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RESEARCH ARTICLE

Will the large-scale vaccination succeed in containing the COVID-19 pandemic and how soon?

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***Background*: The availability of vaccines provides a promising solution to contain the COVID-19 pandemic. However, it remains unclear whether the large-scale vaccination can succeed in containing the COVID-19 pandemic and how soon. We developed an epidemiological model named SUVQC (Suceptible-Unquarantined-Vaccined-Quarantined-Confirmed) to quantitatively analyze and predict the epidemic dynamics of COVID-19 under vaccination.**

***Methods*: In addition to the impact of non-pharmaceutical interventions (NPIs), our model explicitly parameterizes key factors related to vaccination, including the duration of immunity, vaccine efficacy, and daily vaccination rate etc. The model was applied to the daily reported numbers of confirmed cases of Israel and the USA to explore and predict trends under vaccination based on their current epidemic statuses and intervention measures. We further provided a formula for designing a practical vaccination strategy, which simultaneously considers the effects of the basic reproductive number of COVID-19, intensity of NPIs, duration of immunological memory after vaccination, vaccine efficacy and daily vaccination rate.**

***Results*: In Israel, 53.83% of the population is fully vaccinated, and under the current NPI intensity and vaccination scheme, the pandemic is predicted to end between May 14, 2021, and May 16, 2021, assuming immunity persists for 180 days to 365 days. If NPIs are not implemented after March 24, 2021, the pandemic will end later, between July 4, 2021, and August 26, 2021. For the USA, if we assume the current vaccination rate (0.268% per day) and intensity of NPIs, the pandemic will end between January 20, 2022, and October 19, 2024, assuming immunity persists for 180 days to 365 days. However, assuming immunity persists for 180 days and no NPIs are implemented, the pandemic will not end and instead reach an equilibrium state, with a proportion of the population remaining actively infected.**

***Conclusions*: Overall, the daily vaccination rate should be decided according to vaccine efficacy and immunity duration to achieve herd immunity. In some situations, vaccination alone cannot stop the pandemic, and NPIs are necessary to supplement vaccination and accelerate the end of the pandemic. Considering that vaccine efficacy and duration of immunity may be reduced for new mutant strains, it is necessary to remain cautiously optimistic about the prospect of ending the pandemic under vaccination.**

Keywords: COVID-19; vaccination; pandemic; epidemic dynamics; epidemiological model

Author summary: The availability of vaccines provides a promising solution to contain the COVID-19 pandemic. However, it remains unclear whether the large-scale vaccination can succeed in containing the COVID-19 pandemic and how soon. Here, we developed an epidemiological model to quantitatively analyze and predict the epidemic dynamics of COVID-19 under vaccination. Overall, the daily vaccination rate should be decided according to vaccine efficacy and immunity duration to achieve herd immunity. In some situations, vaccination alone cannot stop the pandemic, and NPIs are necessary to supplement vaccination and accelerate the end of the pandemic.

INTRODUCTION

Coronavirus disease 2019 (COVID-19) has rapidly spread to more than 200 countries and territories. As of March 24, 2021, COVID-19 had resulted in more than 131 million infections, causing approximately 2.85 million deaths. Given its high infectivity and limited clinically effective medicines for COVID-19, a variety of nonpharmaceutical interventions (NPIs), such as movement restrictions, gathering bans, and social distancing, have been implemented worldwide to reduce viral transmission and the severity of outbreaks. The effectiveness of NPIs in mitigating viral spread has been reported in previous studies [1–3].

Vaccines are crucial in containing the pandemic. Currently, over 200 severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine candidates with different mechanisms are under accelerated development, including inactivated virus vaccines, live attenuated vaccines, recombinant protein vaccines, replication-incompetent vector vaccines, replication-competent vector vaccines, inactivated virus vector vaccines, DNA vaccines and RNA vaccines [4]. Phase III human clinical trials and efficacy testing have been completed for several candidates [5]. The reported efficacies of the vaccines are 95% for Pfizer/BioNTech (RNA vaccine) [6]; 91.6% for Gamaleya (recombinant protein vaccine) [7]; 94.1% for Moderna (RNA vaccine) [8]; 70.4% for AstraZeneca (replication-incompetent vector vaccine) [9]; 79.34% for Sinopharm (inactivated virus vaccine) [10]; and 50.65% – 91% for Sinovac (inactivated virus vaccine) [11]. The total capacity in 2021 is estimated to be approximately 7.4 billion doses [12], covering less than half of the global population (for most COVID-19 vaccines, 2 doses are required for maximum efficacy). On December 14, 2020, the United Kingdom (UK) became the first region to initiate a vaccination scheme, and as of March 24, 2021, more than 80 countries had initiated vaccinations. Among these countries, Israel has the highest vaccination rate, at 53.83%, and the USA has administered the largest number of vaccination doses, at 130.47 million.

The availability of vaccines is a remarkable step towards ending the COVID-19 pandemic. However, the prospect of pandemic control is still unclear. It is important to quantitatively explore and predict epidemic trends under current vaccination scenarios considering vaccine efficacy and the strengths of NPIs. It is especially important to explore and evaluate the optimal scheme of vaccination. In this study, we developed an epidemic model to explore pandemic dynamics under vaccination and NPI scenarios. We applied the model to analyze and predict pandemic trends in Israel and the USA given their daily vaccination rates and other parameters; we chose these countries because Israel has the highest rate of vaccination and the USA has a much larger population size and has been severely affected by the COVID-19 pandemic. We also provided a formula to help determine the required speed of vaccination considering different vaccine efficacies, immunity durations and NPIs. These results provide insights to guide efficient COVID-19 epidemic control under vaccination scenarios.

RESULTS

Model

Based on our previous work, which outlined the Susceptible-Unquarantined-Quarantined-Confirmed (SUQC) model [33], we developed a new model, named the Susceptible-Unquarantined-Vaccinated-Quarantined-Confirmed (SUVQC) model, to describe the epidemic dynamics of COVID-19 under vaccination. The SUVQC model includes nine variables corresponding to different states of individuals in the population (Fig. 1):

$S(t)$, the number of susceptible individuals in the population at time t. For COVID-19, all individuals are assumed to be susceptible to the disease, except for those who gain immunity through vaccination or infection. Note that immunity against COVID-19 is not permanent, and an infected or vaccinated person becomes susceptible again when the period of protective immunity ends.

$V(t)$, the number of fully vaccinated individuals at time t that are still actively protected by immunity gained through vaccination.

$U(t)$, the number of infected individuals who are infectious and unquarantined. $U(t)$ includes two groups: $U_S(t)$, comprising unquarantined infected individuals from the susceptible population, and $U_V(t)$, comprising unquarantined infected individuals from the vaccinated population. $U(t) = U_S(t) + U_V(t)$. $U_V(t) > 0$ is because COVID-19 vaccines cannot provide 100% protection.

$Q(t)$, the number of quarantined, infected individuals. Quarantined, infected individuals have no contact with susceptible and vaccinated individuals and thus do not contribute to infection in the population. Note that for simplicity, this group also includes infected individuals who have never been quarantined but enter the $Q(t)$ state due to recovery and loss of infectivity.

$R_Q(t)$, the number of individuals among the quarantined population who were originally infected but not confirmed and are currently recovered, with active immunity to the virus.

$A(t)$, the number of confirmed infected patients who are still in an active infection state and have not recovered or died.

$R_C(t)$, the number of recovered individuals with confirmed infection and current immunity to the virus.

$D_C(t)$, the number of dead individuals among the confirmed infected patients.

In addition to the above nine variables, we also define $C(t)$, the cumulative confirmed infected cases, as $\frac{\mathrm{d}C(t)}{\mathrm{d}t} = [\gamma_2 + (1-\gamma_2)\sigma]Q(t)$.

The model includes 12 parameters:

t_s, the average duration of immunological memory in individuals who recover from infection.

t_v, the average duration of immunological memory in vaccinated individuals.

α, the infection rate, which is the average number of newly infected patients in the S population that is caused by an unquarantined infected individual in the U_S group per day.

$\eta(t)$, the daily number of fully vaccinated individuals.

λ_1, the reduced probability of a vaccinated, susceptible individual being infected. Vaccine efficacy is defined as $1-\lambda_1$.

λ_2, the reduced infectivity in vaccinated infected individuals compared to U_S individuals, that is, the average infection rate of U_V is $\lambda_2\alpha$.

γ_1, the quarantine rate among unquarantined infected individuals.

γ_2, the confirmation rate of Q, which is the probability that infection in quarantined infected individuals will be confirmed by a conventional method.

σ, the subsequent confirmation rate of infected individuals who are not confirmed by conventional methods but confirmed with additional testing.

k_1, the ratio of unconfirmed infected cases to confirmed infected cases.

k_2, the ratio of dead to recovered individuals among all confirmed patients.

γ_3, the recovery rate of confirmed actively infected individuals.

The transitions among different states during an epidemic are summarized in Eq. (1), and demonstrated in Fig. 1. Susceptible individuals (S) become vaccinated individuals (V) after vaccination at a constant rate. S can also transition to a U_S status due to infection. Similarly, V still have a chance of becoming infected and thus transitioning to a U_V status. The infected U_S and U_V individuals transition to the Q state due to quarantine measures and subsequently lose infectivity. Among individuals in state Q, some with confirmed infection recover or die. The remaining individuals in the Q state do not have confirmed COVID-19 according to tests or other approaches and transition to the R_Q state directly. Note that the $Q \to R_Q$ flow may be due to a lack of test kits, or infection with no symptoms (asymptomatic infection). It is reasonable to assume that all unconfirmed individuals have mild symptoms and thus do not flow from $Q \to D_Q$ directly. Individuals in the V, R_C and R_Q states finally become susceptible to the disease again after a period of time, since immunity against COVID-19 is likely not permanent. Since we are unable to differentiate unvaccinated individuals in R_Q and S at time t, $\eta(t)$ includes two groups: $k_3\eta(t)$, representing individuals who transition from S to V, and $(1-k_3)\eta(t)$, representing individuals who transition from R_Q to V, where $k_3 = \frac{S(t)}{S(t) + R_Q(t)S(t)/(S(t)+\lambda_1 V(t))}$.

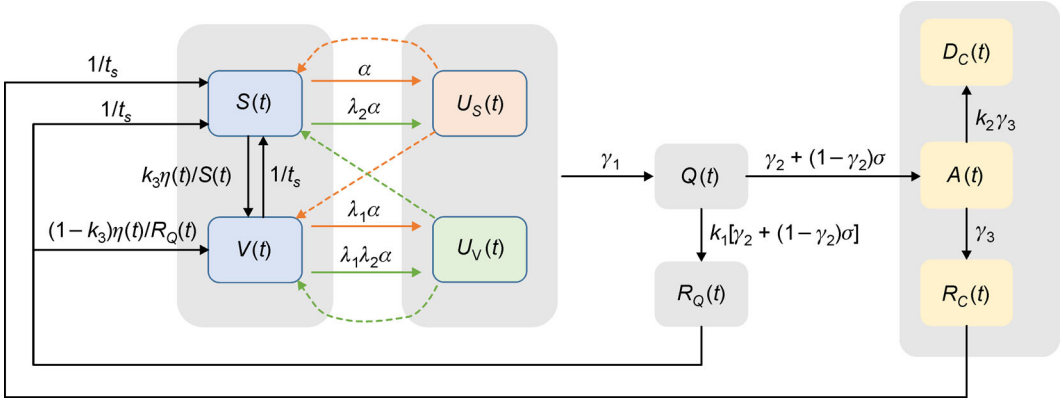

Figure 1. A schematic illustration of the model.

$$
\begin{cases}
\dfrac{\mathrm{d}S(t)}{\mathrm{d}t} = -\alpha\dfrac{U_S(t)S(t)}{N(t)} - \lambda_2\alpha\dfrac{U_V(t)S(t)}{N(t)} - k_3\eta(t) + \dfrac{1}{t_v}V(t) + \dfrac{1}{t_s}(R_C(t) + R_Q(t)) \\
\dfrac{\mathrm{d}V(t)}{\mathrm{d}t} = -\lambda_1\alpha\dfrac{U_S(t)V(t)}{N(t)} - \lambda_1\lambda_2\alpha\dfrac{U_V(t)V(t)}{N(t)} + \eta(t) - \dfrac{1}{t_v}V(t) \\
\dfrac{\mathrm{d}U_S(t)}{\mathrm{d}t} = \alpha\dfrac{U_S(t)S(t)}{N(t)} + \lambda_2\alpha\dfrac{U_V(t)S(t)}{N(t)} - \gamma_1 U_S(t) \\
\dfrac{\mathrm{d}U_V(t)}{\mathrm{d}t} = \lambda_1\alpha\dfrac{U_S(t)V(t)}{N(t)} + \lambda_1\lambda_2\alpha\dfrac{U_V(t)V(t)}{N(t)} - \gamma_1 U_V(t) \\
\dfrac{\mathrm{d}Q(t)}{\mathrm{d}t} = \gamma_1(U_S(t) + U_V(t)) - [\gamma_2 + (1-\gamma_2)\sigma]Q(t) - k_1[\gamma_2 + (1-\gamma_2)\sigma]Q(t) \\
\dfrac{\mathrm{d}R_Q(t)}{\mathrm{d}t} = k_1[\gamma_2 + (1-\gamma_2)\sigma]Q(t) - \dfrac{1}{t_s}R_Q(t) - (1-k_3)\eta(t) \\
\dfrac{\mathrm{d}A(t)}{\mathrm{d}t} = [\gamma_2 + (1-\gamma_2)\sigma]Q(t) - \gamma_3 A(t) - k_2\gamma_3 A(t) \\
\dfrac{\mathrm{d}R_C(t)}{\mathrm{d}t} = \gamma_3 A(t) - \dfrac{1}{t_s}R_C(t) \\
\dfrac{\mathrm{d}D_C(t)}{\mathrm{d}t} = k_2\gamma_3 A(t) \\
\dfrac{\mathrm{d}C(t)}{\mathrm{d}t} = [\gamma_2 + (1-\gamma_2)\sigma]Q(t)
\end{cases}
\tag{1}
$$

Parameter inference

The observed data used for model fitting were daily reported infection cases. The SUVQC model includes multiple parameters, most of which utilize information from other sources, including known facts and previous studies:

• t_s and t_v: A recent study demonstrated that immune memory caused by SARS-CoV-2 infection can last up to 8 months after infection [13]. Several other studies have also suggested an immunization period of at least 6–9 months [14–16]. At present, there is no clear conclusion on how long immune protection induced by the vaccine can last. We set it to $t_s = t_v = 240$ days. Since the duration of immunity is critical in epidemic dynamic modeling, we also analyzed three different durations of immunity, including 90 days, 180 days and 365 days.

• $\alpha = 0.2967$: This value was obtained by fitting an exponential curve of the confirmed case number in Wuhan in the very early phase of the pandemic [3].

• λ_1 and λ_2: The main vaccines administered to date in Israel and the USA are the Pfizer/BioNTech and Moderna vaccines, with efficacies of 95% and 94.1%, respectively [6,8]. Thus, $\lambda_1 = 0.95$. No epidemic data are available for estimating λ_2 yet. It has been reported that vaccination can reduce the incidence of severe illness, which may imply lower infectivity in individuals in the U_v state than in the U_s state. Nevertheless, asymptomatic patients have a viral load similar to that in symptomatic patients [17]. Thus, we assume that individuals in the U_v state have the same infectivity as those in the U_s state; therefore, $\lambda_2 = 1$.

• γ_3: The recovery rate of patients with active confirmed infection is $\gamma_3 = 1/14$, since the mean hospital admission days for survivors and nonsurvivors are 11.3 days and 14.5 days, respectively, according to former studies [18].

The values of some other parameters and variables, *e.g.*, k_1, k_2, η, $V(0)$, and $R_C(0)$, are population specific and will be elaborated in the following sections.

$U_S(0)$, which is the initial number of unquarantined, infected individuals from the susceptible population, $Q(0)$, which is the initial number of quarantined infected individuals, and parameters γ_1 and $\beta = \gamma_2 + (1-\gamma_2)\sigma$ are inferred by fitting the numbers of daily reported cumulative confirmed case number $C(t)$ with the SUVQC model. The loss function is defined as:

$$
err(\gamma_1, \beta, U_0^S, Q_0) = ||\mathbf{C} - \hat{\mathbf{C}}||_2 \tag{2}
$$

where $\hat{\mathbf{C}} = f(\gamma_1, \beta, U_0^S, Q_0)$ is the expected cumulative confirmed case number provided by the model (Eq.(1)), which was obtained with the fourth-order Runge-Kutta method. The values of the four parameters or variables were inferred by optimizing the loss function with the interior-point method (implemented with fmincon in MATLAB).

The epidemic trend in Israel under vaccination

The population size of Israel is approximately 9.05 million. The COVID-19 pandemic in Israel started on February 21, 2020. The country has undergone three waves of outbreaks. We inferred the tem-poral dynamics of R_t as a function of time by applying the SUQC model to daily reported confirmed cases using the sliding window scheme (with a window size of 3 weeks and a step size of one week; blue curve, Supplementary Fig. S1). This demonstrates the development and fluctua-tion of the pandemic during the process, which is consistent with public reports. The Israeli government issued a series of control measures during this period, including social distancing guidelines, home isolation measures, travel bans, restrictions on movement, etc. The Government Stringency Index provided by OxCGRT [19,20] couples well with the $R(t)$ trend, indicating the efficacy of multiple intervention measures (red curve, Supplementary Fig. S1). As of March 24, 2021, 830,028 dynamic individuals had been reported to be infected by COVID-19. The Israeli government procured COVID-19 vaccines from multiple sources: 8 million doses from Pfizer; 10 million doses from AstraZeneca; and 6 million doses from Moderna. Vaccination started on December 19, 2020 and is progressing steadily and rapidly. As of March 24, 2021, approximately 53.83% of the Israeli population had been fully vaccinated. Together with other measures, vaccination demonstrated good efficacy, and newly confirmed cases have shown a continual downward trend since January 20, 2021. We analyzed the epidemic dynamics of COVID-19 in Israel under vaccination and predicted its future trend with the SUVQC model under parameter settings inferred from the reported data up to March 24, 2021. The prediction of future trends starts on March 24, 2021.

Some population-specific parameters and variables were inferred beforehand considering prior knowledge:

1. $k_1 = 0.31/(1-0.31) = 0.45$, the proportion of infected individuals remaining asymptomatic throughout infection was estimated at 31% according to former studies [21].

2. $\eta = 54{,}753$ (0.605% of population), the number of daily vaccinated individuals was estimated as the average number of vaccinations over 30 days (February 23, 2021 to March 24, 2021) according to data from the ourworldindata website (https://ourworldindata.org/). Note that $V(t)$ is defined as the number of fully vaccinated individuals, and η is the daily number of fully vaccinated individuals. This is a simplification of reality since individuals not fully vaccinated are also immune to COVID-19, but a single vaccine dose has a lower efficacy.

3. $V_0 = 3{,}158{,}669$, the number of initial fully vaccinated individuals on February 23, 2021, was obtained from the ourworldindata website (https://ourworldindata.org/).

4. $k_2 = 0.74\%$, the ratio of dead and recovered individuals among confirmed patients was calculated considering $C(0) = 759{,}572$, the number of initial confirmed cases, $D_C(0) = 5{,}634$, the initial confirmed deaths, and $A(0) = 41{,}610$, which were obtained from the Johns Hopkins University Coronavirus Center [22].

5. $R_C(0) = 756{,}439$, the number of initially confirmed recovered individuals who still retain immunological memory to the virus was estimated by the recurrence formula $R_C(t) = (C(t) - R_C(t-1))/t_s$. $R_Q(0)$ was calculated as $R_Q(0) = k_1 R_C(0)$.

Other parameters, including $t_s = 240$ days, $t_v = 240$ days, $\alpha = 0.2967$, $\lambda_1 = 0.05$, $\lambda_2 = 1$, $\gamma_3 = 1/14$, are universal among different countries and were chosen according to the section "Parameter Inference".

We set $U_V(0)$ to 0 since $V(t) \rightarrow U_V(t)$ is small compared to $S(t) \rightarrow U_S(t)$ at the early stage of vaccination. The initial number of unquarantined, infected individuals from the susceptible population $U_S(0)$, the initial number of quarantined infected individuals $Q(0)$, and parameters γ_1 and $\beta = \gamma_2 + (1-\gamma_2)\sigma$ were inferred by fitting the daily reported cumulative confirmed case number $C(t)$ with the SUVQC model. After obtaining all the values of the parameters and initial variables, the initial values of susceptible individuals in population $S(0)$ were calculated as $S(0) = N - V(0) - U_S(0) - U_V(0) - Q(0) - R_Q(0) - A(0) - R_C(0) - D_C(0)$. We explored the trends for two scenarios: one with NPIs, for which we assume the current control measures will continue with the same intensity, and another without NPIs, for which we assume that no more NPIs are imposed under vaccination.

Figure 2 presents the inference and prediction of the epidemic dynamics in Israel assuming an eight-month duration of immunological memory. The SUVQC model was fitted to the daily numbers of confirmed cases from February 23 to March 24, 2021, and the unknown parameters and variables were inferred to be $U_S(0) = 38{,}835$, $Q(0) = 26{,}736$, $\gamma_1 = 0.2714$ and $\beta = 0.0983$. The model fits well with the observed data (Fig. 2A, yellow dots: data for model fitting; green dots: data for testing, from March 25, 2021 to May 3, 2021, $R^2 = 0.9886$). If we assume the intensity of NPIs remains consistent between February 23, 2021 and March 24, 2021 (a corresponding mean Government Stringency Index of 56.82 according to OxCGRT; for comparison, the maximum Government Stringency Index of Israel was 94.44 in mid-April 2020 and 68.33 between March 1, 2020, and March 24, 2021), the epidemic in Israel is estimated to end around May 15, 2021 (with zero new confirmed cases as the criterion), with 836,059 cumulative confirmed infection cases and 6,495 confirmed deaths. The number of active cases ($A(t)$) is estimated to peak on

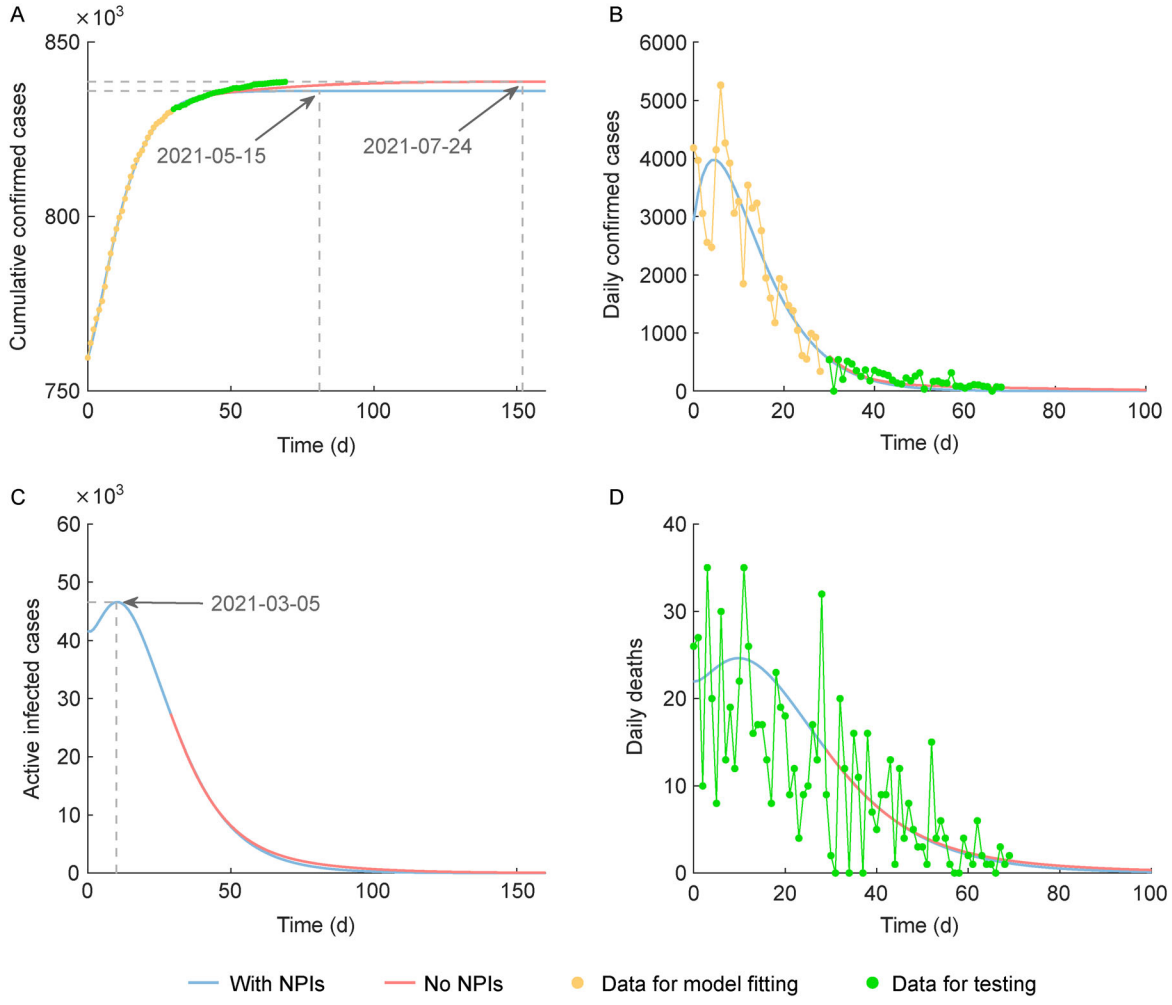

Figure 2. Inference and prediction of epidemic dynamics in Israel. Parameter setting: vaccine efficacy $1-\lambda_1 = 0.95$, daily vaccination rate $\eta/N = 0.605\%$ per day, duration of immunity $t_v = 8$ months. Data for model fitting is from 2021-2-23: (A) Cumulative confirmed cases. (B) Daily confirmed cases. (C) Active infected cases. (D) Daily deaths.

March 5, 2021, with a maximum value of $A(t) = 46{,}629$ (Fig. 2).

For the scenario assuming no more NPIs after March 24, 2021, the epidemic in Israel is estimated to end around July 24, 2021, with 838,632 cumulative confirmed infection cases and 6,520 confirmed deaths. The number of active cases is estimated to peak on March 24, 2021, with a value of $A(t) = 27{,}356$ (Fig. 2).

To assess the impact of the duration of immunity induced by vaccination, we also carried out the same analysis with other possible t_s values, *e.g.*, $t_s = t_v = 90$, 180, 365 days. The results are summarized in Table 1 (see the corresponding plots in Supplementary Figs. S2–S4). Assuming the intensity of NPIs between February 23, 2021 and March 24, 2021, remains stable, the epidemic in Israel will end between May 14, 2021 and May 19, 2021, depending on different durations of immunity. The number of cumulative confirmed infection cases is estimated to be between 835,944 and 836,576, with the number of deaths estimated at between 6,493 and 6,500. The epidemic in Israel is estimated to last for much longer if no NPIs are performed after March 24, 2021, ranging from July 4, 2021 to August 26, 2021, with the number of cumulative confirmed infected cases between 837,656 and 840,383 and the number of deaths between 6,513 and 6,533. However, the epidemic in Israel will never end if the duration of immunity is only 90 days and no NPIs are carried out. After several waves of fluctuation, the epidemic achieved an equilibrium state, with 68,742 active infected cases (Supplementary Fig. S2C and D, Table 1). The fluctuations are due to the initial proportions of vaccinated individuals and susceptible individuals. Overall, the epidemic trend in Israel under vaccination is optimistic if the duration of immunity is longer than 6 months.

Table 1 Prediction of the epidemic trend in Israel with different durations of immunity

Duration of immunity	90 days	180 days	240 days	365 days
With NPIs				
Ending time	2021-5-19	2021-5-16	2021-5-15	2021-5-14
Infected number	836,576	836,169	836,059	835,944
Death number	6,500	6,496	6,495	6,493
Maximum active number	46,658	46,636	46,629	46,623
Date of maximum active number	2021-3-5	2021-3-5	2021-3-5	2021-3-5
Equilibrium value of active number	0	0	0	0
Without NPI after Mar 24, 2021				
Ending time	-	2021-8-26	2021-7-24	2021-7-4
Infected number	-	840,383	838,632	837,656
Death number	-	6,533	6,520	6,513
Maximum active number	125,593	27,368	27,356	27,343
Date of maximum active number	2021-11-30	2021-3-24	2021-3-24	2021-3-24
Equilibrium value of active number	68,742	0	0	0

The epidemic trend in the USA under vaccination

The population of the USA is approximately 327 million. The COVID-19 pandemic in the USA started in late January 2020. The temporal dynamics of $R(t)$ in the USA were inferred by applying the SUQC model to the daily reported confirmed cases with a sliding window scheme (with a window size of 3 weeks and a step size of one week; blue curve, Supplementary Fig. S5). From the $R(t)$ curve, we similarly identified three waves of outbreaks: the early stage before early April, from June 6 to August 8, and from early October to late December. The Government Stringency Index provided by OxCGRT [19,20] aligns well with the $R(t)$ trend, which demonstrates that the fluctuation in the epidemic is highly correlated with public events and the implementation of controls by federal and state governments (red curve, Supplementary Fig. S5). As of March 24, 2021, 30,012,522 confirmed infection cases had been reported. The USA government has ordered 600 million doses of the Pfizer and Moderna vaccines, and before the end of July 2021, each company is expected to deliver 300 million doses in regular increments. Vaccination in the USA started on December 14, 2020. As of March 24, 2021, approximately 13.86% of the USA population had been fully vaccinated.

We inferred some parameters and variables before model fitting considering prior knowledge:

1. As of mid-November 2020, 14.3% of the USA population (approximately 47 million) was estimated to have been infected by SARS-CoV-2 [23], and the reported number of confirmed cases was approximately 11 million. Thus, $k_1 = (47-11)/11 = 3.3$ for the USA.

2. $\eta = 876{,}824$ (0.268% of population), and the number of daily vaccinated individuals was estimated as the average of daily number of vaccinations over 30 days (February 23, 2021 to March 24, 2021), obtained from the ourworldindata website (https://ourworldindata.org/).

3. $V_0 = 19{,}882{,}544$, the number of initial fully vaccinated individuals on February 23, 2021, was obtained from the ourworldindata website (https://ourworldindata.org/).

4. $k_2 = 1.82\%$, which represents the ratio of dead and recovered individuals among confirmed patients, $C(0) = 28{,}302{,}207$, which represents the initial number of confirmed cases, $D_C(0) = 503{,}937$, which represents the initial number of confirmed deaths, were obtained from the Johns Hopkins University Coronavirus Center [22]. $A(0) = 1{,}367{,}655$ was estimated with the recurrence formula $A(t) = A(t-1) + (C(t)-C(t-1)) - A(t-1)/\gamma_3$.

5. $R_C(0) = 28{,}185{,}069$, the number of initial confirmed recovered individuals who still remain immune to the virus was estimated with the recurrence formula $R_C(t) = (C(t)-R_C(t-1))/t_s$. $R_Q(0)$ was calculated with $R_Q(0) = k_1 R_C(0)$.

Figure 3 presents the prediction and inference of the epidemic in the USA assuming an 8-month duration of immunity. The SUVQC model was fitted to the daily numbers of confirmed cases from February 23, 2021 to March 24, 2021, and the unknown parameters and variables are inferred to be $U_S(0) = 1{,}522{,}494$, $Q(0) = 747{,}060$, $\gamma_1 = 0.1672$ and $\beta = 0.1233$ (Fig. 3A, yellow dots: data for model fitting; green dots: data for testing, from March 25, 2021 to May 3, 2021, $R^2 = 0.9887$). Assuming that all the inferred parameters remain constant in the future and that the NPI intensity of is retained at a level similar to that between February 23, 2021 and March 24, 2021 (the mean Government Stringency Index is 63.50 according to OxCGRT; for comparison, the maximum

Government Stringency Index for the USA was 75.46 in late November 2020 and 65.91 from March 1, 2020 to March 24, 2021), the end of the epidemic in the USA is estimated to be July 11, 2022, with 34,186,100 confirmed infection cases and 633,556 confirmed deaths (Fig. 3A and B, Table 2). However, if we assume that no NPIs are carried out and the other parameters remain the same, the epidemic will end much later, on April 17, 2027, with 65,238,549 confirmed infected cases and 1,188,609 confirmed deaths (Fig. 3A and B, Table 2). Notably, given a limited duration of immunity of 3–6 months and the speed of vaccination, there is a probability that the epidemic never ends without the application of NPIs (Table 2, see the corresponding plots in Figs. 3 and 4, and Supplementary Figs. S6 and S7).

We thus explored epidemic dynamics in the USA under other scenarios with different immunity durations and a higher speed of vaccination (Table 3). With an accelerated vaccination rate of $1\%N$ per day (approximately 4 times the current vaccination rate) and with the application of NPIs, the end of the epidemic in the USA ranges between July 21, 2021 and September 17, 2021, depending on different immunity durations of 3, 6, 8 and 12 months (see the corresponding plots in Fig. 5, and Supplementary Figs. S8–S10). The number of cumulative confirmed infections is estimated to be between 31,416,458 and 32,545,275, and the number of deaths is estimated to be between 584,040 and 604,226. The epidemic in the USA will last for a much longer time if no NPIs are carried out after March 24, 2021, ranging from September 6, 2021 to January 23, 2022, with the number of cumulative confirmed infections between 32,896,846 and 45,214,634 and the number of deaths between 610,510 and 830,688.

Significantly, assuming an immunity duration of three months and the current daily vaccination rate of $\eta =$

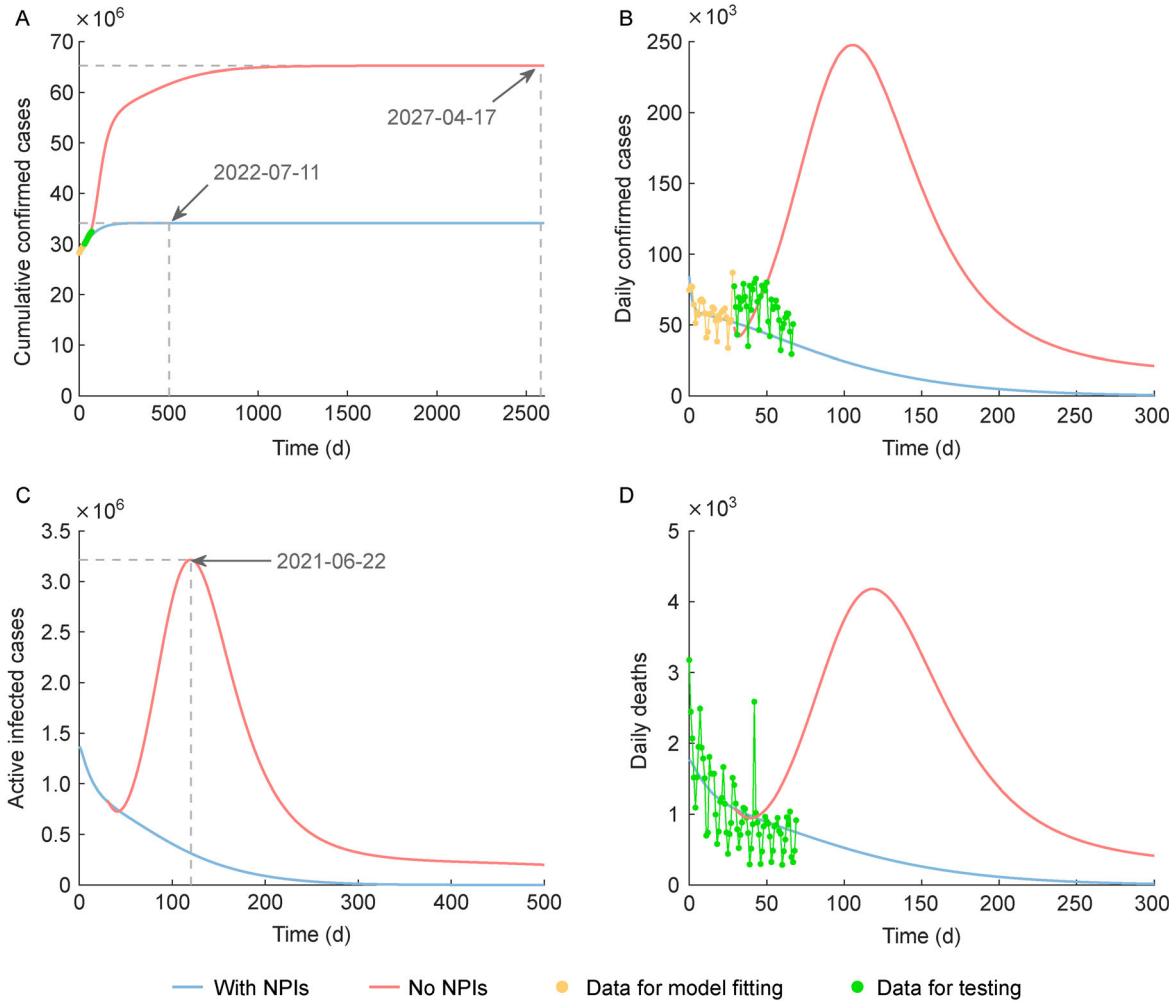

Figure 3. Prediction of epidemic dynamics in the USA with vaccination and multiple parameter settings. Vaccine efficacy $1-\lambda_1 = 0.95$, daily vaccination rate $\eta/N = 0.268\%$, duration of immunity $t_v = 8$ months. Data for model fitting is from 2021-2-23: (A) Cumulative confirmed cases. (B) Daily confirmed cases. (C) Active infected cases. (D) Daily deaths.

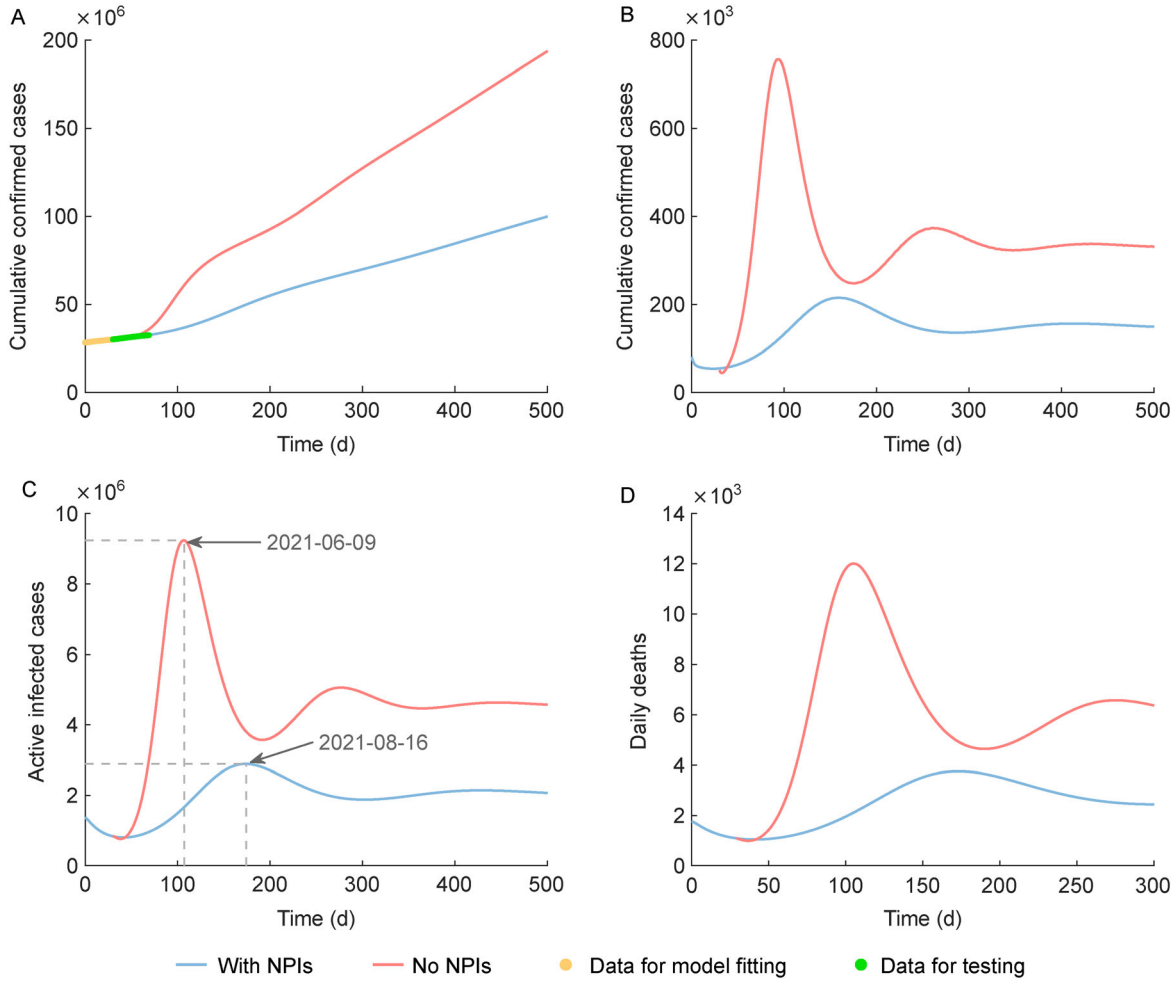

Figure 4. Prediction of epidemic dynamics in the USA under a duration of immunization of three months. Vaccine efficacy $1-\lambda_1 = 0.95$, daily vaccination rate $\eta/N = 0.268\%$. Data for model fitting is from 2021-2-23: (A) Cumulative confirmed cases. (B) Daily confirmed cases. (C) Active infected cases. (D) Cumulative deaths.

$0.268\%N$ per day, the epidemic in the USA will never end (Table 2 and Fig. 4). The epidemic reaches an equilibrium state, with 2,008,797 active infection cases under the current NPI intensity and an equilibrium state of 4,457,975 active infection cases without the application of NPIs.

Formula for optimal vaccination parameters to achieve herd immunity

If f is the proportion of the population that retains immunological memory from vaccination at time t, $f = V/N$. We consider a discrete transmission model for simplicity, where t_i denotes the i-th transmission cycle. $M(t_i)$ denotes the number of new infection cases at time t_i, and includes two groups: unquarantined infected individuals from the vaccinated population, $U_V(t_i) = M(t_i)f\lambda_1/(f\lambda_1 + (1-f))$, and from the susceptible population $U_S(t_i) = M(t_i)(1-f)/(f\lambda_1 + (1-f))$. The number of new infection cases at the next time step t_{i+1} is as follows:

$$M(t_{i+1}) = U_V(t_i)\lambda_2 R_0(f\lambda_1 + (1-f)) + U_S(t_i)R_0(f\lambda_1 + (1-f)) \quad (3)$$

By definition the effective reproductive number at time t_i can be calculated as follows:

$$R(t_i) = \frac{M(t_{i+1})}{M(t_i)} = R_0(\lambda_1\lambda_2 f + 1 - f) \quad (4)$$

For effective control of the epidemic, $R(t_i)$ should be < 1, as follows:

$$f > \frac{1 - 1/R_0}{1 - \lambda_1\lambda_2} \quad (5)$$

Calculating the speed of vaccination is straightforward:

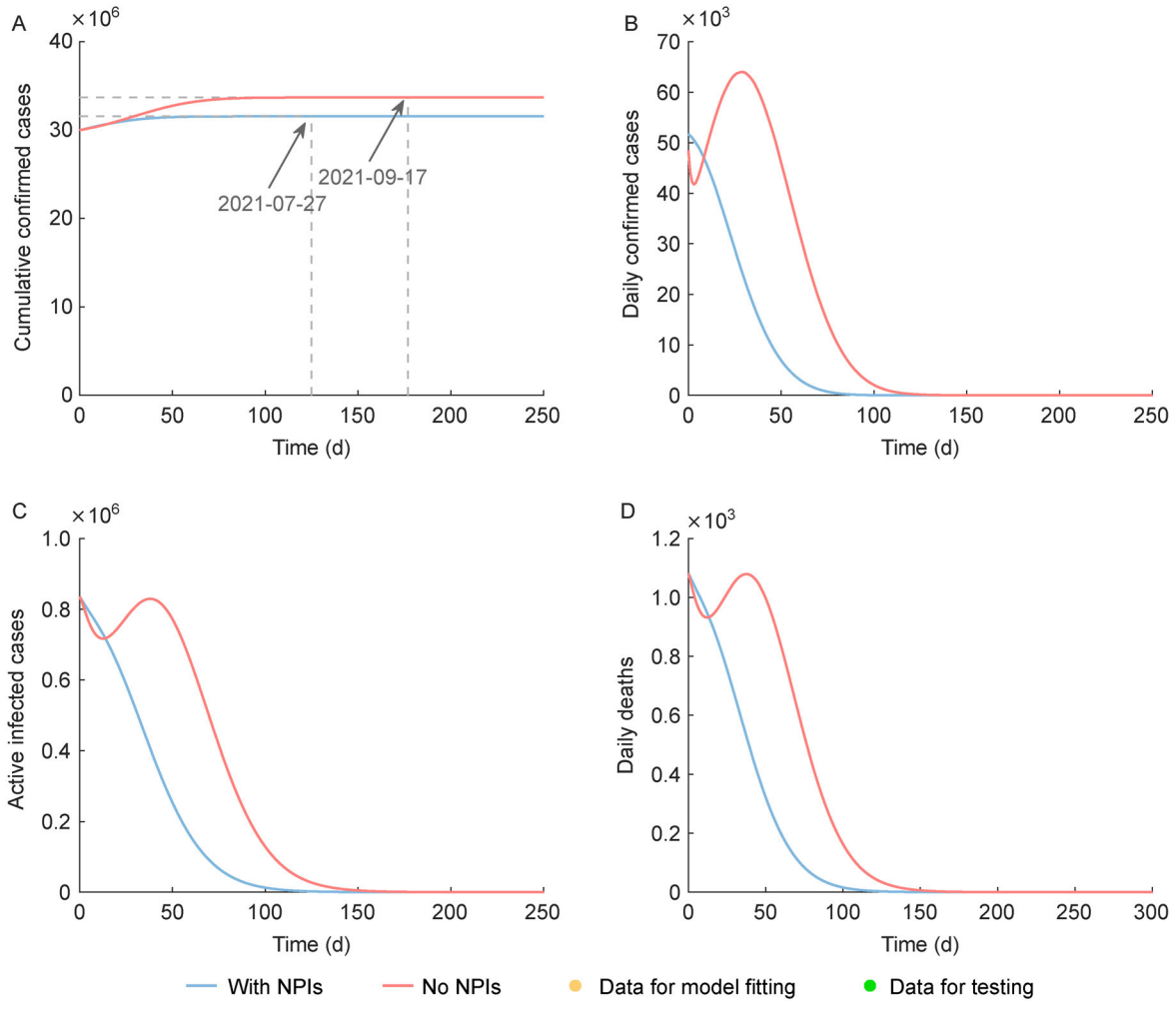

Figure 5. Prediction of epidemic dynamics in the USA with vaccination supposing a higher daily vaccination rate η/N = 1%. Vaccine efficacy $1-\lambda_1 = 0.95$, duration of immunity $t_v = 8$ months (data for model fitting is from 2021-2-23): (A) Cumulative confirmed cases. (B) Daily confirmed cases. (C) Active infected cases. (D) Cumulative deaths.

Table 2 Prediction of the epidemic in the USA with different durations of immunity

Duration of immunity	90 days	180 days	240 days	365 days
With NPIs				
Ending time	-	2024-10-19	2022-7-11	2022-1-20
Infected number	-	39,221,727	34,186,100	32,781,833
Death number	-	723,566	633,556	608,455
Maximum active number	2,889,241	1,367,655	1,367,655	1,367,655
Date of maximum active number	2021-8-16	2021-2-23	2021-2-23	2021-2-23
Equilibrium value of active number	2,008,797	0	0	0
Without NPI after Mar 24, 2021				
Ending time	-	-	2027-4-17	2022-7-23
Infected number	-	-	65,238,549	47,251,025
Death number	-	-	1,188,609	867,087
Maximum active number	9,238,306	4,535,544	3,215,414	1,999,593
Date of maximum active number	2021-6-9	2021-6-20	2021-6-22	2021-6-17
Equilibrium value of active number	4,457,975	1,216,877	0	0

Table 3 Prediction of the epidemic in the USA with different durations of immunity and an accelerated vaccination rate of 1%N per day

Duration of immunity	90 days	180 days	240 days	365 days
With NPIs				
Ending time	2021-9-17	2021-8-3	2021-7-27	2021-7-21
Infected number	32,545,275	31,717,232	31,560,898	31,416,458
Death number	604,226	589,418	586,623	584,040
Maximum active number	842,149	837,787	836,535	835,138
Date of maximum active number	2021-3-24	2021-3-24	2021-3-24	2021-3-24
Equilibrium value of active number	0	0	0	0
Without NPI after Mar 24, 2021				
Ending time	2022-1-23	2021-9-28	2021-9-17	2021-9-6
Infected number	45,214,634	34,795,880	33,703,470	32,896,846
Death number	830,688	644,455	624,928	610,510
Maximum active number	2,435,402	984,639	836,535	835,138
Date of maximum active number	2021-5-29	2021-5-8	2021-3-24	2021-3-24
Equilibrium value of active number	0	0	0	0

$$\eta/N > \frac{1-1/R_0}{t_v(1-\lambda_1\lambda_2)} \tag{6}$$

Note that when $V(t_i) = N$, the maximum value of $\eta(t_{i+1})/N = 1/t_v$, which implies that the long-term upper bound of η/N is $1/t_v$. Thus, from Eq. (6), we conclude that when $1-1/R_0 > 1-\lambda_1\lambda_2$, the epidemic cannot be terminated by vaccination alone. For example, assume that the basic reproductive number of SARS-CoV-2 is $R_0 = 2.5$ and that U_V has the same infectivity as U_S (that is, $\lambda_2 = 1$), λ_1 should be less than 0.4 (correspondingly, the vaccine efficacy is $\geqslant 0.6$) to ensure that the epidemic can be ceased by vaccination alone.

Eq. (6) provides a useful formula for determining the optimal vaccination rate taking into account the different values of R_0, t_v and λ_1 to guarantee the termination of the epidemic. For $R_0 = 2.5$, $t_v = 240$ days, $\lambda_1 = 0.4$ (*e.g.*, the efficacy of vaccination is 0.6), $\lambda_2 = 1$, η should be $>$ 0.42% of the population per day. For $R_0 = 2.5$, $t_v = 240$ days, $\lambda_1 = 0.05$ (*e.g.*, the efficacy of vaccination is 0.95), $\lambda_2 = 1$, η should $> 0.26\%$ of the population per day (Fig. 6, red point). Figure 6 provides a thorough demonstration of the minimum vaccination rate to ensure effective termination of the epidemic for a wide range of R_0 and vaccine efficacy values.

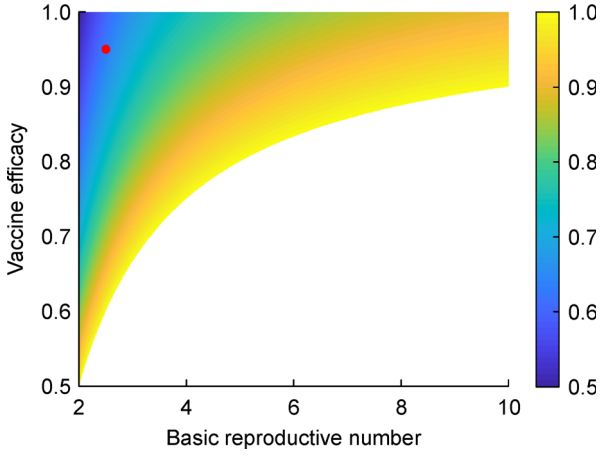

Figure 6. Optimal vaccination parameters to achieve herd immunity. The minimum daily vaccination rate η/N required to effectively end the epidemic without NPIs for different basic reproductive number (R_0) values and vaccine efficacy ($1-\lambda_1$). Here we set $\lambda_2 = 1$. The color scheme indicates the daily vaccination rates in units of $1/t_v$. Red dot: for $R_0 = 2.5$, $t_v = 240$ days and $1-\lambda_1 = 0.95$, the minimum daily vaccination rate should be $\eta/N = 0.26\%$ per day.

DISCUSSION

In this study, we developed the SUVQC model to characterize COVID-19 pandemic dynamics under vaccination and NPI application. In addition to the intrinsic parameters of the epidemic, such as transmissibility and the effect of NPIs, the model also explicitly parameterizes multiple key factors related to vaccination, including vaccine efficacy, the vaccination rate, and the reduced infectivity of individuals who have been vaccinated or infected.

Note that SUVQC model has some strong assumptions, which may bias inference and prediction. The model

assumes that all individuals are equally susceptible to the virus. In reality, individuals in the hot spots of the human interaction network have a higher risk of exposure. A vaccination program prioritizing these individuals is more effective in containing the epidemic, especially when there is a shortage of vaccines. For such a vaccination program, the daily vaccination rate provided by Eq. (6) can be overestimated. Furthermore, the model includes 12 parameters, for most of which the data (daily reported number of confirmed cases) are uninformative and must be inferred beforehand with prior knowledge. Some critical parameters, such as the duration of effective immunity, are still unclear due to limited studies. The prediction of epidemic dynamics by the model is made based on some preselected values. We thus developed a MatLab application for the readers to download and run the model with parameter values on their own.

The model was applied to the numbers of daily reported confirmed cases to project the future trends in Israel and the USA, with the parameters inferred based on their current epidemic statuses and intervention measures. The analysis demonstrates that good vaccine efficacy and a high vaccination rate coupled with intensive NPIs can eliminate the spread of the virus very efficiently. However, for the USA, under some parameter settings, such as a short duration of immunity or the elimination of NPIs, the epidemic will not end and instead reach an equilibrium state, with a proportion of the population remaining actively infected. We provide a unified formula for determining the minimum daily vaccination rate considering different effective reproductive numbers and vaccine efficacy. Considering that vaccine parameters and epidemic parameters are difficult to adjust in operation, a practical scheme is to supplement the vaccination plan with NPIs.

There are many reasons to remain conservative when estimating the efficacy of vaccination in suppressing an epidemic. SARS-CoV-2 genomes are still actively evolving under selection with new mutations, and SARS-CoV-2 may gain the ability to partially escape vaccine-induced immunity, reducing vaccine efficacy [24–28]. It is possible that current vaccines may have reduced efficacy and induce a shorter duration of immunity in the near future. In addition, many COVID-19 reinfection reports imply that immunity may not be strong and long lasting [29,30]. Excessive optimism is undesirable considering the unpredictable factors. Retaining NPIs, at least to some extent, is still necessary to contain the pandemic. If the vaccination program works, the epidemic in Israel should end by mid-May (no later than August 26, 2021, assuming there are no NPIs and the duration of immunity is 180 days). If it does not end by then, we must re-evaluate the role of vaccination.

SUPPLEMENTARY MATERIALS

The supplementary materials can be found online with this article at https://doi.org/10.15302/J-QB-021-0256.

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COMPLIANCE WITH ETHICS GUIDELINES

The authors Shilei Zhao, Tong Sha, Chung-I Wu, Yongbiao Xue and Hua Chen declare no competing financial interests.

All procedures performed in studies were in accordance with the ethical standards of the institution or practice at which the studies were conducted, and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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