severity of disease outbreak. Further the traditional SIR models have been updated as SEIR, SEIRD, SVIR and TSIR models.[21,22] In recent years, researchers have proposed the SVIR model by including the vaccination compartment to study the impact of vaccination on the disease control.[23] Similarly, the SIR model was modified where the recovered compartment includes individuals who have recovered and protected from infection by natural immunity and propose that the transmission rate declines with the inclusion of herd immunity.[24] Naturally acquired and vaccine-induced immunity on the future dynamics of SARS-CoV-2 transmission was investigated by the researchers and found that more frequent revaccinations are linked to fewer total numbers and lower peaks of daily COVID-19 deaths in the assumed scenarios.[25] In the present study SVIR model was used by adding vaccine compartment to SIR model to study the impact of imperfect and perfect vaccine, which may produce either partial or complete immunity against vaccinated populace. Similarly, the study highlighted by assuming the different vaccine coverage at different efficacies in reducing the magnitude of the COVID-19 epidemic

Table-1
State variables and model parameters for the SVIR model.

Parameter/Variable	Description
S	Number of susceptible population
V	Number of Vaccinated individuals
I	Number of Infected population
R	Number of Recovered population
Λ	Force of Infection
B	Transmission rate
Γ	Recovery rate
V	Proportion of vaccinated population
V_{eff}	Vaccine efficacy

Start time *(t = 0)*as of 6thOctober 2020.

Table-2
The differential equations representing the SVIR model for perfect and imperfect vaccine models.

Rate of change of variable	Perfect vaccine	Imperfect vaccine	
		AoN	Leaky
dS(t)/dt	- λ *S(t) - *ν** S (t)	- λ *S(t) - *ν** S(t) * Veff	- λ *S(t) - *ν** S(t)
dI(t)/dt	λ *S(t) - γ *I (t)	λ *S(t) - γ *I(t)	λ *S(t) - γ *I(t) + (1-Veff)*λ* V(t)
dR(t)/dt	γ *I(t)	γ *I(t)	γ *I(t)
dV(t)/dt	*ν* * S(t)	*ν** S(t) * Veff	- (1- Veff)*λ* V(t) + *ν** S(t)

ν = Number of population vaccinated(v)/Total population (N).
λ = β *I(t)/N.

Table-3
Equations used to determine theR_0 and R_t through SVIR model.

Reproduction number	No Vaccine	Perfect vaccine	Imperfect vaccine	
			AoN	Leaky
R_0	β/γ			
R_t		(1−v) × R_0	(1−(v * V_{eff})) × R_0	(1−v) × R_0+ v (1- V_{eff}) × R_0

in India.

2. Methods

The present study was used a generalized Susceptibility-Infected-Recovered (SIR) modelling framework to obtain the epidemiological parameters such as transmission rate, recovery rate and basic reproduction number (R_0) of COVID-19 in India as a nation and to the states (Andhra Pradesh, Gujarat, Kerala and Maharashtra).[26] Similarly, a vaccine model was developed by assuming different settings of vaccine action, vaccine availability with varied vaccine efficacies and different coverage strategies which would affect the magnitude of the disease epidemic. Here, the population is considered as a homogenous and constant, similarly, the transmission and recovery rates are also assumed as constant. However, births and deaths are ignored due to the disease in epidemic. The date of vaccine availability is presumed to be October 06, 2020.

2.1. Data collection and software

The daily confirmed COVID-19 case data from January 30 to October 06, 2020 pertaining to India as whole nation and to the states Andhra Pradesh, Gujarat, Kerala and Maharashtra was used to calibrate the model. The COVID-19 cases were forecasted assuming varied vaccination strategies considering the number of susceptible, infected and recovered population as on October 06, 2020. The data analyses were performed using R software version 4.0.3.

2.2. Disease transmission model

The estimates of transmission and recovery rate of COVID-19 incidence were predicted using deterministic SIR compartmental model by simulating the dynamics of the number of susceptible (S), infected (I), and recovered (R) individuals. Essentially, this standard model can be represented as a set of differential equations as follows.

$$\lambda = \beta \times \frac{I(t)}{N}$$

$$\frac{dS(t)}{dt} = -\lambda \times \mathrm{S(t)}$$

$$\frac{dI(t)}{dt} = \lambda \times \mathrm{S(t)} - \gamma \times \mathrm{I(t)}$$

$$\frac{dR(t)}{dt} = \gamma \times \mathrm{I(t)}$$

where N represents the total population, S(t), I(t), R(t) are the number of susceptible, infected and recovered population at time (t). The impor-

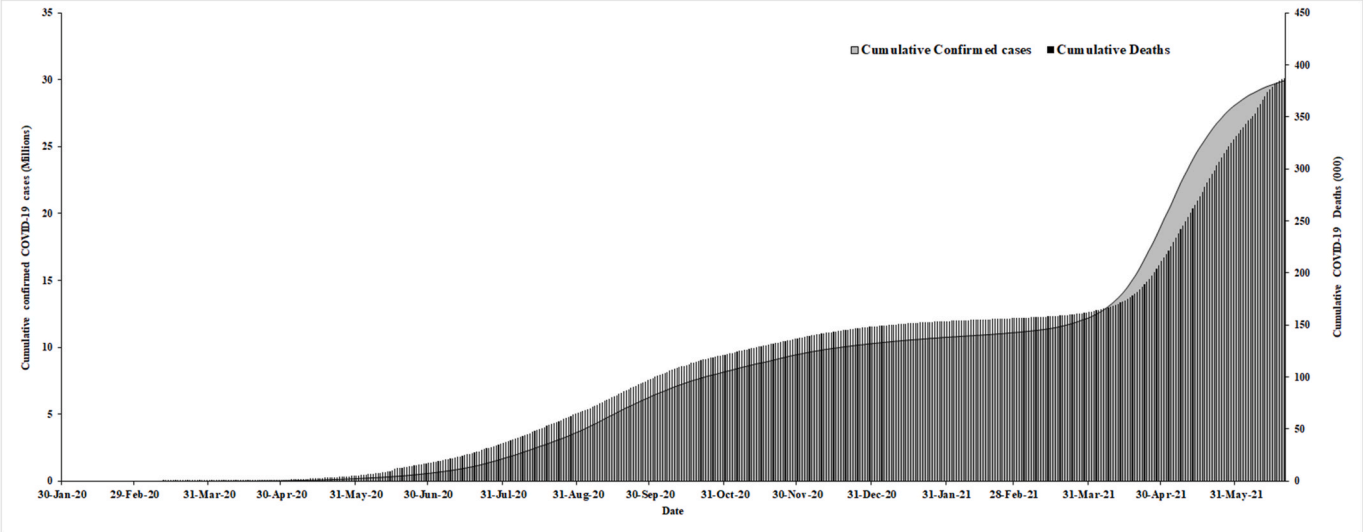

Figure-2. Day wise confirmed cases and deaths of COVID-19 in India.

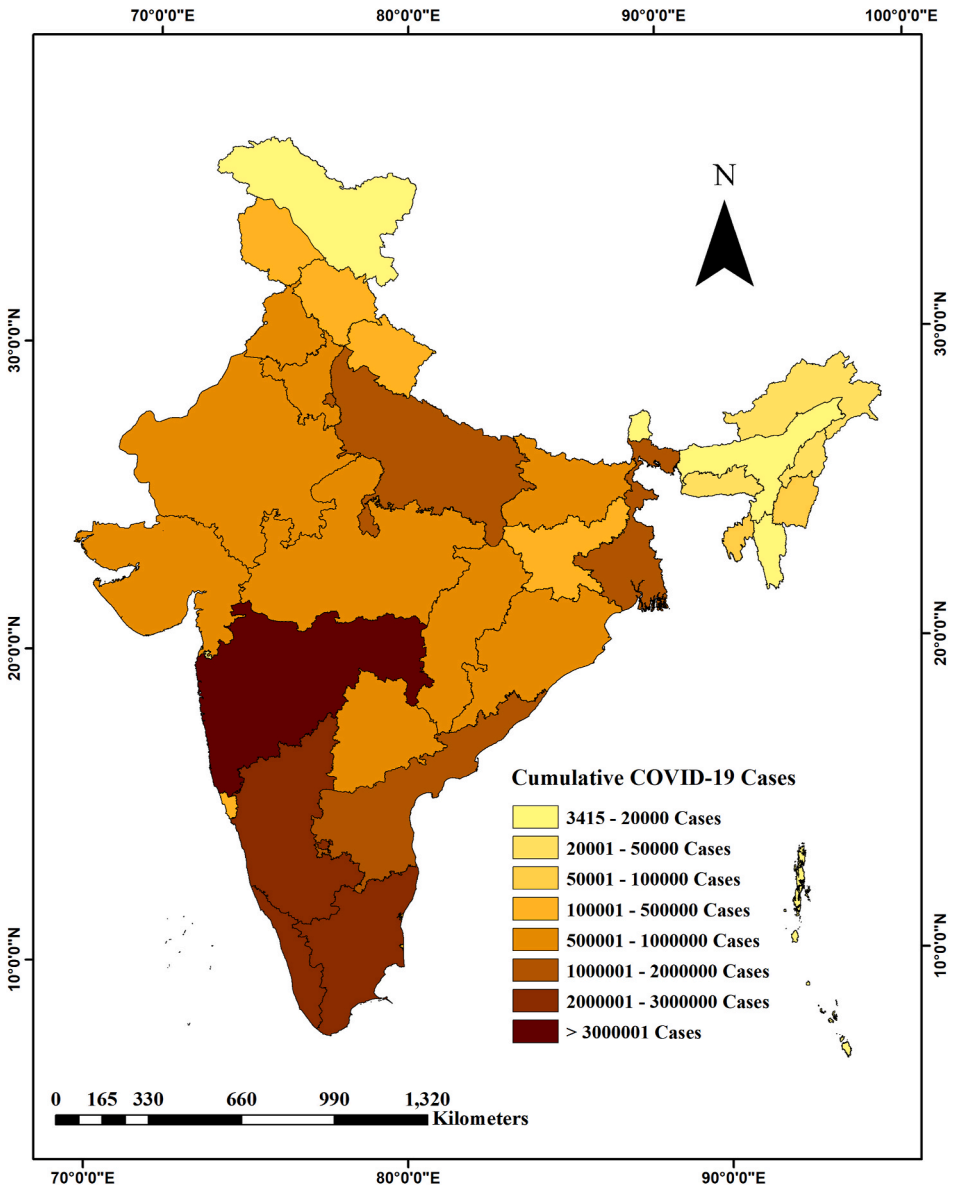

Figure-3. State wise prevalence of COVID-19 cases in India.

Table-4
Epidemiological parameters such as basic reproductive number (R_0), transmission rate (β) and recovery rates (γ) of India and to the states as of October 06, 2020.

State	Reproduction number (R_0)	Transmission rate (β)	Recovery rate (γ)
India	1.188	0.498	0.419
Andhra Pradesh	1.237	0.399	0.322
Gujarat	1.183	0.400	0.338
Kerala	1.182	0.399	0.338
Maharashtra	1.180	0.524	0.444

tant parameters of the model are beta, gamma and lambda represent the transmission rate, recovery rate and force of infection respectively. The β, γ and R_0 parameters of the model were quantified through sum of the square functions and least square optimization approaches.

2.3. SVIR model formulation

We consider a SVIR (Susceptible-Vaccinated-Infected-Recovered) model which is adapted from the basic SIR model with inclusion of vaccination compartment into the model. The population is divided into four compartments which includes all the individuals who are susceptible, vaccinated, infected and recovered. The schematic overview of the SVIR deterministic model used to assess the impact of various vaccination strategies against COVID-19 is shown in figure-1, where the compartments denotes the different epidemiological states of the disease and the arrows signifies the possible flow of individuals between the compartments.

Applying the definitions of state variables and parameters interpretation from table-1 and figure-1, the differential equations in system which describe the COVID-19 dynamics are formulated as below (Table-2). Three different models were developed assuming different vaccination scenarios such as perfect vaccine and imperfect vaccine consist of AoN and Leaky vaccine models.

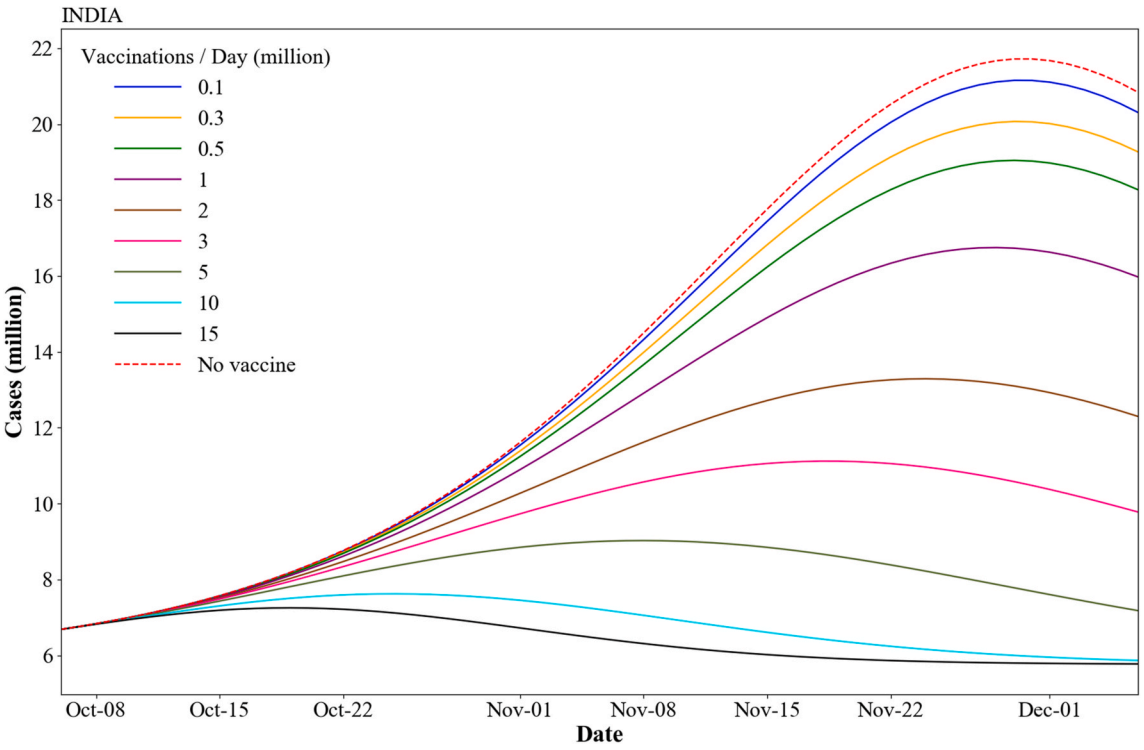

Figure-4. Number of vaccinations with 100% efficacy needed to reduce the epidemic peak in India.

2.4. SVIR model of perfect vaccine

The perfect vaccine model is formulated by including an additional vaccination (V) compartment into the SIR model to analyse the underlying transmission dynamics of epidemic control using the vaccination. The additional compartment V, represents the individuals who have vaccine induced immunity by change at rate of varied proportions of vaccinations ('v') per day from susceptible population. Thus, the susceptible population are divided into vaccinated (V) and unvaccinated (S) individuals (Figure-1). We assume that the available vaccine is perfect with absolute efficacy and provides complete protection to the vaccinated individuals. The differential equations representing the perfect vaccine model are listed in table-2.

2.5. SVIR models of imperfect vaccine: AoN and leaky vaccine models

Using the same strategy of developing compartments, the imperfect vaccine model has been designed considering the mechanism of vaccine action since the vaccination modelling consistently consider all-or-nothing (AoN)[27–29] or leaky type of vaccine.[27,29,30] The compartments are: susceptible-vaccinated (AoN or Leaky)-infected-recovered (SVIR). These models evaluate the impact of introducing a vaccine with varying efficacies and with different vaccine coverage strategies during the epidemic. These models help us to quantify the number of vaccinations is required per day with varied efficacies to prevent or extinguish the epidemic. A set of differential equations representing the SVIR model with different settings of vaccine are listed in table-2. Under the assumption of all-or-nothing vaccine, the parameter effective vaccination coverage which is a product of proportion of vaccinated population and vaccine efficacy ($v*V_{eff}$) is used to compute the size of population in the vaccinated state. Similarly, for a leaky vaccine, v (proportion of vaccinated population) is used to compute the number of individuals in vaccinated state. Similarly, force of infection (1-Veff) λ is included to determine the size of population is Infectious state (Figure-1). In the present study we assumed that an epidemic with no vaccination as an initial scenario followed by vaccinated individuals with varied vaccine efficacies (e.g. 100%, 70%, 50% and 30% efficacy) at different population coverage's pattern in India and to the states of Andhra Pradesh, Gujarat, Kerala and Maharashtra.

2.6. Estimation of reproduction number (R_o) and effective reproduction number (R_t)

The basic reproduction number (R_0) represents the number of secondary infections caused by a single infectious case in a totally susceptible population. R_0 determines whether a disease can invade a population or not. When $R_0 < 1$ every infected individual produces on average less than one new infected individual, and the disease perishes. Whereas if $R_0 > 1$, each infected person produces more than one new infected person and the disease can invade the population. Effective reproduction number (R_t) is the average number of secondary infections caused by a single infectious case, with a given level of immunity in the susceptible population (vaccination intervention). In the present study the R_0 and R_t was determined for India and to the states using the equations listed in table-3.

3. Results

3.1. COVID-19 in India

India reported its first COVID-19 infection on January 30, 2020 in Kerala and few weeks later there were few more infections reported across the country. Among all the states the states of Maharashtra, Karnataka, and Kerala, has reported more than two million COVID-19 cases followed by Tamilnadu, Uttar Pradesh, Andhra Pradesh, Delhi and West Bengal has reported more than one million cases in India. Similarly, other states also observed COVID-19 cases considerably. Figure-2 shows the day wise COVID-19 cases and deaths and Figure-3 shows the state wise COVID-19 prevalence in India.

Table-5
Effect of vaccination strategies on epidemic peak reduction in India and other states.

v*	100%	70%		50%		30%	
		AoN	Leaky	AoN	Leaky	AoN	Leaky
Number of cases (% Reduction)							
India (Date of peak cases without vaccination 30-11-2020 (n = 21.719 million))							
0.1	21.15(4)	21.32(3)	21.33(3)	21.43(2)	21.44(2)	21.54(1)	21.55(1)
0.3	20.06(11)	20.54(8)	20.57(8)	20.87(6)	20.90(5)	21.20(3)	21.23(3)
0.5	19.02(18)	19.79(13)	19.83(13)	20.32(9)	20.37(9)	20.87(6)	20.91(5)
1	16.69(33)	18.05(24)	18.12(24)	19.02(18)	19.12(17)	20.06(11)	20.15(10)
2	13.01(58)	15.07(44)	15.20(43)	16.69(33)	16.88(32)	18.53(21)	18.72(20)
3	10.48(75)	12.71(60)	12.89(59)	14.69(47)	14.96(45)	17.13(31)	17.42(29)
5	7.69(93)	9.54 (81)	9.74(80)	11.62(67)	12.01(65)	14.69(47)	15.19(43)
10	5.97(105)	6.54(101)	6.68(100)	7.69(93)	8.12(90)	10.48(75)	11.35(69)
15	5.79(106)	5.93(105)	6.00(105)	6.38(102)	6.70(100)	8.18(90)	9.17(83)
Andhra Pradesh (Date of peak cases without vaccination 29-11-2020 (n = 1.179 million))							
0.01	1.127(11)	1.143(8)	1.143(8)	1.153(6)	1.154(6)	1.164(4)	1.164(3)
0.05	0.961(48)	1.016(36)	1.019(35)	1.057(27)	1.062(26)	1.103(17)	1.108(16)
0.1	0.831(76)	0.900(61)	0.906(60)	0.961(48)	0.970(46)	1.036(31)	1.046(29)
0.2	0.719(101)	0.770(90)	0.777(88)	0.831(76)	0.846(73)	0.929(55)	0.949(51)
0.3	0.687(108)	0.714(102)	0.720(101)	0.759(92)	0.775(89)	0.852(72)	0.880(66)
0.4	0.677(110)	0.690(107)	0.695(106)	0.719(101)	0.734(98)	0.797(84)	0.830(77)
0.5	0.674(111)	0.681(109)	0.684(109)	0.698(106)	0.711(103)	0.759(92)	0.795(84)
Gujarat (Date of peak cases without vaccination 16-12-2020 (n = 0.599 million))							
0.01	0.552(10)	0.566(7)	0.566(7)	0.575(5)	0.576(5)	0.585(3)	0.585(3)
0.05	0.407(42)	0.454(32)	0.456(32)	0.491(24)	0.492(23)	0.531(15)	0.532(15)
0.1	0.292(67)	0.354(54)	0.356(53)	0.407(42)	0.410(42)	0.472(28)	0.476(27)
0.2	0.186(91)	0.236(80)	0.240(79)	0.292(67)	0.299(66)	0.379(48)	0.388(46)
0.3	0.149(99)	0.180(92)	0.184(91)	0.225(82)	0.234(80)	0.311(63)	0.325(60)
0.4	0.136(102)	0.153(98)	0.157(97)	0.186(91)	0.195(89)	0.261(74)	0.279(70)
0.5	0.131(103)	0.141(101)	0.143(100)	0.163(96)	0.171(94)	0.225(82)	0.245(78)
Kerala (Date of peak cases without vaccination 22-11-2020 (n = 0.618 million))							
0.01	0.578(11)	0.590(8)	0.590(7)	0.598(5)	0.598(5)	0.606(3)	0.607(3)
0.05	0.444(45)	0.489(34)	0.492(33)	0.522(25)	0.526(24)	0.558(16)	0.562(15)
0.1	0.333(74)	0.394(59)	0.398(57)	0.444(45)	0.451(44)	0.505(30)	0.512(28)
0.2	0.221(104)	0.275(90)	0.282(88)	0.333(74)	0.345(71)	0.418(52)	0.433(48)
0.3	0.178(115)	0.214(105)	0.221(104)	0.263(93)	0.279(89)	0.351(70)	0.374(64)
0.4	0.162(119)	0.184(113)	0.190(112)	0.221(104)	0.237(100)	0.301(83)	0.330(75)
0.5	0.155(121)	0.168(117)	0.173(116)	0.194(111)	0.210(107)	0.263(93)	0.297(84)
1	0.150(122)	0.151(122)	0.153(121)	0.155(121)	0.163(119)	0.178(115)	0.214(106)
Maharashtra (Date of peak cases without vaccination 13-11-2020 (n = 2.620 million))							
0.01	2.588(3)	2.598(2)	2.599(2)	2.605(1)	2.605(1)	2.611(1)	2.612(1)
0.05	2.465(13)	2.510(10)	2.512(9)	2.541(7)	2.543(7)	2.572(4)	2.575(4)
0.1	2.324(25)	2.407(18)	2.411(18)	2.465(13)	2.470(13)	2.525(8)	2.530(8)
0.2	2.086(46)	2.223(34)	2.230(33)	2.324(25)	2.335(25)	2.436(16)	2.445(15)
0.3	1.896(62)	2.065(48)	2.076(47)	2.198(36)	2.214(35)	2.351(23)	2.366(22)
0.4	1.746(75)	1.930(59)	1.944(58)	2.086(46)	2.106(44)	2.272(30)	2.293(28)
0.5	1.627(85)	1.816(69)	1.832(68)	1.985(54)	2.010(52)	2.198(36)	2.226(34)
1	1.328(111)	1.463(99)	1.484(97)	1.627(85)	1.669(82)	1.896(62)	1.953(57)
2	1.215(120)	1.252(117)	1.266(116)	1.328(111)	1.372(107)	1.535(93)	1.631(85)

v* = vaccination/day.

3.2. Estimation of COVID-19 prevalence through SIR model

Table-4 represents the epidemiological parameters which are simulated through deterministic SIR model consist of basic reproduction number (R_0), transmission rate (β), and recovery rate (γ) for India and the states of Andhra Pradesh, Gujarat, Kerala and Maharashtra as of October 06, 2020. The simulated parameters were considered as constant for the prediction of COVID-19 cases considering the non-availability of vaccine as an initial scenario. In Figure-2 the dotted red line represents the projected COVID-19 cases when is no vaccine is available and tends to peak during November and December months.

3.3. SVIR model of perfect vaccine

The SVIR model for perfect vaccine shows what would happen if vaccines having 100% efficacy are administered during the epidemic. Figure-4 shows the epidemic curves of COVID-19 in India and how the vaccines with 100% efficacy, if 0.1, 0.3, 0.5, 1, 2, 3, 5,10 and 15 million population are vaccinated daily from the day of vaccine availability (i.e. October 06, 2020) can reduce the size of the peak when compared with the peak without vaccination. The model suggest that an epidemic would start to decline in India when greater than five million population are vaccinated per day. It is evident from the plot that the cases peaked on November 30, 2020 (n = 21.71 million) when no vaccine was available and subsequently the epidemic peak decreased by 18% (n = 19.02 million cases), 58% (n = 13.01 million) and 75% (n = 10.48 million) when 0.5, 2 and 3 million vaccinations per day are administered across the country (Figure-4, Table-5).

Similarly, the Figure-S1 illustrates the epidemic curves of Andhra Pradesh, Gujarat, Kerala and Maharashtra and how the different vaccinations strategies (i.e., 0.01, 0.05, 0.1, 0.2, 0.3, 0.4, 0.5, 1 and 2) alters the peak of epidemic in different states of India. The plot reveals that the threshold vaccinations required to start the decline of epidemic peak in Andhra Pradesh, Gujarat, Kerala and Maharashtra are 0.2, 0.2, 0.2 and 1 million vaccinations per day respectively. Table-5 shows how the number of vaccinations impact the total number of cases deterred compared with no vaccination in different states of India (Figure-S1, Table-5).

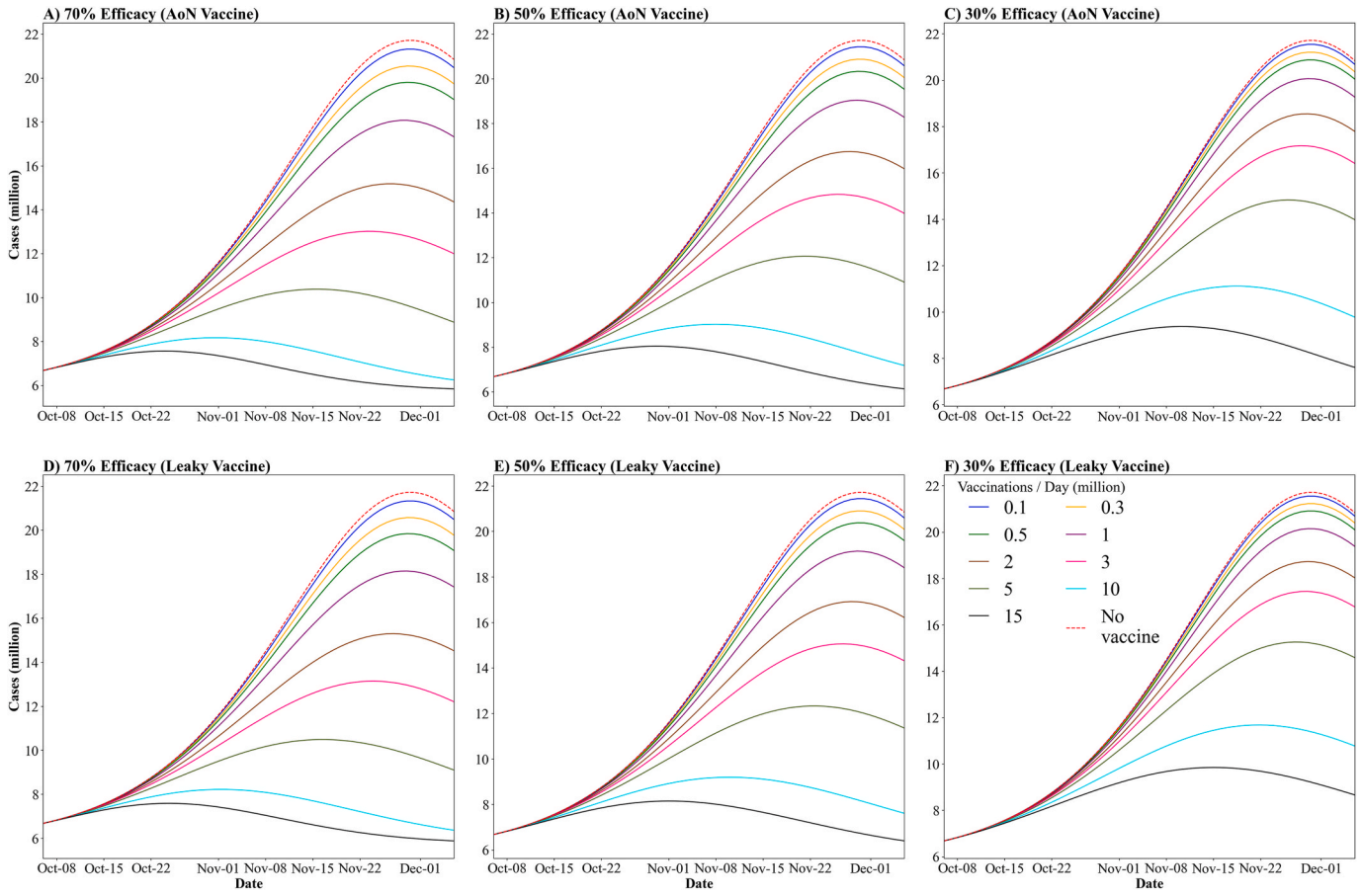

Figure-5. Number of AoN (A–C) and Leaky (D–F) vaccinations with 70%, 50% and 30% efficacy needed to reduce the epidemic peak in India.

3.4. AoN and leaky vaccine models

The next step of analysis is what would occur if vaccination took place with varied efficacies and with different mechanism of vaccine action and at what extent the vaccination could bring down the epidemic curve. Figure-5 illustrates the epidemic curves of India assuming both AoN (Fig-5A-C) and leaky (Fig-5D-F) vaccines with 70%, 50% and 30% vaccine efficacies with different vaccination strategies in comparison with the epidemic curve of no vaccine.

Figure-5 determines that the epidemic outbreak in India would start declining, if the vaccinations (both AoN and Leaky) with 70% efficacy are administered at 5 million/day, whereas the vaccine requirement increases to 10 and 15 million/day if the efficacy threshold drops to 50% and 30% respectively. Figure-5A-C and D-F shows how the vaccine efficacy and coverage can reduce the size of the epidemic peak and influence the total number of cases decrease compared with no vaccination when AoN and Leaky vaccines are administered. The model suggests that the epidemic peak in India decreases by 24% (n = 18.05 million cases), 60% (n = 12.71 million) and 81% (n = 9.54 million) when 1, 3 and 5 million AoN vaccinations per day with 70% efficacy respectively are administered across the country. Similarly, when the Leaky vaccines with 70% efficacy are given at the same coverage, the epidemic peak decreases by 24% (n = 18.12 million cases), 59% (n = 12.89 million) and 80% (n = 9.74 million) only. The study suggest that the AoN vaccine was found to be marginally effective than leaky at lower efficacies (<70%) when administered at the higher coverage strategies. The influence of AoN and Leaky vaccines with 50% and 30% efficacy in reducing the magnitude of the epidemic peak in India are represented in table-5.

Similarly, figure-6 & 7 shows the epidemic outbreak in Andhra Pradesh, Kerala, Gujarat and Maharashtra would start declining, if the vaccinations (both AoN and Leaky) with 70% efficacy are administered at 0.2, 0.1, 0.3 and 0.5 million/day. However, if the efficacy of vaccinations (both AoN and Leaky) is 50%, the disease epidemic peak start reducing when vaccinations are administered at 0.3, 0.2, 0.4 and 1 million/day to the states. Likewise, 0.4, 0.3, 1 and 1.5 million vaccinations are required per day to decline the epidemic peak in Andhra Pradesh, Kerala, Gujarat and Maharashtra states respectively when the vaccine efficacy is 30% (Figure-6 & 7).

Figure-6 shows the vaccine efficacy and coverage can reduce the size of the epidemic and influence the total number of cases decreased compared with no vaccination in Andhra Pradesh, Kerala, Gujarat and Maharashtra when AoN vaccine is administered with varied efficacies. The model estimates that the epidemic peak in Andhra Pradesh decreases by 8% (n = 1.14 million cases), 36% (n = 1.01 million) and 61% (n = 0.90 million) when 0.01, 0.05 and 0.1 million AoN vaccinations per day with 70% efficacy are administered (Figure-6A-C). Similarly, when the Leaky vaccines with 70% efficacy are given at the same coverage, the epidemic peak decreases by 8% (n = 1.14 million cases), 35% (n = 1.01 million) and 60% (n = 0.90 million) (Figure 7A–C). Further, the epidemic peak of Kerala state reduces by 34% (n = 0.48 million cases), 59% (n = 0.39 million) and 90% (n = 0.27 million) when 0.05, 0.1 and 0.2 million AoN vaccinations per day with 70% efficacy are administered. However, when the leaky vaccines with 70% efficacy are given at the same coverage, the epidemic peak in Kerala state decreases by 33% (n = 0.49 million cases), 57% (n = 0.39 million) and 88% (n = 0.28 million) (Figure-6 & 7D-F) respectively.

Furthermore, the epidemic peak in Gujarat state decreased by 32% (n = 0.45 million cases), 54% (n = 0.35 million) and 80% (n = 0.23 million) when 0.05, 0.1 and 0.2 million AoN vaccinations per day with

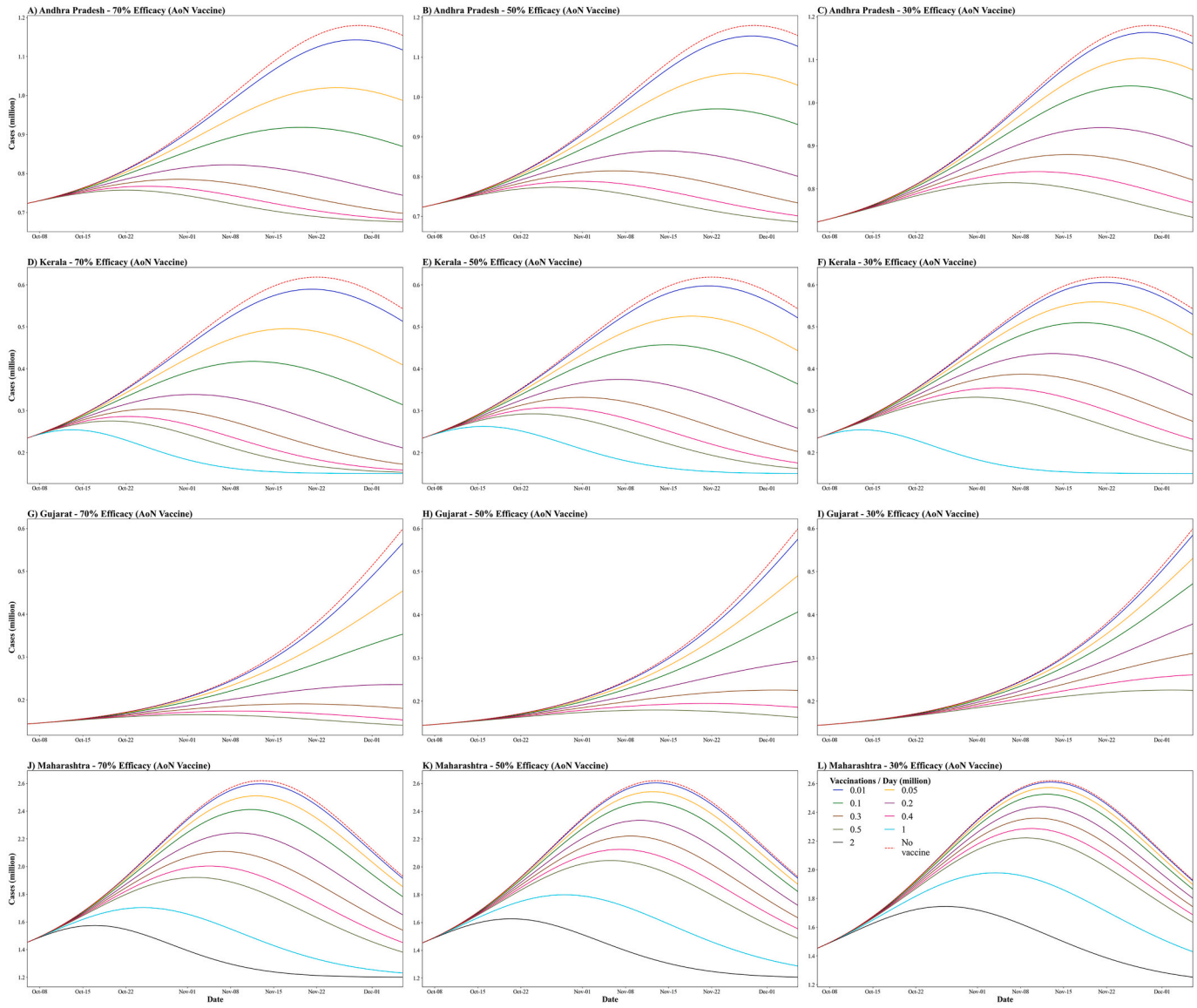

Figure-6. Number of AoN vaccinations with 70%, 50% and 30% efficacy needed to reduce the epidemic peak in Andhra Pradesh (A–C), Kerala (D–F), Gujarat (G–I) and Maharashtra (J–L).

70% efficacy are administered. At the same time the vaccine coverage and with vaccine efficacy can reduce the epidemic peak in Gujarat state by 32% (n = 0.45 million cases), 53% (n = 0.35 million) and 79% (n = 0.24 million) when leaky vaccinations are vaccinated (Figure-6 & 7G-I). Similarly, the epidemic peak of Maharashtra state drops by 34% (n = 2.22 million cases), 48% (n = 2.06 million) and 69% (n = 1.81 million) when 0.2, 0.3 and 0.5 million AoN vaccinations per day with 70% efficacy are vaccinated (Figure-6J-L). The leaky vaccines with same vaccine coverage, and 70% efficacy can reduce the epidemic peak in Maharashtra by 33% (n = 2.23 million cases), 47% (n = 2.07 million) and 68% (n = 1.83 million) (Figure-7J-L).

The influence of AoN and leaky vaccines at different vaccine coverage with 50% and 30% efficacies can reduce the magnitude of the epidemic in India, as well as in the states of Andhra Pradesh, Kerala, Gujarat and Maharashtra states are presented in the Table-5. Considering the different mechanisms of vaccine action, both AoN and Leaky vaccines does not have marked difference in their effectiveness due to vaccine coverage or efficacies. However, the AoN vaccinations are marginally effective than leaky vaccines for Indian and in the states of Andhra Pradesh, Kerala, Gujarat and Maharashtra.

3.5. Basic reproduction number (R_0) and effective reproduction number (R_t)

The vaccination strategies applied in the present study strongly influences the basic reproduction number. In India and in all the studied states, the R_0 is registered as >1 (India, Gujarat, Kerala, Maharashtra R_0 = 1.18 and Andhra Pradesh R_0 = 1.23) when the no vaccine scenario is considered. This suggests that the disease can persist for a longer time if no vaccine is available. The effective reproduction number is > 1 in India (R_t = 1.03) when a vaccine with 100% efficacy is available at less than or equal to 3 million vaccination per day, however when the vaccine coverage is increased to 5 million per day the R_t is decreased to <1 (R_t = 0.9) indicating that the decline in the epidemic peak which is also confirmed by reduction in cases. Similarly, the R_t in Andhra Pradesh, Gujarat and Kerala is > 1 and decline to <1 if vaccination coverage of 0.1 and 0.2 million per day. Whereas the R_t of Maharashtra state is > 1 (R_t = 1.0) and decline to <1 (R_t = 0.8) if the coverage ranges from 0.5 to 1 million vaccinations per day (Figure-8).

Moreover, the vaccines with 70% and 50% efficacy influences the R_t in India and it is recorded as >1 at 5 million and <1 l0 million vaccination per day respectively. However, with 30% efficacy the R_t is > 1 at

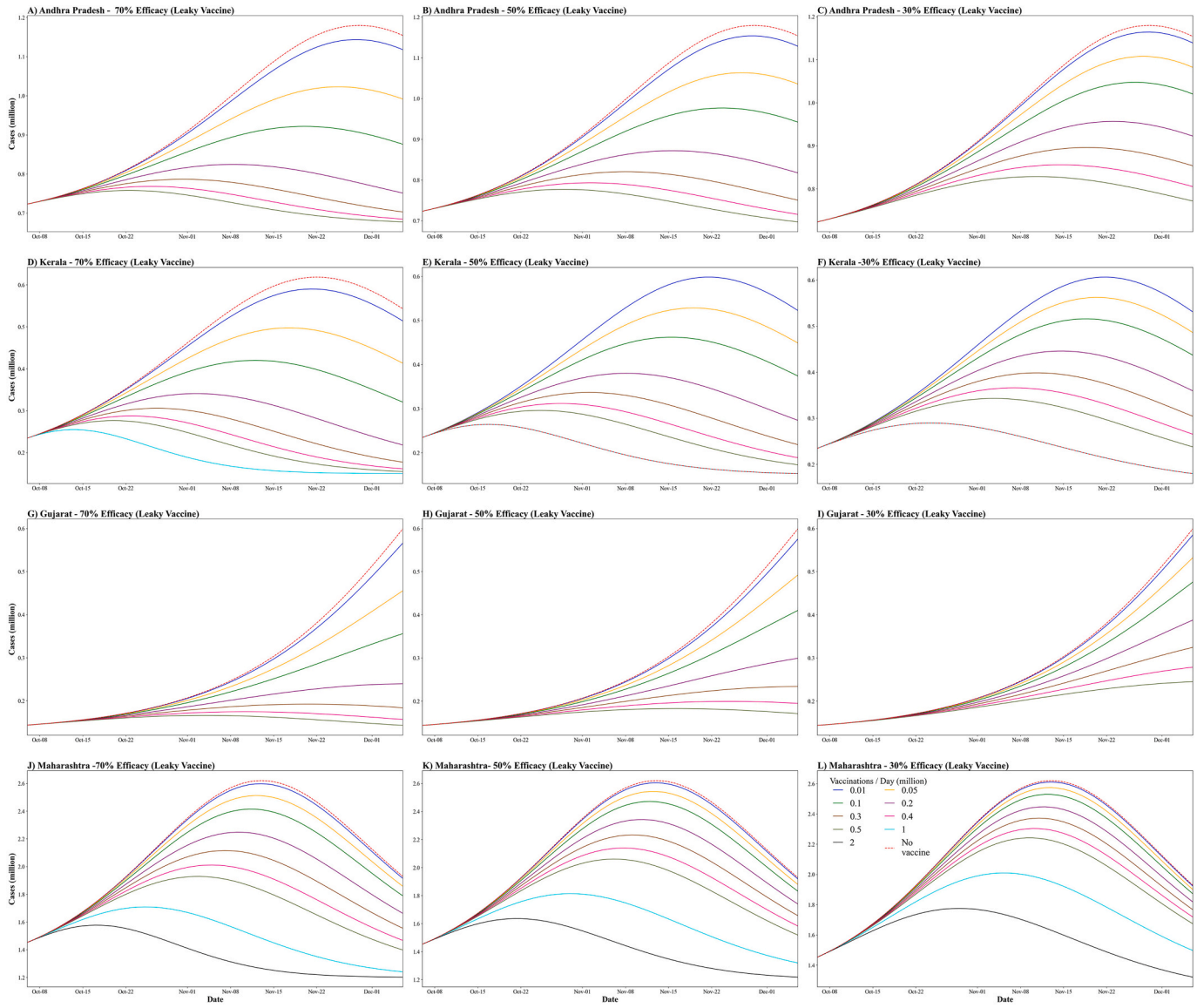

Figure-7. Number of Leaky vaccinations with 70%, 50% and 30% efficacy needed to reduce the epidemic peak in Andhra Pradesh (A–C), Kerala (D–F), Gujarat (G–I) and Maharashtra (J–L).

10 million vaccination coverage required to decline <1 at high vaccination coverage of 15 million per day. The effective reproduction number in Andhra Pradesh is recorded as >1 at 0.2 million vaccination and it decline to <1 at 0.3 million vaccination per day with a vaccine coverage of 70% and 50% efficacy. Gujarat state experienced $R_t > 1$ at 0.2 million vaccination coverage with 70% and 50% efficacy and declined to $R_t < 1$ at 0.3 million coverage with same efficacy, whereas with 30% efficacy the vaccination coverage required to reduce the $R_t < 1$ in Gujarat is 0.5 million vaccination per day. Similarly, In Kerala the effective reproduction number is observed as >1 at 0.1 and 0.2 million vaccination coverage and declined to <1 if vaccination coverage increases to 0.2 million with 70% efficacy. However, with 50% efficacy R_t is observed as >1 at 0.2 and < 1 at 0.3 million vaccines administered per day respectively. Likewise, the state Maharashtra experienced $R_t > 1$ at 0.5 million vaccination coverage and $R_t < 1$ at 1 million coverage with 70% efficacy, while 50% and 30% efficacy the R_t in Maharashtra state is observed as $R_t > 1$ at 1 million coverage and $R_t < 1$ at 2 million vaccinations per day (Figure-8).

4. Discussion

The eradication of infectious diseases like smallpox in humans and rinderpest in bovine's vaccination highlights the potentiality to induce preventive response against the epidemic infections.[31–33] The outcome of the vaccination impact varied widely based on the locale in which it is implemented, making it difficult for policy decision.[34] Therefore, from public health perspective it is essential to understand what extent of vaccination could control the disease. In this study, we present a realistic compartmental model, able to optimally suggest the required vaccination strategies to control the COVID-19 disease in India and other states. The present study reported the extent to which a vaccination program could reduce the basic reproduction number, and the projections for the upcoming COVID-19 epidemic curves for India and states show a pessimistic scenario unless the vaccines are highly efficacious and population coverage is high. We have shown that, over a wide range of assumptions, availability of perfect vaccine could reduce majority of disease burden in India and its states. Furthermore, we propose that an increase in vaccine efficacy and vaccination coverage results in reducing the disease burden early in the highly populated states which is evident from the disease reducing scenario of Maharashtra and Andhra Pradesh.

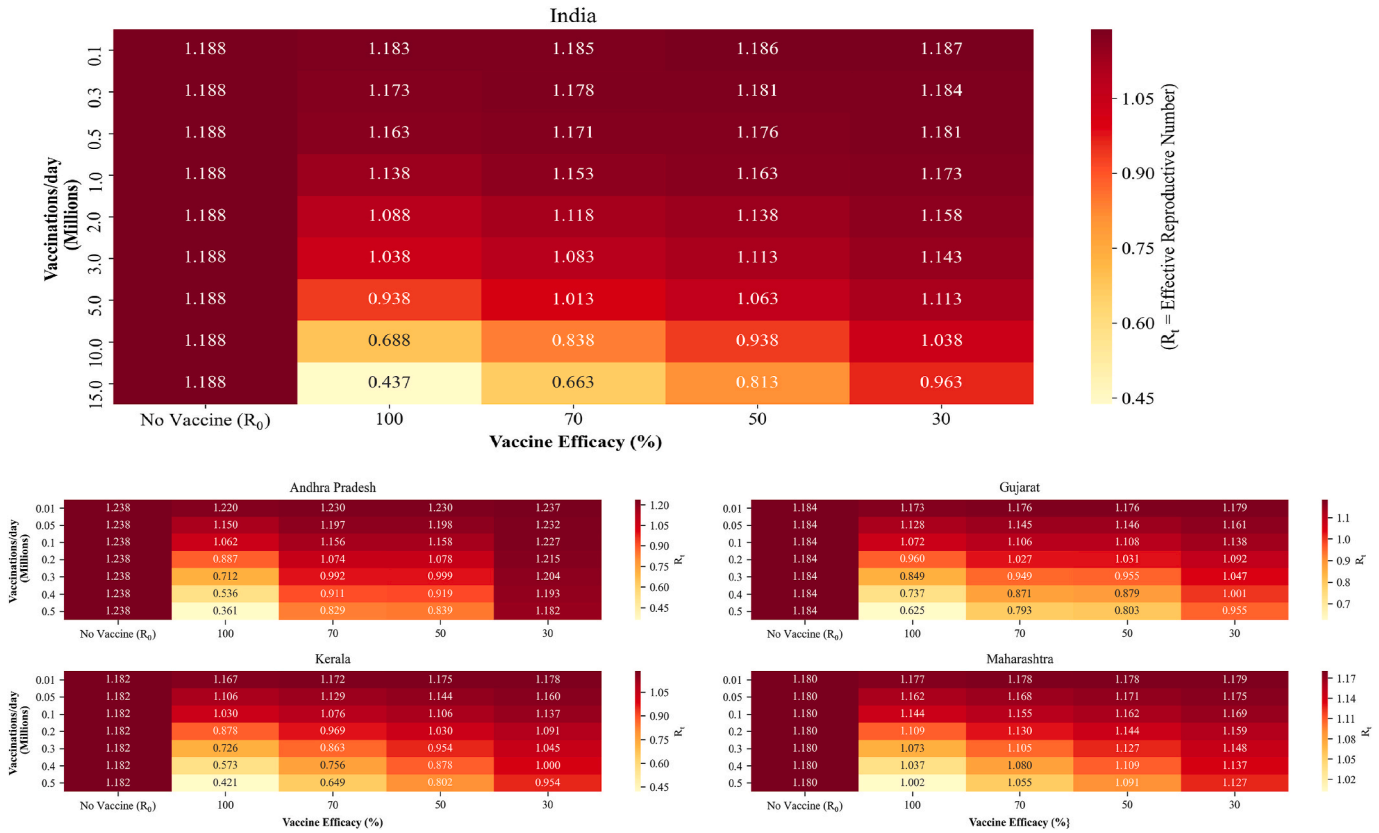

Figure-8. Heat maps representing basic Reproduction and Effective Reproduction number of India, Andhra Pradesh, Gujarat, Kerala and Maharashtra.

Notably, our results confirmed that the findings of a previous vaccination model in showing similar trends with respect to the effectiveness of AoN vaccine in reducing the disease burden.[35]

This study found that in the absence of non-pharmaceutical interventions, to prevent an epidemic of COVID-19 in India, at least 3 million populations per day are to be vaccinated with the assumption of 100% vaccine efficacy. To extinguish an ongoing epidemic in India and alleviate the need for restrictive lockdown measures, the vaccination should cover at least >5 million population per day with 100% vaccine efficacy. However, achieving the above said vaccination coverage is difficult as 23% of Indians are still hesitant to take the COVID-19 vaccine according to a survey and would get the vaccine only if assured and it was safe.[36] But, it is unlikely that the first vaccines will provide 100% protective efficacy nor protection from asymptomatic carriers. Current reports from well-known COVID-19 vaccine candidates indicate that the vaccine efficacy against >90% of confirmed cases.[37] Even if enough people are willing to take the vaccine, there should be an adequate production capacity, vaccine supplies and trained staff to reach the target. The recent vaccination programs of rotavirus and pneumococcal conjugate vaccines in India have shown that the new vaccines can be rolled out effectively with the existing public health infrastructure.[38] These experiences of deploying vaccines in pandemic settings can be helpful to enhance current vaccine allocation plans.

The WHO has indicated that a successful vaccine should be 50% efficacious,[39] and there are some circumstances in which a vaccine with assumed efficacy of 70%, 50%, 30% and with different mechanism of action could prevent or extinguish an ongoing epidemic at different vaccination coverages. In this line the present study has demonstrates that an AoN vaccine with higher efficacy has greater potential to prevent the disease in India and states by reducing the basic reproduction number than the Leaky vaccines, but these would require a potentially unachievable population coverage. Hence, the study suggests that availability of vaccine alone does not allow the conditions to become normal instantaneously unless both vaccination coverage and vaccine efficacy are fairly high. Thus, it is very important to educate the public who may think that no more lockdown measures to be followed as soon as a vaccine becomes available, particularly when the vaccine efficacy is critically low.[40] Still, the vaccine with lower efficacy when combined with other non-pharmaceutical control measures can be helpful in reducing the burden on health care system through targeted vaccination. This study reported that, the vaccines with higher efficacy when administered at high population coverage the disease can be controlled in India and its states. This study also highlights the need and importance of improving the vaccine manufacturing infrastructure in highly populated countries like India to fight against the epidemic diseases. Thus, the present study helps to understand the dynamics of vaccination to fight against the COVID-19 disease and the same approach can be applicable to a broad range of emerging infectious diseases, although more focused study is needed.

5. Limitations

The models developed in this study has some limitations. First, the underreporting of cases during the study period is uncertain. Second, the developed models suggest different number of vaccinations required with varied efficacies at different coverages. We are aware that the result of the present study does not reflect the reality of present scenario in controlling the disease. The main reason for this asynchrony is, the incidence of COVID-19 in India started declining even before the availability of vaccine due to strict implementation of lockdown guidelines and preventive measures like social distancing, hand washing and wearing of face masks. Hence, we believe that the models developed in this study still represents the best approach currently available. It should be noted that this kind of models can be helpful in controlling the epidemics of other infectious diseases during the pandemic when no vaccine is available.

Ethical statement

The authors declare that an ethical statement is not applicable.

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Declaration of competing interest

The authors declare no competing financial interests exist.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cegh.2022.101052.

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