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Vaccine efficacy and SARS-CoV-2 control in California and U.S. during the session 2020–2026: A modeling study

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ABSTRACT

Background: Besides maintaining health precautions, vaccination has been the only prevention from SARS-CoV-2, though no clinically proved 100% effective vaccine has been developed till date. At this stage, to withhold the debris of this pandemic-experts need to know the impact of the vaccine efficacy rates, the threshold level of vaccine effectiveness and how long this pandemic may extent with vaccines that have different efficacy rates. In this article, a mathematical model study has been done on the importance of vaccination and vaccine efficiency rate during an ongoing pandemic.

Methods: We simulated a five compartment mathematical model to analyze the pandemic scenario in both California, and whole U.S. We considered four vaccines, Pfizer (95%), Moderna (94%), AstraZeneca (79%), and Johnson & Johnson (72%), which are being used rigorously to control the SARS-CoV-2 pandemic, in addition with two special cases: a vaccine with 100% efficacy rate and no vaccine under use. SARS-CoV-2 related data of California, and U.S. were used in this study.

Findings: Both the infection and death rates are very high in California. Our model suggests that the pandemic situation in California will be under control in the last quartile of the year 2023 if vaccination program is continued with the Pfizer vaccine. During this time, six waves may happen from the beginning of the immunization where the case fatality and recovery rates will be 1.697% and 98.30%, respectively. However, according to the considered model, this period might be extended to the mid of 2024 when vaccines with lower efficacy rates are used. On the other hand, the daily cases and deaths in the U.S. will be under control at the end of 2026 with multiple waves. Although the number of susceptible people will fall down to none in the beginning of 2027, there is less chance to stop the vaccination program if vaccinated with a vaccine other than a 100% effective vaccine or Pfizer, and at that case vaccination program must run till the mid of 2028. According to this

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study, the unconfirmed-infectious and infected cases will be under control at the end of 2027 and at the mid of 2028, respectively.

Interpretation: The more effective a vaccine is, the less people suffer from this malign infection. Vaccines which are less than 90% effective do not have notable contribution to control the pandemic besides hard immunity. Furthermore, specific groups of people are getting prioritized initially, mass vaccination and quick responses are required to control the spread of this disease.

1. Introduction

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) induced disease SARS-CoV-2 has a devastating impact on every sector of human life (Nicola et al., 2020). A Global emergency was declared due to this SARS-CoV-2 outbreak on January 30, 2020, by the World Health Organization (WHO) (Sohrabi et al., 2020). To contain the rapid spread of the virus (Kamrujjaman et al., 2020a; Burkert, 2020), governments initially followed different approaches, including the shutdown of the borders, restrictions on both local and international travel, quarantine, and nationwide lockdown (Al, 2020; Guidance on social distancing for everyone in the UK, 2020; Kamrujjaman et al., 2021; Mahmud, Kamrujjaman, Jubyrea, Islam, & Islam, 2020). The education system from pre-school to university education has been affected by SARS-CoV-2, and in most cases, authorities have closed the educational institutions. According to UNESCO, approximately 900 million students have faced the detrimental effect of this closure (COVID-19 Educational Disruption and Response, 2020). An international survey has been carried out by the International Association of Universities (IAU) to estimate the impact of this outbreak on the global education system. 78% of participants are convinced by the fact that SARS-CoV-2 will engender an adverse influence on the number of students who will enroll in the upcoming academic year. Approximately half of the respondents (46%) think both local and international students will face problems due to this ongoing pandemic (Marinoni, van't Land, & Jenssen, 2020). As well as the influence on undergraduate education (Alsafi, Abbas, Hassan, & Ali, 2020), the most critical impact on post-graduate research is that many irrelevant COVID-19 research topics have been halted. The national funding body for health research in the U.K. stopped all non-COVID-19 research to facilitate the opportunity for clinically trained staff to return to the frontline (News, 2020). In the USA, similar action was taken by the National Institute for Health to stop all non-critical research. Apart from healthcare research, many institutions of Harvard University closed laboratories in the Faculty of Arts and Sciences in order to abstain from researching humanities and social sciences (NIH shifts non-mission-critical laboratory operations to minimal, 2020; Information, 2021). Moreover, the concern is raised about the canceled scientific conferences. Conferences are now taking place on online platforms, and this medium is not that viable for networking compared to physical conferences as these conferences are considered significant to many fields of scientific research and opportunities for collaboration (Impey, 2020). The approach to social isolation due to SARS-CoV-2 has had a severe outcome on the psychological and mental health of the people in the society. Suicide, self-harm, substance misuse, domestic and child abuse are many of the presumed repercussions of this isolation. Since March 9, 2020, in the U.K., 4000 offenders have been arrested due to domestic abuse that is equating to 100 per day, indicating the negative result of social isolation (Grierson; Holmes et al., 2020). According to a report (Usher, Bhullar, Durkin, Gyamfi, & Jackson, 2020), France and the USA have seen 32–36% and 21–35% surge in domestic abuse. In the U.K., there has been an increase in domestic abuse hotline calls by 25% and 75% enhancement in the Google search regarding support for domestic abuse. This abuse is mainly due to the reduction of the opportunities for support, enhanced contact to manipulative relationships, and disaster-related indoor uncertainty (Holmes et al., 2020; Usher et al., 2020).

However, the outbreak of SARS-CoV-2 by coronavirus in Wuhan is not the first outbreak by the virus. Before this, there were two outbreaks known as Severe Acute Respiratory Syndrome (SARS) in China in 2002, followed by Middle East Respiratory Syndrome (MERS) in 2012 in Saudi Arabia (Peiris, Guan, & Yuen, 2004; Raj et al., 2014). To treat the 2003 SARS infection, scientists quickly developed different vaccines, and VRC-SRSDNA015-00VP was one of them, which is a DNA vaccine that consists of a circular plasmid DNA macromolecule (VRC-8318) (Huang, Yang, Kong, & Nabel, 2004). Phase I human trial started after 17 months of evaluating the preclinical safety and efficacy of the vaccine candidate (Yang et al., 2004). Ten healthy volunteers aged 21–49 took part in this trial from December 13, 2004, to May 2, 2005. Four milligrams (4 mg) of the vaccine were injected three times at four weeks intervals, and the subjects were monitored for 32 weeks (Catanzaro et al., 2006, 2007; Martin et al., 2006). However, 9 participants out of 10 completed the recommended doses and, one of them was withdrawn from the list to treat poison ivy contact dermatitis after receiving the second vaccination (Martin et al., 2008). While analyzing the vaccine's effectiveness, it was found that the VRC DNA SARS vaccine generated response against T-cell and antibody of SARS virus and neutralized antibody in 8 out of 10 subjects. After completing the phase I clinical trial of the VRC DNA SARS vaccine, it was declared that the safety and tolerability were within the favorable range (Buchholz et al., 2004; Catanzaro et al., 2006, 2007; Chen & Subbarao, 2007; Lu et al., 2004; Martin et al., 2006, 2007). Unfortunately, no data/information of this vaccine regarding the further trial phases is available. For MERS coronavirus, GLS-5300 was the first vaccine that entered the phase I clinical trial,

and it was also a DNA vaccine. Initially, the vaccine was given to 75 adults, from 18 to 50 years old. 0.67 mg, 2 mg, or 6 mg of GLS-5300 vaccine was administered on the 0, 28th, and 84th days. Safety assessment of the volunteers of this study was monitored up to 48 weeks after completing the doses (Modjarrad et al., 2019). After analysis of phase I clinical trial results, it was found that 93% of participants experienced a reaction at the injection site and 92% experienced pain. Infection was the most common unwanted adverse effect reported in 36% of participants. Also, the antibody neutralizing effect was observed in 27 volunteers at 14th weeks, 25 volunteers at 24th weeks, and 2 volunteers at 60th weeks (Yoon & Kim, 2019).

To date, there are many outbreaks of infectious diseases apart from these outbreaks of infectious disease by a coronavirus. Cholera is such a kind of disease that is induced by the bacterium *Vibrio Cholerae* and the intestine is usually damaged when infected by this bacterium. Although this disease is endemic in few Asian and African countries, several cholera epidemics have been noticed worldwide. It is estimated that about 1.3–4 million people get affected by this disease, and among them, 21,000–143,000 face death per year (Ali, Nelson, Lopez, & Sack, 2015). In 2017, 1,227,391 cases and 5654 deaths were reported in 34 countries worldwide (Weekly Epidemiological Record (WER), 2018). Rapid dehydration and the inconsistency of electrolytes in our bodies are common scenarios of this disease. Without swift action, cholera might be the reason for the death of a person due to dehydration within a few hours (Codeço, 2001). Enhanced water and sanitation systems are indeed useful to prevent the disease, but the most effective way is a vaccination. This strategy is following to contain the spread of this infectious disease, particularly in Haiti (NPR Cookie Consent and Choices, 2012). Among 200 serotypes of the bacterium, two of them are responsible for the disease cholera, and they are *V. cholerae* O1 and O139. Dukoral (WC-rBS) and Shanchol are two available vaccines for cholera that are administered orally. mORCVAX is an identical vaccine similar to Shanchol (World Health Organization, 2016). Dukoral is available in more than sixty countries worldwide, and it consists of the deadly strains of *V. cholerae* and recombinant cholera toxin beta (CTB) (Cholera, 2021; Dukoral suspension and effervescent granules for oral suspension, 2021). Whereas Shanchol contains three deadly strains of *V. cholerae* O1 and single O139, but it does not contain any CTB like Dukoral (Trach et al., 1997). Different doses of Dukoral are given depending on age. Those who are more than 6 years old are given 2 doses, whereas children below 6 years receive three doses of this vaccine at least a week interval (Dukoral suspension and effervescent granules for oral suspension, 2021). On the other hand, two doses of Shanchol are administered to those who are $\geq$ 1-year-old at 14 days apart (Charles et al., 2014). These vaccines' most potent protective action is observed against the disease in the first 2 years of vaccination. According to the efficacy report of these vaccines, their efficacy ranging from 86% to 66% at 4–6 months, 62%–45% at 1 year and, 77%–58% at 2 years (World Health Organization, 2016). Another infectious disease is malaria which roughly abounds in 91 countries globally. Out of 120 species, only six species of Plasmodium are responsible for infecting the human (Ashley, Pyae Phyo, & Woodrow, 2018). According to the latest World malaria report published by WHO on November 30, 2020, there were 229 million malaria cases and 409,000 death worldwide. Although the number of deaths was comparatively lower compared to 2018, which was 411,000. African countries were responsible for almost 94% of all malaria cases, and deaths (Fact sheet about malaria). To date, only RTS, S/AS01 is the most effective anti-malarial vaccine studied the most. Interestingly, this vaccine is the result of a collaboration started in the 1980s between the Walter Reed Army Institute of Research in the USA and GSK biologicals (Ballou & Cahill, 2007). An experiment of this vaccine was conducted initially in African children, and the significant effect was measured against infection of *P. falciparum* and this species is regarded as the deadliest parasite worldwide and prevalent in Africa. The vaccine was capable of resisting the malarial infection in 4 out of 10 cases over 4 years in children who received four doses during the clinical trial period (Fact sheet about malaria).

To eradicate any pandemic disease, vaccination is the most prominent way. The immune system is boosted by vaccination. Neither any diseases nor vaccination indeed provides immunity. Vaccination becomes successful because, in most cases, every disease has a recovered/immune stage (Kamrujjaman et al., 2020b; Mahmud, Kamrujjaman, & Islam, 2021). Vaccination plays an integral role in ameliorating of living and health standards of people (Bacci & Massimo, 1997; Bloom, 2004). After the emergence of SARS-CoV-2, scientists started developing vaccines relentlessly worldwide. Finally, for the first time on November 9, 2020, NEW YORK & MAINZ, GERMANY (BUSINESS WIRE) Pfizer Inc. (NYSE: PFE) and BioNTech S.E. (Nasdaq: BNTX) announced their vaccine BNT162b2 that has made based on the mRNA as effective against SARS-CoV-2. This result was from the phase III clinical trial of the vaccine where the volunteers did not have any prior symptoms of SARS-CoV-2 infection. Forty-three thousand five hundred thirty-eight volunteers were recruited in this part of the trial, and it was found that the vaccine was 90% effective in resisting the viral infection. Also, the analysis confirmed 94 SARS-CoV-2 cases in participants during this trial period (Pfizer.Com, 2020). Later on December 10, 2020, an article published in The NEW ENGLAND JOURNAL of MEDICINE regarding the safety and efficacy of the vaccine of further study where; it was found that the vaccine is 95% capable of protecting the disease. In this part of the trial, 43,548 took part; among them, 43,448 were injected. 21,720 participants were given either BNT162b2, and 21,728 received placebo. All of them received two doses, and the second dose was given after 21 days of the first dose, and the concentration was 30 μg. After the first dose, 10 severe SARS-CoV-2 cases were raised, and 9 related to those assigned to placebo, and the remaining one was BNT162b2 recipient. After 7 days of administration of the second dose, there were 8 confirmed cases of SARS-CoV-2 among the participants who received BNT162b2 whereas 162 cases were observed in the case of placebo. The most common side effects were pain at the injection site, fatigue, headache, muscle pain, chills, joint pain, and fever which remained a few days. Notably, most volunteers had these side effects after completing the final dose (Polack et al., 2020). More than a month later after the first declaration, on December 11, 2020, the U.S. Food and Drug Administration (FDA) approved the vaccine for emergency use authorization (EAU) in individuals who are 16 years old and older to prevent the disease SARS-CoV-2 (Office of the Commissioner, 2021a). The USA, the UK, Canada, Bahrain, Mexico, and Singapore are some countries that approved this vaccine rapidly to use throughout the country after

getting approval from the U.S. FDA (Associated Press, 2020; The Straits Times, 2020). Pfizer has announced that they are expecting to produce 50 million doses at the end of this year and 1.3 billion by the end of the following year (Pfizer.Com).

Another vaccine that is being used extensively is ChAdOx1 nCoV-19 (AZD1222) that Oxford-AstraZeneca has developed. Report from the clinical trial has shown that this vaccine can also protect against the SARS-CoV-2 infection. From April 23 to November 4, 2020, 23,848 volunteers took part in a clinical trial, and 11,636 (7548 in the U.K., 4088 in Brazil) were taken randomly to analyze the interim primary efficacy. Participants received either ChAdOx1 nCoV-19 vaccine or control (meningococcal group A, C, W, and Y conjugated vaccine or saline). Two doses of the vaccine were injected composed of 5×10^{10} units of viral (Standard dose: SD/SD cohort). 70.4% found the overall vaccine efficacy. Twenty-one days after the first administration of the first dose, 10 cases of SARS-CoV-2 induced who received the control where two were regarded as severe cases, including one death. One hundred seventy-five severe adverse reactions were observed in 168 people, and among them, 84 were associated with ChAdOx1 nCoV-19, and 91 in control (Voysey et al., 2020). The latest report on the efficacy published on March 25, 2021, suggests that the Oxford-AstraZeneca vaccine efficacy is 76%. The interim analysis of the vaccine efficacy showed that it was 79% effective against the virus. This result was from a trial where 32,449 adults participated from the U.S., Peru, and Chile. During the trial period, no one was reported to get admitted to the hospital or died, although 60% of the participants had previous health issues like diabetes or obesity (Callaway & Mallapaty, 2021; Mallapaty & Callaway, 2021). However, recently a severe issue, rare-blood clotting, has been reported due to this vaccine. This happens mostly in women age over 55 years old. Considering this critical issue, 20 European countries have halted vaccination (Mallapaty & Callaway, 2021). Among these countries, Denmark has stopped using the vaccine completely. Due to this, 2.4 million doses of vaccines will be withdrawn until the following announcement. The Danish authority decided to do this after reporting two cases of blood-clotting, one of them was fatal in a 60 years old woman (BBC News, 2021). On the other hand, Germany has suspended the regular use of the vaccine but decided to continue using it for people over 60. This decision was made when few cases of rare blood clotting were observed for younger people (Deutsche Welle (www.dw.com), 2021). Sweden, Latvia, Italy, Spain, France, Luxembourg, Cyprus, Portugal, Slovenia, Netherlands, Ireland are some other European countries that have suspended the use of the Oxford-AstraZeneca vaccine (Al, 2021).

Moderna SARS-CoV-2 vaccine mRNA-1273, developed by Moderna TX, Inc got approval for emergency use for the first time by the FDA on December 18, 2020 (Meo, Bukhari, Akram, Meo, & Klonoff, 2021). In phase, I clinical trial, 45 adults aged from 18 to 55 participated, and they were given two doses of the vaccine with a 28 days interval. They were divided into three different groups and administered 25 μg. 100 μg, or 250 μg per dose for each group. After the first dose of the vaccine, it was found that the higher doses were capable of inducing a higher effect (Geometric mean titer (GMT) was 40,227 in 25 μg, 109,209 μg, and 213,526 in 250 μg of the vaccine recipients, respectively). After the 2nd dose of the vaccine, a similar pattern was observed: a higher amount of the vaccine generated higher responses. At that time, the GMT were 2999,751, 782,719, and 1,192,154, respectively (Jackson et al., 2020). On the other hand, 30,420 volunteers from the U.S. participated in phase III clinical trial of mRNA-1273. They were divided into two groups (15,210 in each group) and given either the vaccine (100 μg) or placebo. Symptomatic illness was observed due to SARS-CoV-2 infection was detected in 185 and 11 volunteers who were given the placebo and vaccine, respectively (Baden et al., 2021). The most common observed side effects of the vaccine were pain at the injection site (92%), fatigue (70%), headache (64.7%), muscle pain (61.5%), chills (45.4%), joint pain (46.4%), fever (15.5%), swelling at the injection site (14.7%), erythema at the injection site (10%), nausea, vomiting (23%), and lymphadenopathy, axillary tenderness (19.8%). No serious events were observed for the vaccine or placebo (Meo et al., 2021). However, after the phase III clinical trial, the efficacy of the mRNA-1273 was found 94.1% to prevent the severe illness due to the SARS-CoV-2 infection (Baden et al., 2021).

Ad26.COV2.S is another vaccine that the FDA has approved, U.S. developed by the Janssen Pharmaceutical Companies of Johnson and Johnson. The mechanism of action of this vaccine is different from the Pfizer and Moderna vaccine. According to the developer, it can combat moderate to severe SARS-CoV-2 infection in people age 18 and over. Here, the modified DNA of adenovirus is used that can make a similar viral particle of SARS-CoV-2. When the vaccine is administered, the body will make an immune response against that particle. Eventually, this immune response will protect from the SARS-CoV-2 infection. Notably, the adenovirus is responsible for respiratory infection. From the phase III clinical trial, different efficacy was found. A single dose of the vaccine was 66% and 67% effective against moderate to severe-critical SARS-CoV-2 condition after 14 and 28 days of the administration, respectively. Interestingly, higher efficacy was observed for the severe-critical condition that 77% and 85% after 14 and 28 days of vaccination, respectively (Livingston, Malani, & Creech, 2021; Sadoff et al., 2021). However, a report published on April 13, 2021, reveals that the U.S. has stopped using this vaccine due to forming blood clots. Six cases were found having blood clotting combined with low platelets. All of them were females aged from 18 to 48 years old. This condition appeared after 6–13 days of vaccination (Mahase, 2021).

Apart from these four vaccines, few other vaccines got approval and using in many countries. The list of those vaccines is given below [Updated on April 20, 2021] (Zimmer, Corum, & Wee, 2021):

Scientists are investigating 89 vaccines where 52 are in the phase I clinical trial and 37 are in phase II clinical trial stage. On the other hand, 23 vaccines have reached the phase III stage (Zimmer et al., 2021).

2. Model overview

The mathematical model in infectious disease is one of the most crucial issues in epidemiology. From mathematical models, we get translucent ideas about the pattern of disease behavior.

2.1. Model formulation and parameter description

In this study, we propose a non-demographic SEIR (Susceptible-Exposed-Infected-Recovered) type vaccination model to illustrate the dynamics of SARS-CoV-2 infectious disease.

We assume that among any locality, almost all the active population are susceptible at the beginning of the virus circulation since a sudden introduction of an unknown and highly contagious virus takes few days to make the population conscious of its consequences. Meanwhile, specific types of contacts between the susceptible individuals and already infected and/or infectious individuals keep spreading the infection silently. When the virus-induced disease has started showing symptoms and mass fatality begins as a consequence, it is almost too late. It becomes impossible to identify and isolate all infected and infectious individuals from the healthy but susceptible population.

After some specific types of contacts with a SARS-CoV-2 patient, a susceptible individual may have two different scenarios: His enough precautions and/or strong immune system may immediately refuse to let the sufficient amount of virus enter in his body, and so the body is still not infected rather susceptible yet. Another scenario may happen: he got to permit many viruses in his body because of his ill knowledge and/or inadequate safety measures, and his immune system starts fighting against the virus. This person must appear for a clinical test. A positive clinical test result is the confirmation of a SARS-CoV-2 infection case. For this kind of infection, a clinical test supports disease diagnosis, not treatment. If there are not enough facilities to provide an immediate test to the susceptible individuals who have come to contact with a confirmed infected person, or who have been asymptomatic throughout their entire infection period which refers to the person who have been pauci-symptomatic (sub-clinical), or pre-symptomatic (going to develop symptoms later), or post-infection (with still detectable viral RNA fragments from an earlier infection) (Pollock & Lancaster, 2020). Muge Cevik et al. showed that SARS-CoV-2 infected individuals might become infectious one to two days before the exposure of symptoms and also can continue to be infectious up to the seventh day after that (Cevik et al., 2021). Now, it has been proved that symptomatic and pre-symptomatic transmission have a major role in the proliferation of SARS-CoV-2 than the truly asymptomatic transmission (Buitrago-Garcia et al., 2020; Byambasuren et al., 2020; Cevik, Kuppalli, Kindrachuk, & Peiris, 2020; Hassan, Mahmud, Nipa, & Kamrujjaman, 2021; Qiu et al., 2021).

Multiple pieces of research have found that the transmission rates can be 3 to 25 times higher for people with symptoms than those who are asymptomatic (Buitrago-Garcia et al., 2020; Koh et al., 2020; Madewell, Yang, Longini, Halloran, & Dean, 2020; Qiu et al., 2021). A study in Wuhan casting almost 10 million people concluded with no proof of asymptomatic transmission till their study had published (Cao et al., 2020). Usually, the viral particles may shed from infectious people via talking, breathing, and/or coughing, where coughing may cause more viral particles to be spread than the other two mediums; which makes people with symptoms more contagious, as coughing is a major symptom of SARS-CoV-2 (Chen et al., 2021). In addition, pre-symptomatic and asymptomatic individuals naturally have more contacts than the isolated symptomatic individuals (Pollock & Lancaster, 2020). Now it is clear that there are always some infected and so infectious people out there who are not intended to undergo the clinical test at the very primary stage and will keep spreading the infection as long as s/he gets her/his clinical result and has been taken to isolation/hospital.

In most of the cases (approximately 97% worldwide (Coronavirus Cases: Statistics and Charts - Worldometer)) for SARS-CoV-2 out-break, the symptomatic clinically tested confirmed infected individuals get recovered with proper health maintenance and regular medications. These recovered/discharged populations can hold herd immunity against the virus in maximum cases, while some recovered/discharged populations may be reinfected according to their immune ability and/or age. World Health Organization declared the reinfection case percentage may lie up to 0.01% (Coronavirus disease (COVID-19), 2021). Moreover, till now, the SARS-CoV-2 virus has taken 3% (Coronavirus Cases: Statistics and Charts - Worldometer) lives of the clinically tested confirmed cases. Mainly, the old aged and people with the vulnerable immune system because of other illnesses, and people with unhealthy lifestyles are the major victims to not survive.

In our model, we introduce a vaccinated compartment to the modified SEIR model being activated from the day when an authorized, hence clinically effective vaccination program has been started in any specific locality or among any particular population/group. Since no vaccine may work 100% effectively, there remains a slight risk of being infected though a complete dose of vaccination has been taken. We include this concept by considering the vaccine inefficacy parameter in the model. Like many other COVID-19 vaccine models, we consider perfect immunity for recovered individuals from natural infection, i.e., no susceptibility to reinfection. Although, a small portion might be susceptible to reinfection, which we ignore to keep the model simple. Since the effect of vaccination is the core of this study, so we did consider the susceptibility to reinfection for vaccinated individual. While in close contact with another infectious individual without proper health precautionary measures, this parameter may lead a small number of vaccinated population to the infectious class or pre-symptomatic situation, and then to the infected class. We observe and assume, as being vaccinated, such contacts merely transmit vaccinated individuals to the infected compartment, but the exposed (unconfirmed infectious) class; since most of the vaccines may cause fever for 1–2 days to activate the immune system against SARS-CoV-2 virus and this situation is considered as being in the exposed class to avoid model complexity. And this population easily move to the recovered compartment from the exposed class without costing additional parameter to the model. The primary focus of this study is to realize the role of vaccination in controlling the pandemic situation along with the importance of vaccine efficiency rates in this aspect.

Virus mutations are playing another very sophisticated role in causing new clusters in different corners of the world after every couple of weeks/months. Firstly, the primary host of this SARS-CoV-2 virus was a completely different species, bats; and

all of a sudden it made a jump to the human being (Zhou et al., 2021). There are some other examples of such epidemics, from flu pandemics to Ebola outbreaks, making such jump and then accelerating (Zhou et al., 2021).

For SARS-CoV-2, the basic reproduction number (R_0) was around 2.50 at the starting of the pandemic in Wuhan and now can be as high as 6.1 for the different variants (Ke, Romero-Severson, Sanche, & Hengartner, 2021; WHO, 2020). It has been seen that two lineages (Alpha and then Delta) each is 50% more transmissible, which makes it obvious to expect a further bounce in transmission over an upcoming couple of months/years (Brown, 2021).

Naturally, viruses improve their ability to spread through different tricks like:

1. Improving the process of opening the doorway to host's body cells
2. Enriching the amount of microbial in host's body so that host spreads out more viruses through breathing, talking, or coughing
3. Promotes the ability to survive longer in the non-host environment.

Considering all these scopes of mutations, there is still space for the SARS-CoV-2 virus to mutate (Brown, 2021; Research Square, 2021). But this does not refer that by the course of time the virus can keep mutating and will end up as an unstoppable adversary. According to Dr. Katzourakis, "Ultimately, there are limits and there isn't a super-ultimate virus that has every bad combination of mutations" (Gallagher, 2021). Also, there is the concept of the ubiquitous trade-off, which says, one often gets worse at one/several thing/s to become better at something else. The hope is, the execution of the fastest vaccination program in history will end up giving a hard time for the virus to overcome and strengthen itself in another evolutionary direction.

We adapt this idea of mutation in our model by taking the transmission rates as step functions inside the model algorithm. The rates stage up periodically for certain times and start falling as the vaccination program continues for a long time, and ends up rounding off to zero. For this reason, it is natural to have several waves before the pandemic is eradicated.

3. Numerical results

Numerical simulation is the most incredible way to observe and present the outcomes of mathematical models. In this section, we will demonstrate the numerical results of our proposed model. Model prediction and actual data of infected cases of the SARS-CoV-2 virus may confer a better conception about this disease pattern. Moreover, we present a clear idea about forecasting and controlling the disease with different vaccines.

We use the Crank–Nicolson finite difference method for the model, and the graphical presentations are executed with MATLAB.

3.1. Parameter estimation

In this subsection, we are to fit the clinically confirmed SARS-CoV-2 cases with the proposed model parameters. We simulate the model outcomes in the fitting methodology known as longitudinal daily case notification data.

We try to fit the model parameters to multi-day longitudinal time series data collected from reliable sources (Coronavirus Cases: Statistics and Charts - Worldometer; Zimmer et al., 2021; Wikipedia contributors; California) in a similar way Goeyvaerts et al. estimated dynamic transmission model parameters for seasonal influenza by fitting to season-specific influenza-like illness incidence (Goeyvaerts et al., 2015). Here, we strictly accept only laboratory-confirmed SARS-CoV-2 specimen cases instead of influenza-like symptoms rather than laboratory-confirmed cases of SARS-CoV-2.

We apply a least-squares approach to better fit the model for an assumed and estimated set of parameters. The model output is compared to the corresponding exploratory daily incidence of positive SARS-CoV-2 cases. The empirical number of reported cases on the day d and the number of incidences predicted by the model on the day d is denoted by I_d^E and I_d^M, respectively. The comparison between these two numbers on the day d are done using the parameter α introduced by Goeyvaerts et al. (Goeyvaerts et al., 2015) to scale the model outcome, where, α captures the probability of an infected individual being symptomatic, prescribed to undergo the clinical test for SARS-CoV-2, and ends up being tested positive. The sum of squares error is calculated as

$$\sum_{\forall d}\left(I_d^H - (\alpha I_d^M)\right)^2$$

The parameter space is evenly sampled using the Latin hypercube sampling (Blower & Dowlatabadi, 1994) to generate 35,000 parameter combinations (see Table 1). Parameter descriptions and Latin hypercube sampling ranges (that is, fitting ranges) are shown in Table 2. Later on, we determined the sum of squares score for each parameter set over a simulation run, which we call one 'Run Iteration'. After that, we exploit the MATLAB GlobalSearch algorithm and look for the optimal parameter combinations about the set of parameters that have conferred the minimum sum of squares values.

Because of the stochastic trait of this method, more 'Run Iteration' may end up with lower least-squares fits. We use the 30 best performing set of parameter values executed from the Latin hypercube sampling as the initial points for the MATLAB GlobalSearch algorithm.

Table 1
List of vaccines that have been approved for emergency use.

Developer	Vaccine name	Type	Efficacy	Doses
Gamaleya (Russia)	Sputnik V	Adenovirus	91.6%	2 doses, 3 weeksapart
CanSino Biologics(China)	Convidecia	Adenovirus	65.28%	Single dose
Vector Institute(Russia)	EpiVacCorona	Peptides	Unknown	2 doses, 3 weeksapart
Sinopharm (China)	BBIBP-CorV	Inactivated	79.34%	2 doses, 3 weeksapart
Sinovac Biotech(China)	CoronaVac	Inactivated	50.65% in Brazil,91.25% in Turkey	2 doses, 2 weeksapart
Bharat Biotech(India)	Covaxin	Inactivated	80.6%	2 doses, 4 weeksapart

3.2. Case: California U.S.

California is one of the most important states of the United States. It is the third-largest state by size (423,970 km^2) with a total population of 39, 512, 223 (approximately on July 01, 2019) which makes it the most significant state by population (Population Clock). Corresponds to this data, California has also been affected by SARS-CoV-2 very hardly till the beginning. On January 25, 2020, California reported its first SARS-CoV-2 case, where the first confirmed case in the U.S. was reported on January 21, 2020, by the case of a Washington resident who returned from Wuhan, China on January 15, 2020 (Staff, 2021; Wikipedia contributors). Now, California is on the top of the list among U.S. states with the highest 11.38% confirmed cases and 10.65% reported deaths of the total U.S. data till date (Coronavirus (COVID-19) statistics data - Google Search Help, 1470). As the well-tuned data of our sample population is publicly available online, we collect the daily case data and fit our model with possible parameter values and observe the results in this subsection.

Moreover, California is offering the most advanced treatment for the SARS-CoV-2 virus. It has already started a vaccination program from December 15, 2020 (Money, 2020). Nevertheless, it is very crucial to reach the vaccine to such a vast population overnight. So, the public health administration has taken some effective initiatives to provide vaccines to the people who need them the best. In the beginning, the authority decided that the people who have lived more than 50 years of their lives were being the most vulnerable against the virus. The front-line health workers are also straightforward to get infected, and some people have a weak immune system for other health issues. Californian health authority started assuring vaccines for these individuals in the first place. However, over time it also has declared that any 16+ aged individual will be eligible for vaccination from April 15, 2021 (California). Overall, the vaccination program is prioritized according to risk and age. Only high-risk patients and old-aged individuals are getting prioritized for vaccination, and younger people are comparatively at low risk to be infected by the SARS-CoV-2 virus. We consider the 30-day average vaccination number and imply for the numerical study, and when saying vaccinated, we indicate the population who have taken at least one dose of vaccine, whichever the vaccine is. Also, we considered that the pandemic is under control when the number of active cases drops below 100 per day and is still decreasing. This situation has remained for more than 20 weeks.

The vaccination program is ongoing in hospitals, community vaccination sites, Doctor's offices, clinics, and pharmacies. Effective vaccine curbs against the SARS-CoV-2 virus spreading. It takes a few weeks after the first dose for the body to build protection against the virus. However, after taking the vaccine, it is still possible to get infected by the SARS-CoV-2 virus. After taking the full dose of the vaccine, it may work more effectively against the severe SARS-CoV-19 virus. But, new stain of the SARS-CoV-2 virus is being identified all around the world very frequently. The Food and Drug Administration of U.S. governance body has demonstrated the safety and effectiveness of some vaccines by clinical trials and then authorized for public usage (Center for Biologics Evaluation and Research, 2020; Office of the Commissioner, 2021b). Moreover, the authorized vaccines are up to 95% (Pfizer) effective with a base effectiveness value of 72% (Johnson & Johnson) against the SARS-CoV-2 disease. However, from the beginning of the vaccination program, California is using the Pfizer and Moderna vaccine. In this study, for different vaccine efficacy ('Pfizer' 95%, 'Moderna' 94%, 'AstraZeneca' 79%, and 'Johnson & Johnson' 72% (Martichoux, 2021)), we illustrate the proposed model predictions with figures which correlate with the actual data within an acceptable range. The United States' vaccine safety system ensures that all vaccines are safe, though not entirely practical. The federal government is working on it (Ensuring the Safety of COVID-19 Vaccines in the United States, 2021) (see Fig. 1).

Fig. 2 illustrates the plausibility fit of the considered model for the available SARS-CoV-2 data for California with the usage of the 'Pfizer' vaccine from December 15, 2020, to April 17, 2021. From the actual data of daily cases, it is clear that, till April 2021, there have been two waves of infection in California. Moreover, the figures in Fig. 3 depict the model fitting with the actual fatality data in California. To fit the wave data, we include the viral mutation parameter in the transmission rates as step functions with an average intervention of 20 weeks. Furthermore, this model data forecasts several waves upwards.

The linear regression analysis of the data fitting is presented in Fig. 4 which implies that the proposed model fits the daily reported cases with substantial R^2 value ($R^2 = 0.861\,944$). Thus, we may decide more than 86% accuracy to forecast California's real confirmed SARS-CoV-2 cases. The result indicates that the model acceptance is substantial for the underlining data set for California's taken set of parameter values.

Fig. 5 shows all the possible upcoming waves of SARS-CoV-2 in California, U.S., even if the people are continuously being vaccinated with the Pfizer vaccine, whose effectiveness rate is 97% against the symptomatic SARS-CoV-2 cases, hospitalizations, severe and critical hospitalizations, and deaths (94% against asymptomatic SARS-CoV-2 infections) even in case of the

Table 2
Parameter estimation: California vs U.S.

Notation	Interpretation		Fitting Range		Source
			California	U.S.	
		Pfizer	5%		(Martichoux, 2021; Pfizer, 2021)
ω	Vaccine inefficacy				
		Moderna	6%		(Martichoux, 2021; STAT, 2021)
		AstraZeneca	21%		(Martichoux, 2021; AstraZeneca, 2021)
		J&J	28%		(Martichoux, 2021; Johnson & Johnson, 2021)
κ	Daily vaccination		25, 674 – 110, 250	556, 208 – 1, 387, 585	(California; Ritchie, 2020)
σ	Transition rate for I_S		0.08–0.25	0.08–0.25	Assumption
β_1	Transmission rate for S		$0 - 1.81 \times 10^{-7}$	$0 - 1.27 \times 10^{-}7$	Estimated
β_2	Transmission rate for S_V		$0 - 3.58 \times 10^{-8}$	$0 - 1.24 \times 10^{-}7$	Estimated
γ_1	Recovery rate from I_S		0.61–0.81	0.62–0.82	Assumption
γ_2	Recovery rate from I		0.86–1.0	0.82–1.0	Ritchie (2020)
δ	Disease induced death rate		0–0.02	0–0.03	Ritchie (2020)

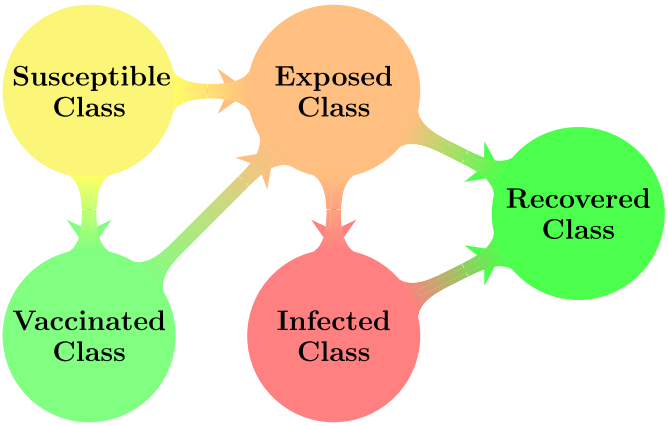


Fig. 1. Compartmental model scheme visualization.

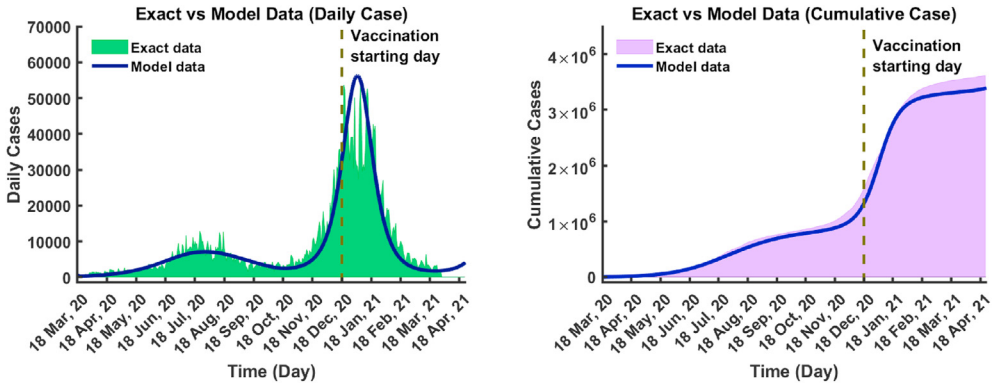


Fig. 2. Model plausibility check for SARS-CoV-2 pandemic: Daily reported cases (left), and cumulative cases (right) with 'Pfizer' vaccine.

full vaccine dose completion (Pfizer, 2021). The model forecasts 6 (six) waves in total from the day of the vaccination program started in this state, December 15, 2021 (seven waves during the total pandemic period). It is also observable that the wave peaks are reducing as time passes, and the epidemic seems to be under control by the mid of 2023. In the meanwhile, 7,814,589 cases will be confirmed according to this study, with 132,636 deaths (Fig. 6) which is 1.697% of a total case with 98.30% recovered patients. Till the mid of 2023, about 20% of the total population of California will be infected with SARS-CoV-2.

We have considered additional cases for alternative vaccine scenarios other than the Pfizer vaccine: Moderna, AstraZeneca, Johnson & Johnson, an imaginary vaccine of 100% effectiveness, and the no vaccine case. Fig. 7 depicts the impacts of

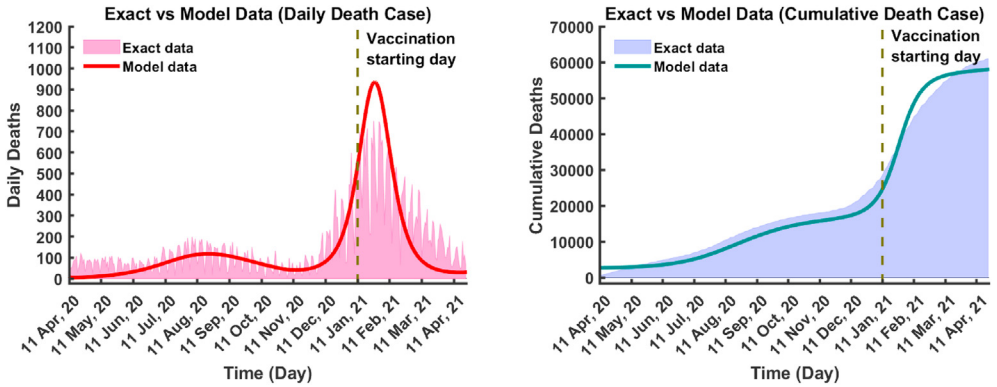


Fig. 3. Model plausibility check for SARS-CoV-2 pandemic: Daily reported death cases (left), and cumulative death cases (right) with 'Pfizer' vaccine.

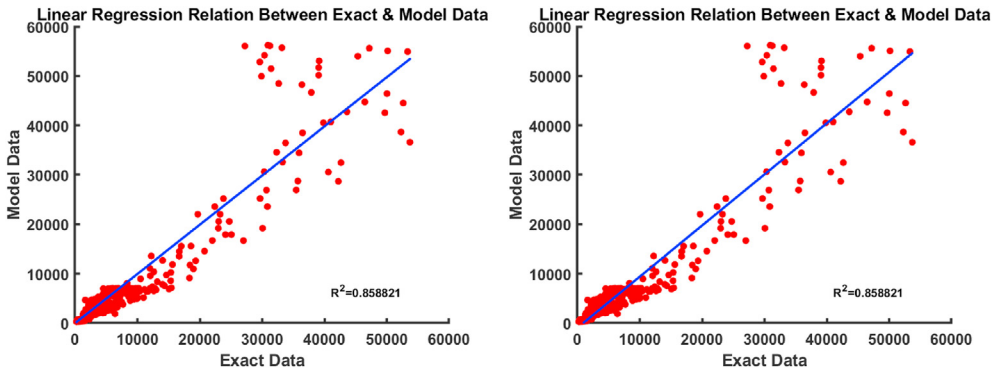


Fig. 4. Two types of regression analysis for exact and proposed model data for California, where (left) linear regression, and (right) linear regression (modified) based on MATLAB.

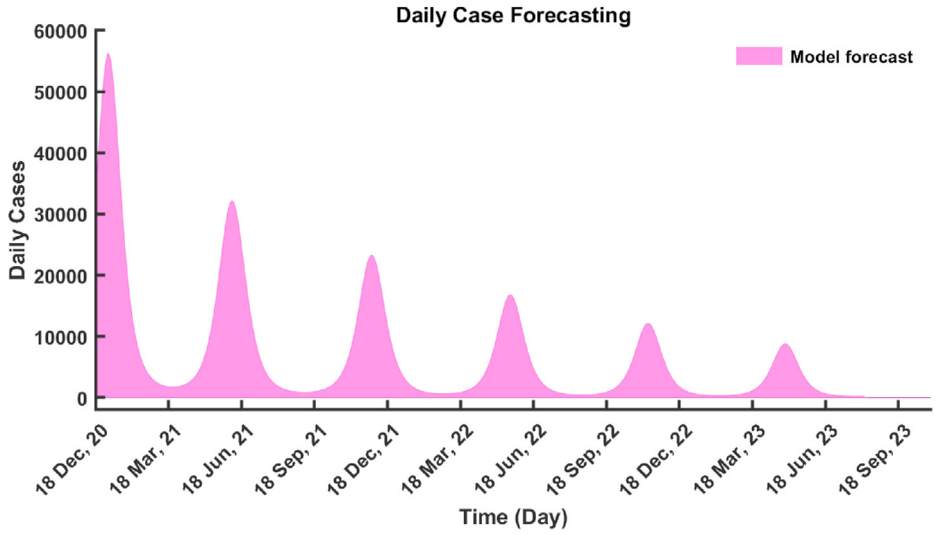


Fig. 5. Model forecasting: Daily confirmed cases with 'Pfizer' vaccine.

each vaccine cases for each compartments: Susceptible (7a,7b), Vaccinated (7c,7d), Unconfirmed Infectious (7e,7f), Infected (7g,7h), Recovered (7i,7j) in subfigure 7a-7j, respectively. The undulating reduction in the susceptible compartment is obvious in Fig. 7a because of the infection waves throughout the pandemic span. The rapid mutation rate in the RNA structure of this

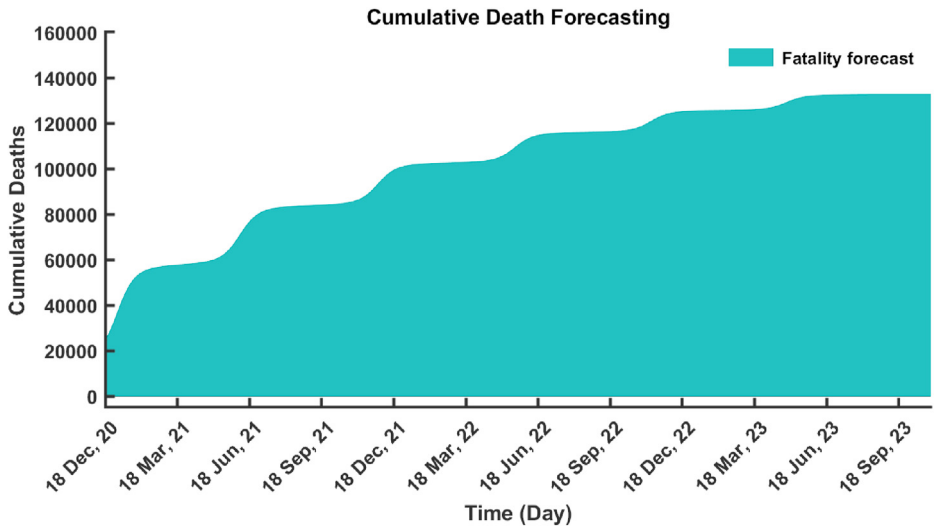


Fig. 6. Model forecasting: Cumulative death cases with 'Pfizer' vaccine.

SARS-CoV-2 virus is the major reason for these infection waves. Moreover, at the mid of June 2023, the breakdown is noticeable. It happens as the model predicts that the mutation rate of the SARS-CoV-2 virus will be meager. Until that date, most of the population will gain vaccine or hard immunity, so susceptible populations rush to the recovered compartment via the susceptibly infectious compartment.

As mentioned above, we have considered the 30-day average vaccination number, and that causes a step function and hence a piece-wise defined dynamics in the vaccinated compartment in Fig. 7c and d. These two figures also suggest that the authority may extenuate the vaccination program when the pandemic is under control. However, the vaccinated population must still be given the boost dose of the vaccine to remain in the vaccinated compartment. Another very trivial observation from Fig. 7d is that the less efficacy rate of the vaccine, the longer the vaccination program is required as per the model outcome. This gives us the sense that the vast control strategy depends on the rate of transition to the recovered compartment after infection and the effectiveness of the vaccine that is being applied.

SARS-CoV-2 is changing its RNA structure very rapidly, and new variants are hitting harder to the civilization. So, there are going to happen some more infection waves (Fig. 7e and f) in the next couple of years till the beginning of 2024. Another reason for these waves is not maintaining and practicing health and daily lifestyle etiquette mentioned by the World Health Organization like using a good face-mask properly (even if vaccinated), maintaining social distancing, avoiding crowds, washing hands, or using hand sanitizers frequently, and many more. Each wave of the unconfirmed infectious compartment results in a wave in the confirmed infected compartment with a delay of one to two weeks (compare Fig. 7e-h). In the short time limit Fig. 7h, we see the infection eradicates in the shortest time (first week of September 2023) in the case of the presence of a 100% effective vaccine, and then for Pfizer simulation, and then for Moderna, AstraZeneca, J&J vaccine, and without vaccine scenario almost at the same time. Every wave is much smaller than the previous wave peak for all vaccine scenarios, and the compartment vanishes gradually, which means the end of the SARS-CoV-2 pandemic. Only the Pfizer vaccine (97% effectiveness) controls the pandemic one wave earlier than the other vaccines; when a hypothetical presence of a 100% adequate vaccine controls before Pfizer. Surprisingly, other vaccines whose effectiveness rates are below 95% cannot make much difference from the 'no vaccine' scenario. The same cases are shown for the recovered class in Fig. (7i, and 7j).

The figures of the recovered class (Fig. 7i and j) indicates that at the end of this pandemic, most of the population of California will get recovered and so a considerable percentage of the locals will be able to develop an immunity against SARS-CoV-2 through a vaccine or getting recovered. However, a number of populations in this compartment also depends on the vaccine efficacy as less effective vaccine causes more confirmed cases, and so more recovered population, and vice-versa for the highly effective vaccine. Finally, most of the individuals of California end staying in the recovered class.

Fig. 8 depicts compare among all vaccine scenarios at the foretasted end of the pandemic situations for all compartments (Susceptible, Vaccinated, Exposed, Infected, and Recovered). The numerical study also takes into account that when the number of active confirmed cases decreases down to less than 100 in the whole state (California) and remains less than 100 active cases for more than 20 weeks, then the pandemic will be considered as under control and going to be eradicated forever. As a result, after that moment-the vaccination program will be no longer necessary and so will be shut down step-by-step amidst the next 5–6 weeks.

The model has also been simulated for the SARS-CoV-2 data for the United States of America in Appendix A. The model is well fitted for the real data of the U.S. (Fig. 9). There will be seven to eight big waves of infection from December 2020 to

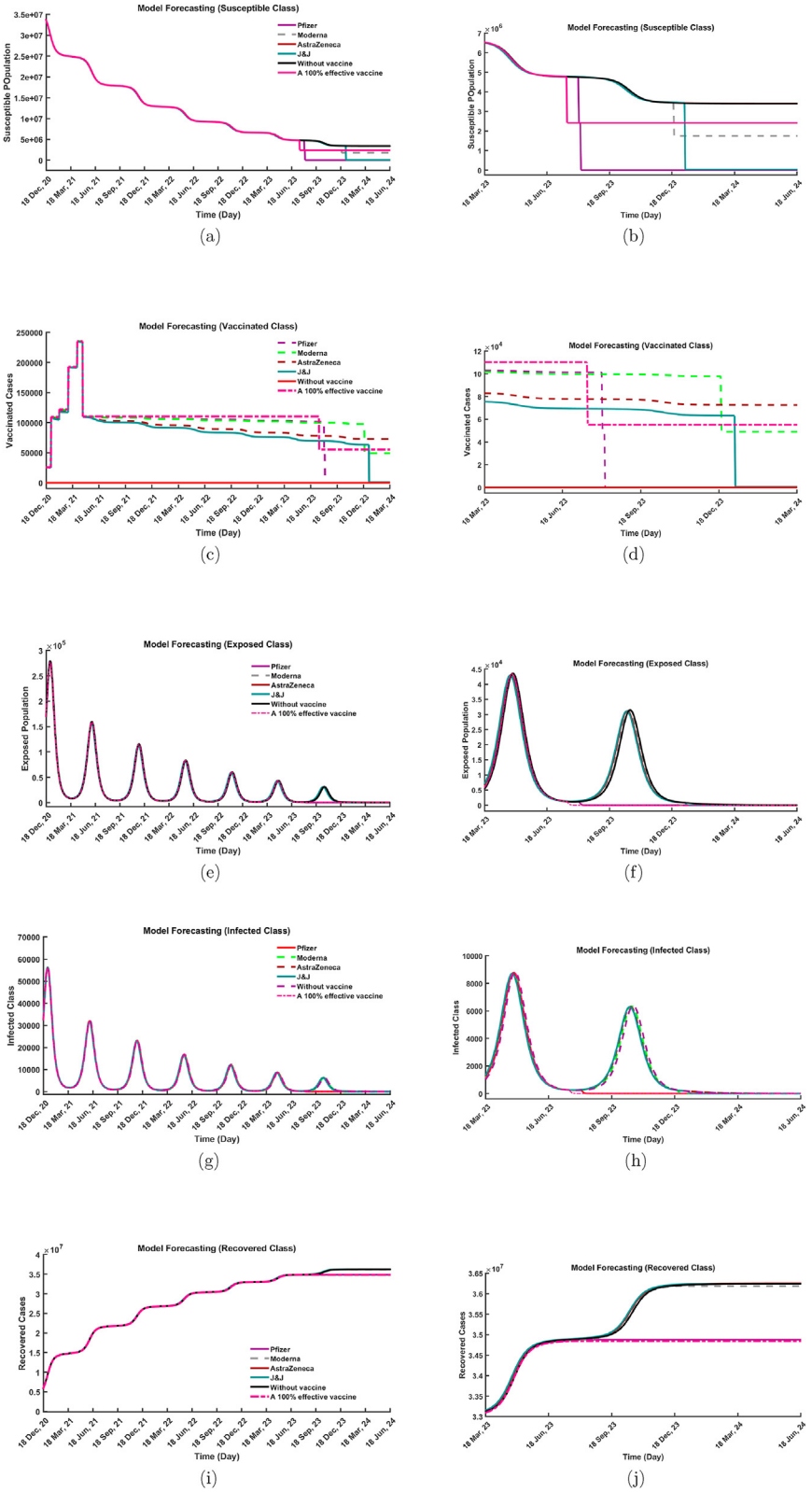
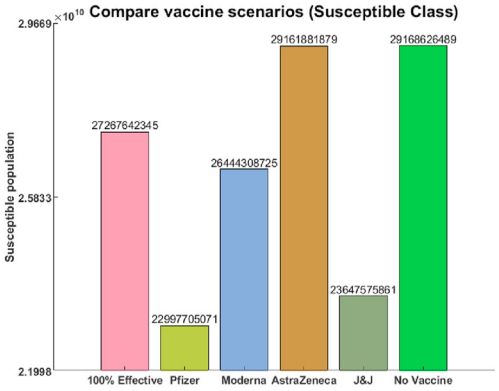
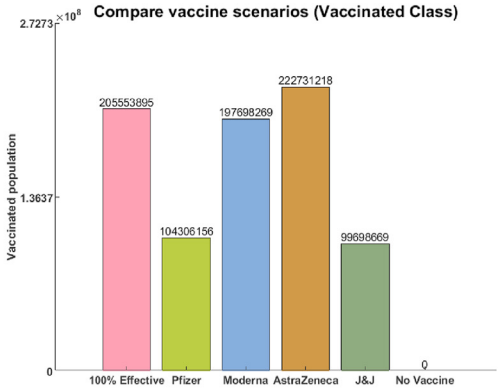


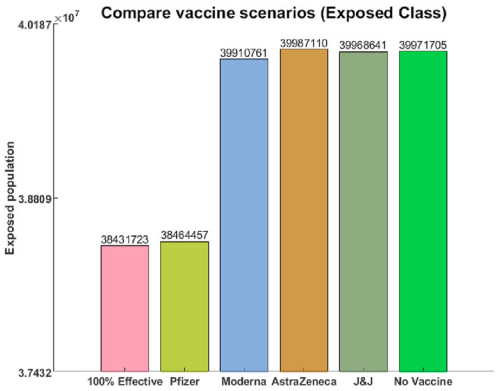
Fig. 7. Model forecasting against all available vaccines. (left column shows the dynamics for long time period, where the right column shows the ending short time dynamics of the corresponding left figure.)



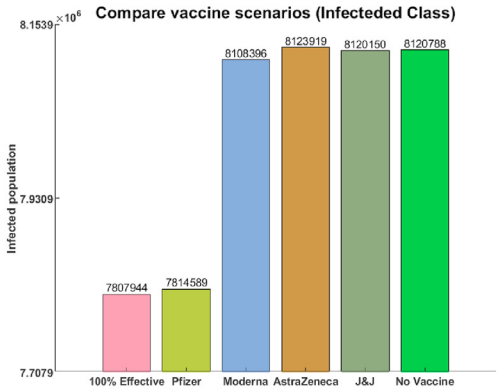
(a)



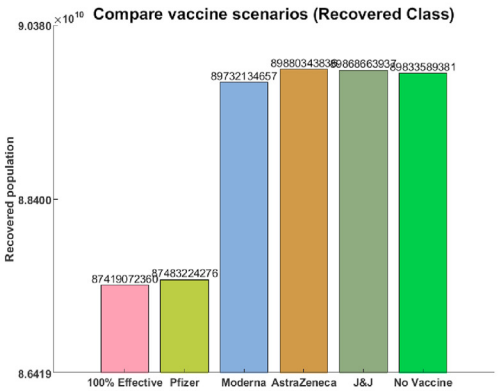
(b)



(c)



(d)



(e)

Fig. 8. Effects of different vaccine situations in California, U.S.

December 2023 and five to six minor waves afterward, and the pandemic is gone entirely by the end of 2026 (Figs. 11 and 12). According to this study, 73, 766, 040 infection cases and 1,442,772 death cases may get reported at the end of 2026 in the U.S.

The compartmental dynamics for different vaccine scenarios has been shown in Fig. 13. The sub-figures 13a,13c,13e,13g, and 13i depicts the gradual change of the corresponding compartment up to the stable situation from the December 2020, but since it's being difficult to visualize the vaccine related variation the sub-figures 13b,13d,13f,13h, and 13j displays the same results from June 2024 to June 2028 where the crucial changes are happening due to the different vaccine efficacy rates for the Susceptible-Vaccinated-Exposed-Infected-Recovered compartments, respectively.

4. Findings & decisions

Like many other epidemics, the vaccine may pull down the death tolls by SARS-CoV-2 virus. There is no way to erase this infectious disease overnight; rather, we have to be used to this virus and live our everyday life with all prescribed precautions, not only as long as we are in this pandemic, but for the rest of our lives to maintain a hygienic and healthy life, and to make sure another pandemic is never coming. Besides all these lifestyles, everyone must be involved in the vaccination program as soon as possible.

Our study finds that a 100% clinically feasible vaccine for all variants of this virus is necessary to reduce the disease-induced loss. The vaccines which are less than 90% adequate should not be recommended, as they will make no good than the cost of both time and resources.

Since the vaccine efficacy rates for all these considered vaccines are not strict per virus variants, physical nature/condition of people from different localities and ethnicity, vaccine allocation is not perfect, and many more (Islam et al., 2021; Pfizer, 2021; AstraZeneca, 2021; STAT, 2021), the efficacy rates we have considered throughout this study resembles any other kind of vaccines which are of the same efficacy rates of the mentioned vaccines with a maximum deviation of 2–3%.

Another interesting observation is that the model suggests California's pandemic ending time is earlier than the U.S. There are many reasons for these predictions. One of the critical factors is the vaccination rate. On March 10, 2021, the vaccination rate in the U.S. for the first dose is 64.9%, and 56.5% of people are fully vaccinated, whereas, in California, the first dose is given to 71.9% of people and 59.1% of people are fully vaccinated. Many states, e.g., Wyoming, Idaho, Alabama, and Mississippi, etc., where vaccination rates are much lower than the national average. The median household income in California is $80,440, whereas on the national average $67,521. Most tech companies are located in California, and they are allowing their employees to work remotely from the beginning of the pandemic. Therefore, many people there can maintain the social distance, whereas advantages like working from home in many other states are minimal. For example, even many universities in Texas did not allow their employee to work remotely, and low-income families have no better alternative instead joining their work in person. Moreover, the percentage of people who are not interested in getting vaccinated outside of California is also higher. There are many other reasoning which also can be enlisted here.

5. Concluding remarks

There are no other effective ways to fight against any pandemic diseases except precaution and vaccination. Although specific groups of people get prioritized initially, mass vaccination is needed to control the spread of SARS-Cov-2. The world is still suffering due to the SARS-CoV-2 pandemic that started more than one and a half years ago. Several vaccines with different efficacy rates have been used globally; infection is still on the rise in many countries. It is hard to predict when a pandemic will be eradicated. In this mathematical modeling study, we used California, and U.S. data, and forecast the possible upcoming SARS-CoV-2 situations for six different vaccine scenarios. Since the considered vaccines have different efficacy rates, we have also demonstrated the impact of efficacy rates on controlling this pandemic.

Author contributions

Conceptualization, M.K. and M.S.M.; methodology, M.S.M., M.M.I.Y.A and M.A.H; software, M.S.M., M.M.I.Y.A and M.K.; validation, M.A.H, M.M.R., and M.M.; formal analysis, M.S.M., M.K. and M.A.H; investigation, M.S.I; resources, M.M.M. and M.M.R; data curation, M.S.M., M.M.I.Y.A and M.A.H; original draft preparation, M.S.M., M.K., M.M.I.Y.A and M.A.H; review and editing, M.M.M., M.M.R., M.M. and M.S.I; supervision, M.K. All authors have read and agreed to the published version of the manuscript.

Disclaimer/data availability statement

All data are provisional and subject to change. Probable cases are not included in the total case numbers. No consent is required to publish this paper.

Declaration of competing interest

The authors declare no conflict of interest exists.

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Appendix A

6 Proposed model: Mathematical overview

We propose the following non-demographic deterministic modified SEIR type epidemic model with vaccination

$$\dot{S} = -(\beta_1 I_S + \beta_2 I)S - \kappa \tag{6.1}$$

$$\dot{S}_V = \kappa - \omega(\beta_1 I_S + \beta_2 I)S_V \tag{6.2}$$

$$\dot{I}_S = (\beta_1 I_S + \beta_2 I)(S + \omega S_V) - (\sigma + \gamma_1)I_S \tag{6.3}$$

$$\dot{I} = \sigma I_S - (\gamma_2 + \delta)I \tag{6.4}$$

$$\dot{R} = \gamma_1 I_S + \gamma_2 \tag{6.5}$$

with initial conditions

$$S(0) = S_0,\ \ S_V(0) = 0,\ \ I_S(0) = I_{S0},\ \ I(0) = I_0 \ \text{ and } \ R(0) = R_0, \tag{6.6}$$

and

$$N(t) \equiv S(t) + S_V(t) + I_S(t) + I(t) + R(t), \tag{6.7}$$

Table 3
Model parameters and their descriptions

Notation	Interpretations	Unit	Base value
$S(t)$	Susceptible class at time t	–	–
$S_V(t)$	Vaccinated class at time t	–	–
$I_S(t)$	Unconfirmed infectious class at time t	–	–
$I(t)$	Infected (confirmed) class at time t	–	–
$R(t)$	Recovered class at time t	–	–
ω	Vaccine inefficacy	per head	0.3
κ	Daily vaccination	per day	Uncertain
σ	Transition rate for I_S	phpd*	$[\frac{1}{4.5}, \frac{1}{12}]$
β_1	Transmission rate for S	phpd*	Uncertain
β_2	Transmission rate for S_V	phpd*	Uncertain
γ_1	Recovery rate from I_S	phpd*	Uncertain
γ_2	Recovery rate from I	phpd*	0.568 7**
δ	Disease induced death rate	phpd*	0.021 6**

*per head per day.
**worldwide.

7 Case: The United States of America

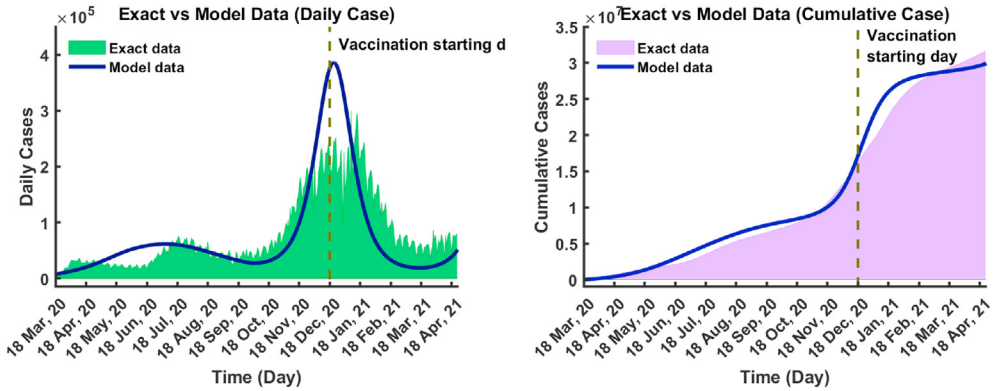

Fig. 9. Model data fitting to U.S. SARS-CoV-2 data.

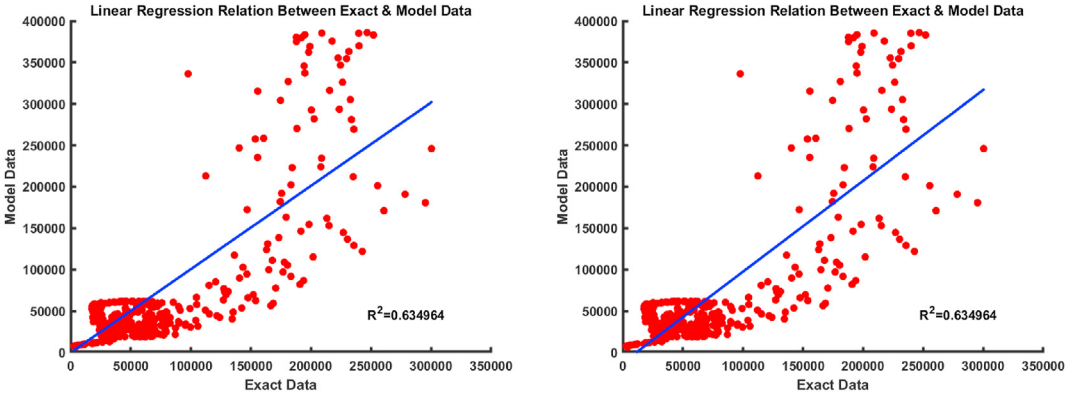

Fig. 10. Two types of regression analysis for exact and proposed model data for U.S., where (left) linear regression, and (right) linear regression (modified) based on MATLAB software.

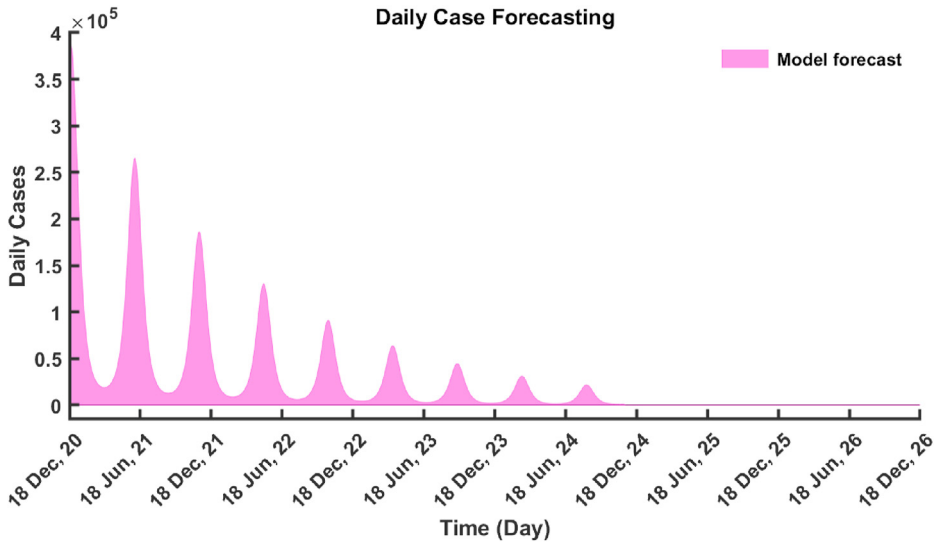

Fig. 11. Model forecasting to U.S. SARS-CoV-2 situation.

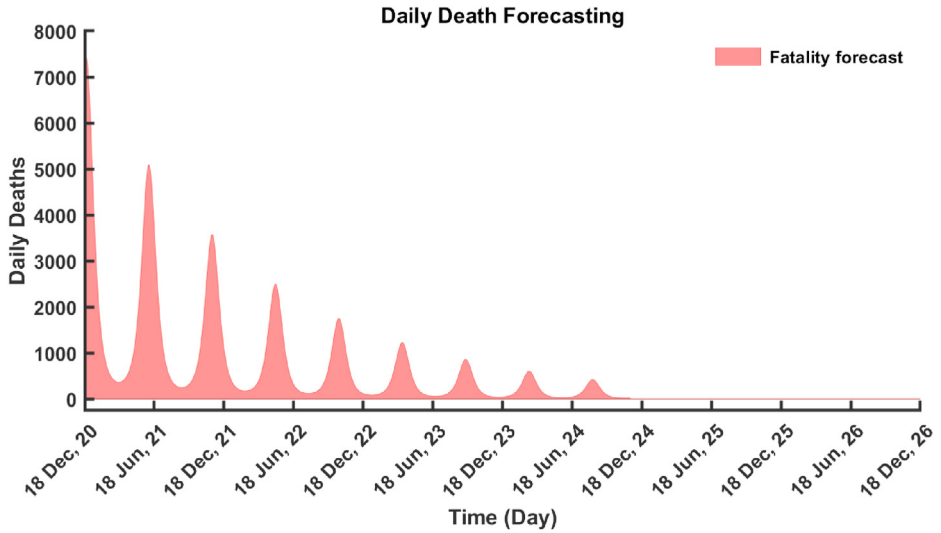

Fig. 12. Model forecasting to U.S. SARS-CoV-2 fatalities.

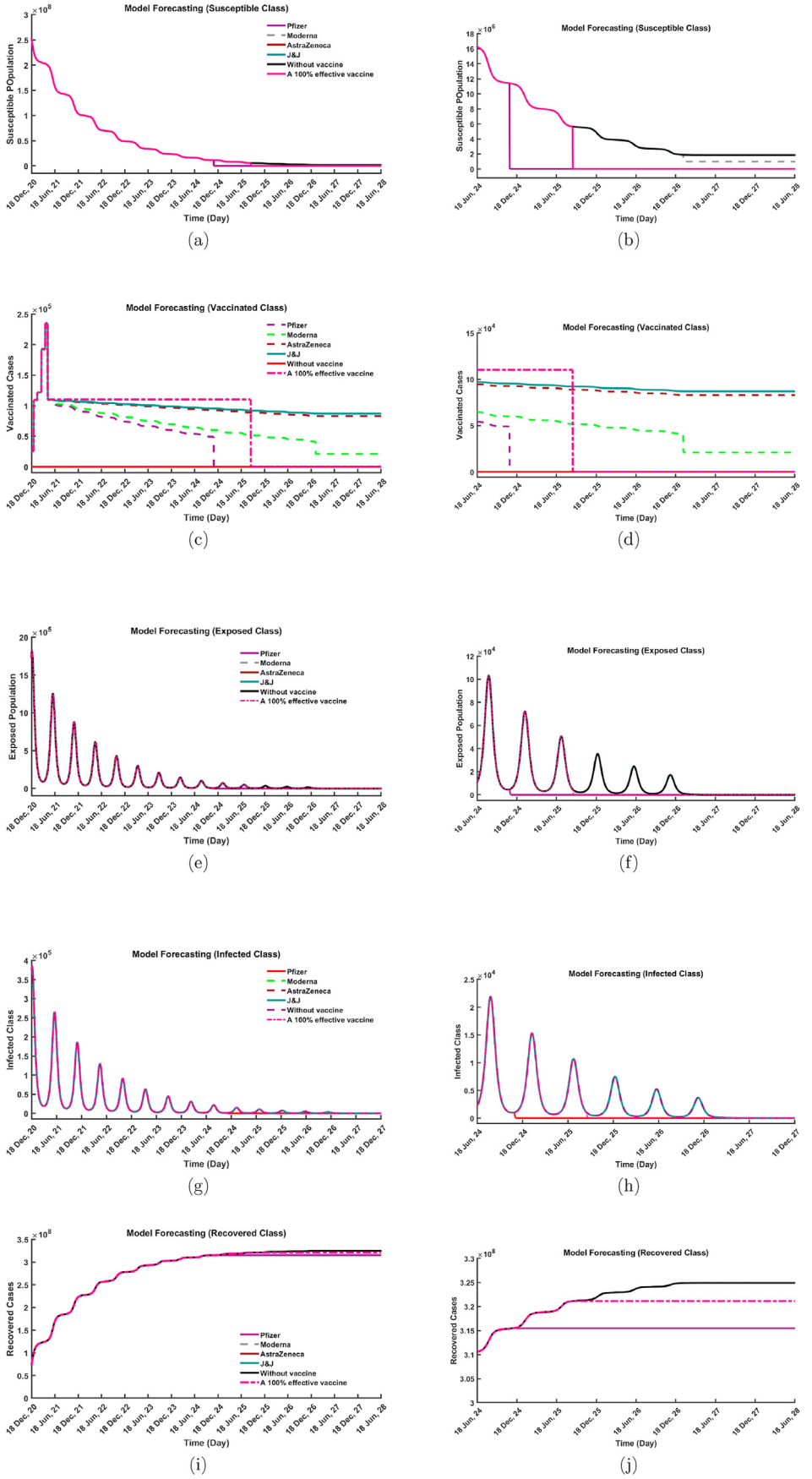

Fig. 13. Model forecasting against all available vaccines for the U.S. pandemic situation.

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