Novel deterministic epidemic model considering mass vaccination and lockdown against coronavirus disease 2019 spread in Israel: a numerical study

Motoaki Utamura1*, Makoto Koizumi2 and Seiichi Kirikami3

1Research Laboratory for Nuclear Reactors, Tokyo Institute of Technology, Tokyo, Japan
2Hitachi Research Laboratory, Hitachi Ltd, Chiba, Japan
3Hitachi Works, Hitachi Ltd, Hitachi, Japan

*Correspondence address. Research Laboratory for Nuclear Reactors, Kamiyoga 2-5-2-612, Setagaya-ku, Setagaya, Tokyo 158-0098, Japan. Tel: +818054940224; Fax: +81354773464; E-mail: titech02715@gmail.com

Abstract

Why public health intervention by the Israeli government against coronavirus disease 2019 spread has been successful while the majority of other countries are still coping with it? To give a quantitative answer, a simple numerical epidemic model is prepared to simulate the entire trend of various infection-related variables considering the first and second vaccination campaigns against the alpha variant and simultaneous lockdown. This model is an extension of our previously published deterministic physical model, that is, Apparent Time Lag Model, which aims at predicting an entire trend of variables in a single epidemic. The time series data of both vaccine dose ratio and lockdown period are employed in the model. Predictions have been compared with observed data in terms of daily new cases, isolated people, infections at large and effective reproductive number, and, further, the model is verified. Moreover, parameter survey calculations for several scenarios have clarified the synergy effects of vaccination and lockdown. In particular, the key element of Israel’s success has been suggested to lie in a high-dose vaccination rate that prevents the onset of a rebound in daily new cases on the recision of the lockdown.

Keywords: COVID-19; Israel; vaccination; ATLM; epidemic model; discrete delay differential equation

Introduction

At present, the world is still facing the crisis caused by the coronavirus disease 2019 (COVID-19) pandemic. The introduction of a lockdown cannot completely prevent the onset of a pandemic. Mass vaccination of the population is the most radical method of limiting its spread. Therefore, the Israeli government authority started the first and second vaccination operations against severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2) alpha variant on 19 December 2020, earlier than most other countries. Because of the fairly small size of the Israeli population, cumulative doses exceeded 100% towards the end of March 2021, the fastest in the world. In parallel, the lockdown was also implemented. As a result, daily new cases drastically decreased from a peak of 10 000 to 500 at the end of March 2021. This successful experience should be shared in other countries. Hence, a prediction model that counts the number of infected people should be established given the data on vaccination dose rate and lockdown period. Few deterministic models based on the standard Susceptible, Infectious and Removed (SIR) model [1] have been recently investigated. The ABM [3–7] is a kind of stochastic approach and differs from mathematical models, such as SIR and Susceptible, Exposed, Infectious and Removed (SEIR), in that it can set up a virtual society that consisted of a large number of autonomous decision making and action actors (agent) with various attributes and can analyse complex social events involving interactions between actors. Based on the rules we set on a computer, agents spontaneously act while interacting in a given environment. Previous reports simulated the comparative and joint impact of COVID-19 vaccine efficacy and coverage together with non-pharmaceutical interventions (NPI) by taking the population of US cities as an example [6, 7]. They suggested that non-pharmaceutical interventions, such as masking and social distancing, among others, are still required to reduce infections against SARS-CoV-2 even after achieving a higher vaccine coverage and efficacy. In this method, a detailed setting is possible; however, many empirical constants are required because of its stochastic approach, and the calculation may be time-consuming depending on the scale. Moreover, a comparison was made based only on a cumulative basis. Prediction should be examined with factors such as in-patients and daily new cases, among others, by available observations.

Due to these difficulties in previous literature, a new deterministic approach, known as the apparent time lag model (ATLM) different from SIR, was developed [8]. The benefits of the
model include the derivation of the final size equation and a simple analytic form of the fundamental reproductive number. In particular, ATLM should be emphasized based on the capability of calculating the trend of the effective reproductive number to foresee an infection turning point from growing to shrinking. These equations or correlations may provide a perspective on a pandemic of interest.

In the present study, ATLM was extended to be capable of evaluating the vaccine effects and NPI in Israel. The validity of the present model was shown using publicly available data. This model is characterized by a small number of empirical constants, which are all measurable.

Methods

Data

Infectious data of COVID-19 in Israel were referred to Worldometers [9] and vaccination statistics, and the reproductive number of COVID-19 was cited by Our World in Data [10]. The first and second nationwide mass vaccination in Israel started on 19 December 2020, and the total dose rate per habitant exceeded 100% towards the end of March 2021. Lockdown was issued from 27 December 2020 to 5 February 2021 [11, 12]. Data for time lags [period from infection until the polymerase chain reaction (PCR) reporting date], V (period of quarantine) and T (period from infection until quarantine) were set to 14 [13], 12 [14] and 14 days, respectively.

We adopted the SARS-CoV-2 infection data in Israel from 8 November 2020 to 31 March 2021 for analysis. Various data such as daily new cases, cumulative infections, currently isolated, current hospitalizations, discharge/death, time lags, etc. were collected. Various data such as daily new cases, cumulative infections, currently isolated, currently hospitalizations, discharge/death, time lags, etc. were collected.

ATLM with vaccine model

SARS-CoV-2 that caused the COVID-19 includes several delayed events in the spread of infection as follows:

1) every infected individual onset being PCR positive and eventually quarantined T days post-infection;
2) we count infections at large at the time t as $x(t) - x(t - T)$ where $x(t)$ is cumulative infected persons until t and infected individuals before $t - T$ are all quarantined;
3) the portion of susceptibility may be expressed by $1 - x(t)/M(t)$;
4) we assume the rate of new infection $dx(t)/dt$ is proportional to the product of infections at large and the portion of susceptibility;
5) individuals once infected are eventually removed and never infected again during the same pandemic;
6) there is no breakthrough infection; and
7) we consider infection spread by the alpha variant only in the present study although observed data are a mixture of alpha variant and conventional strains with portions not negligible early in the time horizon.

Hence, the governing equation of ATLM becomes

$$\frac{dx(t)}{dt} = \alpha(t) \{x(t) - x(t - T)u(t - T)\} \left(1 - \frac{x(t)}{M(t)}\right),$$  \hspace{1cm} (1)

$$M(t) = M_0 \left(1 - \frac{\mu(t)}{100}\right), \quad \alpha(t) = \alpha_0 (1 - \rho(t)),$$  \hspace{1cm} (2)

where $x(t)$ indicates cumulative infected individuals, $dx(t)/dt$, rate of new infection; $\alpha_0$, transmission rate (1/day); $M_0$, virtual collective population; $\mu(t)$, effectiveness of vaccination (%); $\rho(t)$, disability of the people and $u(t)$, step function. As the influence of vaccination corresponds to reduced susceptibility, we expressed the net collective population of a group as $M(t)$ with consideration of plural piecewise solutions to the respective small periods. Conversely, ATLM introduces a virtual collective population (M) instead of the real population (N) of a community in concern. As $M$ is neither known a priori nor modeled so far, it must be estimated by the parameter fitting based on real-world infection data collected. Empirically, $M$ is known to be much smaller than $N$ [8], which matches the observation that the mobility of ordinary people in daily life is limited and the topological space is loosely closed. Thus, infections are likely to happen and cease in the area within the mobility. Random-based mass vaccinations are assumed to play a role in reducing $M$. Therefore, the following assumptions were considered in the analysis:

- every infected individual onset being PCR positive and eventually quarantined $T$ days post-infection;
- we count infections at large at the time $t$ as $x(t) - x(t - T)$ where $x(t)$ is cumulative infected persons until $t$ and infected individuals before $t - T$ are all quarantined;
- the portion of susceptibility may be expressed by $1 - x(t)/M(t)$;
- we assume the rate of new infection $dx(t)/dt$ is proportional to the product of infections at large and the portion of susceptibility;
- individuals once infected are eventually removed and never infected again during the same pandemic;
- there is no breakthrough infection; and
- we consider infection spread by the alpha variant only in the present study although observed data are a mixture of alpha variant and conventional strains with portions not negligible early in the time horizon.

### Table 1: Time delays adopted in ATLM

| Variable | Definition | Value | Reference | Remark |
|----------|------------|-------|-----------|--------|
| T        | Elapsed time until quarantine | 12–15 |          | $T = L + F + G$ |
| L        | Virus latent period | 5     | [21]      |        |
| F        | Elapsed time of pre-symptomatic state until PCR tested (temp ≥37°C) | 5–7   |          |        |
| G        | Go to the hospital for testing and test result reported | 2–3   |          |        |
| V        | Isolation period | 12    | [14]      |        |
| S        | Elapsed time from infection until discharge/death | 26    |          | $S = T + V$ |
| H        | From infection until PCR testing results reported | 14    | [13]      |        |
of the vaccination effectiveness. Then, the effects of lockdown were understood as the decrease in people’s mobility, resulting in decreased transmission rate \( x_0 \) as in Equation (2). Given the initial value of \( x(0) \), Equations (1) and (2) were solved numerically using the fourth-order Runge–Kutta–Gill method with a time step of half-day and obtained \( x(t) \).

Furthermore, other important infection-related parameters were calculated using \( x(t) \) as follows:

Cumulative positive reported cases \( Y(t) \) appears in the delay of \( H \) days. Then,

\[
Y(t) = x(t - H),
\]

where \( H \) is the period from the onset of infection until the PCR test result report reaches the public health authority. \( H \) was assumed to be 14 days [13], that is days when the present data were collected. Equation (3) also indicates the number of cumulative isolated patients.

Similarly, daily new cases reported by the public health authority \( dY(t)/dt \) are daily new infections \( dx(t)/dt \) at \( H \) days before:

\[
\frac{dY(t)}{dt} = \frac{dx(t - H)}{dt}
\]

–Infections at large \( W(t) \) is assumed to be the sum of new infections in the period \([t−T, t] \):

\[
W(t) = x(t) - x(t - T),
\]

where \( T \) is a period during which an infected person remains infected at large (or until quarantined). It was assumed to be 14 days because \( T = L + F + G \), where \( L \) is the incubation period of 5 days [21], \( F \) is the period of pre-symptomatic state before a temperature of 37.5°C becomes reached \( 5-7 \) days and \( G \) is the PCR testing and result reported 2–3 days, yielding \( 12(5 + 5 + 2) < T < 15(5 + 7 + 3) \) with an average of \( T = 14 \).

–The number of isolated people \( P(t) \) consisting of hospitalizations, self-isolated at hotels and home and people who are still undecided on where to undergo treatment was counted based on the difference between those isolated and discharged using the following equation:

\[
P(t) = x(t - T) - x(t - S),
\]

where \( x(t - S) \) is the number of recoveries or deaths. Denoting the isolation period as \( V \), then \( S \) can be written as the sum of \( T \) and \( V \), that is \( S = T + V \). Israel’s Health Ministry decided to shorten the mandatory coronavirus isolation period from 14 to 12-days, provided that the patient had two negative tests from 12 November 2020 [14]. Then, \( V = 12 \) holds in Israel. Therefore, \( S = T + V = 14 + 12 = 26 \).

The effective reproductive number is understood as the average number of secondary cases to a primary case. ATLM defines the effective reproductive number \( Rt(t) \) as

\[
Rt(t) = a(t)T \left( 1 - \frac{x(t)}{M(t)} \right)
\]

where \( a(t)T \) is the basic reproductive number [8].

In subsequent sections, predictions in Equations (3)–(7) will be compared with the available data from Worldometer [9] and Our World in Data [10] and examine the present analysis method.

In summary, the values of delayed parameters adopted in the prediction are \( H = T = 14 \), \( V = 12 \) and \( S = 26 \), which will be used throughout this study.

**Vaccination modelling in Israel**

Let the number of people vaccinated per 100 habitants be \( A \), those vaccinated twice, \( B \), and cumulative doses per 100 habitants \( C \), then those vaccinated only once become \( A - B \) and \( A + B - C \) holds at any instance. When vaccination was completed, that is everyone has become a recipient twice, then \( C \) would be 200%.

Trends of data for \( A \), \( B \) and \( C \) in Israel [10] are shown in Fig. 1. The target value of \( B \) is considered to be 5.5 million among 9 million citizens, which has been almost completed before the end of March. Let the vaccination efficacy for a single-dose recipient be \( \beta \) and that of double-dose one be \( \gamma \), then the average efficacy \( \mu(t) \) of a group consisting of both \( A \) and \( B \) is written as follows for a single-type vaccine:

\[
\mu(t) = \beta(A(t)−B(t)) + \gamma B(t)
\]

The type of virus in the third wave of the pandemic in Israel is mainly the alpha strain [15]. The efficacy of the BNT162b2 mRNA COVID-19 vaccine (Pfizer-BioNTech COVID-19 vaccine) in a nationwide mass vaccination campaign in Israel is reported in peer-reviewed articles [18–20]. Based on these, we adopted \( \beta = 0.8 \) and \( \gamma = 0.95 \) in Equation (8) and assumed the vaccine was activated after 10 days for both single and double injection recipients.

The data plot of \( \mu(t) \) (Equation (8)) in blue circles and its polynomial approximation Equation (9) in broken red line are presented in Fig. 2.

\[
\mu(t) = -0.000034 t^3 + 0.007073 t^2 + 0.297875 t - 33.064707
\]

Since the vaccine effectiveness becomes activated in \( \xi \) days post-injection, \( \mu(t) \) in Equation (9) was replaced by \( \mu(t-\xi) \). Based on the previous literature [16, 17], we assumed \( \xi = 10 \) in the computation. It is observed that the vaccination speed was quick and the collective vaccine effectiveness (CVE) reached ~40% 60 days after starting the vaccination.

**Lockdown modelling**

Lockdown suppresses human contact to reduce infections in society. The Israeli government executed a national lockdown as a necessary step to block the increased morbidity [10] on 27 December 2020 (63 days after 25 October) for 2 weeks with an option of extending it. Actually, a national lockdown was extended until 5 February 2021 (103 days) due to delayed turn-around time from the health and economic crises on 31 January 2021 (98 days) [12].

We modelled the lockdown effects by a sudden decrease in the transmission rate as shown in Fig. 3. \( (1−\rho(t))_{\text{min}} \) was set to 0.72 as a result of parameter fitting. Other parameter values determined after fitting were \( x(0) = 650 \), \( x_0 = 0.117 \) and \( M_s = 1 \ 500 \ 000 \), respectively. First, their values were identified as the first approximation using data in an early phase of the second wave (for details, see Appendix 1). Further, these values were graphically tuned so that they should be consistent with those of other measurements, such as the number of infections at large, in-patients and the trend of the reproductive number. Table 2 summarizes calculation conditions and actual event sequences.
Daily new cases and total cases

Daily new cases were obtained from the Worldometer data source [9] first for comparison with the prediction by ATLM equipped with vaccination and lockdown models. The study was conducted from 8 November 2020 to 31 March 2021, covering a whole span of the third wave of the COVID-19 pandemic in Israel in which mass vaccination and a nationwide lockdown were involved. We regarded the term ‘daily new cases’ in Worldometer as daily new positives observed behind a new infection based on \( H \) days. The computation started ahead of 8 November 2020, by \( H \) days, that is 25 October 2020, the original calculation time.

Figure 4 compares the prediction using the observed data. Both are expressed on a 7-day average basis to prevent fluctuation using the difference in the number of PCR tests in a week. The prediction is a 7-day average of \( \frac{dY}{dt} \) (Equation (4)). The following important findings were observed:

- Impacts at the start and the release of lockdown are apparently observed in data on both dates as 10 January 2021 and 19 February 2021, respectively, whereas the actual dates when the public health interventions were 27 December 2020 and 5 February 2021, respectively [12]. The former reduces the infection rate resulting in the appearance of a peak, whereas the latter produces a plateau as a result of an antagonist between the rebound of the lockdown rescission and the vaccination efficacy. These characteristics are found to have been well simulated. This fact validates the assumption that \( H = 14 \) (infection becomes apparent in a 14-day delay). Both observed data were simulated within 10% error in terms of both time and magnitude.
- At the early stage of the pandemic, the prediction is found to underestimate the observed data. This fact can be interpreted as follows. The observed data contain tailing effects of the preceding second wave, which were not considered in the present study.
- The above-mentioned plateau was not reproduced during computation. This might be caused by an initial additional lockdown intervention on 8 January 2021, as disclosed in the recent literature [22].

Overall, however, the simulation of the entire trend of daily new cases was satisfactory.

Figure 5 presents cumulative positives \( Y(t) \) (Equation (3)). The overall agreement was achieved between the prediction and observed data. Underestimation was obtained from the fact that the observed data contain the tailing effect of the preceding second wave, which was not considered in the present study. Remarkably, the number of cumulative positives attained was approximately 500 000, which is approximately one-third of the virtual collective population \( M_0 \). Then, two-third of the total population remains uninfected because the term \( \bullet \) of RHS in Equation (1) governs infection phenomenon towards the endemic rather than the term \( \left( 1 - \frac{\rho}{C(t)} \right) \) due to the lower transmission rate. Our previous study [8] showed this may become dominant.
provided that $a_0 T < 2.5$, whereas the value in the present study is 1.64.

**The number of isolated patients**

The number trend of isolated patients is presented in Fig. 6. Although the calculation using Equation (6) overestimates the actual data by 15% at a peak on 20 January 2021, the overall trend is simulated fairly well and also proves the assumption that $T = 14$ in the model that is correct because of a larger value of $T$, resulting in overestimation and vice versa for a smaller one.

**Reproductive number**

Figure 7 compares the prediction using Equation (7) with data [10] based on the reproductive number ($R_t(t)$). The $R_t(t)$ data in Our World in Data have been compiled using the method described in the literature [23] and contain real-time estimates of the effective reproductive number. Their $R_t(t)$ estimates for COVID-19 in 124 countries worldwide are provided and used to assess the effectiveness of non-pharmaceutical interventions in a sample of 14 European countries. Thus, the data could be most reliable at this moment.

Aside from an early phase, prediction for the third-wave pandemic in Israel coincides well with estimates from the observed data, especially during the vaccination and lockdown periods. The discrepancy between data and calculation in the early phase could be accounted for based on the co-existence of the aforementioned tail of the second-wave pandemic.

In the early phase, the reproductive number is a compound of the second and third waves, which may be estimated by a weighted average $R_{	ext{mixed}} = R_{2nd} \times (0.83) + R_{3rd} \times (0.17)$ on 15 November. In Fig. 7, substituting the tail part value of $R_{3rd}$ for $R_{2nd}$ would provide $R_{2nd} = 0.5$. Then, with $R_{3rd} = 1.64$, $R_{mixed} = 0.5 \times (0.83) + 1.64 \times (0.17) = 0.70$. As the tail shrinks, $R_t$ grows, which could explain such a tendency of the observed data in the early phase.

The basic reproductive number $a_0 T$ for Israel was estimated using the ATLM as 0.117/14 = 0.008, which is smaller than those evaluated by [24] in the USA and eight European countries using data without pharmaceutical intervention. The reason for its difference remains unknown yet; however, the accumulation of data with pharmaceutical intervention would be recommended for future work.

**The number of infections at large**

Infections at large should be recognized as an important variable to determine when the pandemic will end, a finding much more accurate than daily new cases because the time to reach $W(t) = 0$ rigorously indicates the end of a pandemic.

Next, infections at large may be obtained using data processing as follows. The substitution of daily new cases $Y(t)$ to RHS of Equation (5) would yield $W(t-T)$. $W(t)$ would be obtained by shifting the $W(t-T)$ profile leftward by $T$ along the time axis. To confirm the validity of the obtained $W(t)$ in this method, an agreement was confirmed with a numerical prediction with the precision that has already been examined through arguments described in the previous section. As shown in Fig. 8, an
excellent agreement is observed between the two, suggesting the correctness of the data processing mentioned above. The $\frac{W(t)}{pt} \cdot \frac{dY(t)}{dt}$ ratio was evaluated to be approximately 13 times.

**Estimation of the separate effects of vaccination and lockdown**

Based on the confirmed epidemic model, parameter survey calculations were conducted for the following four scenarios:

1) Without vaccination, without lockdown: case C
   \[ \mu = \rho = 0 \]

2) With vaccination, without lockdown: case D
   \[ \mu \neq 0, \rho = 0 \]

3) Without vaccination, with lockdown: case B
   \[ \mu = 0, \rho 
eq 0 \]

4) With vaccination, with lockdown: case A (real intervention)
   \[ M \neq 0, \rho \neq 0 \]

Results are presented in Fig. 9.

Without lockdown, the blue line (A) would have shifted to the yellow line (D). If the vaccination dose rate had been slower, then the blue line (A) would have approached the red line (B). In general, the lockdown has decreased the transmission rate, whereas vaccination accelerates the convergence of a pandemic.

Next, the separate effect of either vaccination or lockdown was investigated.

We will introduce D/C and B/C ratios in which B, C and D mean daily new cases of case B, C and D. Without lockdown, the peak value would increase 2–2.5 times larger than in the real one denoting C/B. Without vaccination, the pandemic would decelerate in a later stage C/D and even worse on the earlier release of the lockdown.

Figure 10 presents the joint impact of both ratios.

Here, the ratio means a relative infection rate to C. The smaller the ratio, the lower the infection rate. As vaccinations proceed, the D/C ratio monotonously decreases. Conversely, the B/C ratio of the lockdown has a minimum due to rebound during the rescission of lockdown. It is observed until 22 February 2021, the impact of lockdown exceeds that of the vaccination. Thereafter, the effects of vaccination are superior to lockdown.

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**Table 2: Calculation conditions and actual event sequence**

| Item                | Variable | Unit     | Value       | Remark                        |
|---------------------|----------|----------|-------------|-------------------------------|
| Transmission rate   | $x_0$    | 1/day    | 0.117       |                               |
| Initial susceptible | $M_0$    | –        | 1 500 000   |                               |
| Initial infected    | $x(0)$   | –        | 650         | 25 October 2020               |
| Delay until quarantine | $T$     | Day     | 14          |                               |
| Period of quarantine | $V$     | Day     | 12          |                               |
| Delay until discharge | $S$    | Day     | 26          | $S = T + V$                   |
| Delay until reporting | $H$    | Day     | 14          |                               |
| PCR positive result |          |          |             |                               |
| Start of calculation | $t$     | Day     | 0           | 25 October 2020               |
| Start of investigation | $t$   | Day     | 14          | 8 November 2020               |
| Start of vaccination | $t$     | Day     | 55          | 19 December 2020              |
| Start of lockdown    | $t$     | Day     | 63          | 27 December 2020              |
| End of lockdown      | $t$     | Day     | 103         | 5 February 2021               |
| End of calculation   | $t$     | Day     | 157         | 31 March 2021                 |

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Figure 3: Lockdown modelling. The axis represents $1 - pt$ in Equation (2). Lockdown was operated from 27 December 2020 to 5 February 2021. Its effect is anticipated to become apparent on 10 January 2021 and 19 February 2021, because of a 14-day delay in reporting.
The combined effects of A/C are presented in a broken line, indicating that rebound suppression may be to some extent caused by vaccination. A period (25 January 2021 to 25 February 2021) of synergy was observed when the black broken line has the smallest ratio among the three. It is inferred that the faster the dose rate, the smaller the rebound magnitude, which would contribute to the earlier ending of the pandemic.

**Sensitivity analysis**

Time delay constant T may vary from country to country depending on many factors, such as the type of virus strain, public health regulation, intervention, governmental economic policy, medical resources and knowledge of the virus strain and variant, among others. Sensitivity analysis was conducted to determine what T value is appropriate for the present Israeli COVID-19 pandemic. Taking 16, 15, 14, 12 and 10 days as candidates, the transmission rate $\alpha_0$ and initial virtual collective population $M_0$ were estimated using the method in Appendix 1 with data corresponding to the growing phase of the pandemic before lockdown or starting the mass vaccination. Numerical simulations using Equations (1) and (2) were conducted from the beginning until the end of the pandemic and compared with the data. This calculation should be started on a different day based on T. The number of initial infectors $x(0)$ in each case was defined as a value on T days before 8 November so that the new reported 7-day average delay (=238) should be common to all on 15 November 2020.

Results are presented in Table 3 and Fig. 11. It is observed as T decreases and $M_0$ decreases, whereas $\alpha_0$ and $\alpha_0 T$ increase. In Fig. 11, each calculation shows an excellent agreement with the data trend until the peak, except at the very early stage, but is underestimated in most of the descending stages after the peak, except for $T = 16$. One possible reason for the underestimation may be obtained from the fact that senior citizens received injections first before the younger generation whose social activity is much higher. However, this model is not sophisticated as to accommodate such an inhomogeneity. As a result, the predicted effectiveness of the society may overestimate the real one and hence underestimate infections at an early phase of vaccination. Among the four cases, the discrepancy was found smallest in the case $T = 14$. Noting this fact and empirical knowledge on the allowable range of time delay (Table 1), $T = 14$ was adopted. Furthermore, these are finely tuned so that they should be consistent with the other measurements, such as the number of infections at large (Fig. 8), in-patients (Fig. 6) and trend of effective reproductive number (Fig. 7).

The final results are presented in Table 2. Moreover, the portion of daily new reported cases during the second wave of the pandemic on 15 November was estimated to be one-third of the total population (observed data).
Figure 5: Trends of cumulative positives. Equation (3) was used to calculate cumulative positives, $Y(t)$.

Figure 6: Trend of currently isolated patients. Data cited from Worldometer with a notation of ‘currently infected’ [9]. The prediction using ATLM. Coincidence in timing implies the assumption $T = 14$ is proper. The time to provide the peak is behind that of daily new cases (Fig. 4) based on a week.
Figure 7: Effective reproductive number. Observed data were cited from our World in Data [10] and Equation (7) was used for calculation.

Figure 8: Infections at large.
Discussion

Primary findings

The ATLM equipped with a newly developed vaccination and lockdown model simulated a whole trend of various infection variables for the third wave of the COVID-19 pandemic in Israel within a 15% error. In particular, the number of isolated PCR positives and infections at large was separately evaluated with high resolution. Moreover, in the mid-span and after the pandemic, the prediction of an effective reproductive number using Equation (7) derived from ATLM agreed in the period of the later half of the pandemic with real-time estimates in Israel [10] using this method [23]. It provides estimates of Rt for COVID-19 in 124 countries worldwide, which are used to assess the effectiveness of non-pharmaceutical interventions in a sample of 14 European countries. A huge difference appearing during the initial phase of the pandemic was quantitatively explained, that is it was affected by the tailing part of the preceding pandemic that occupies two-third of the total population.

These facts confirm the present vaccination model whose concept is to reduce the virtual collective population based on the acquired vaccination effectiveness. Conversely, most previous studies mainly using ABM disclosed to date were limited to the total and daily new cases [4–6] and were unlikely to show prediction of the trend of the effective reproductive number.

A separate effect of vaccination and lockdown was attempted to be explored. Although lockdown most effectively suppresses the infection rate in the ascending phase of the pandemic, inducing a rebound on its release is inevitable. Vaccination is found to be a strong tool to suppress it. To make this effective, it was inferred from parameter survey calculations that the vaccination dose rate should be sufficiently rapid to achieve at least 40% effectiveness during the rescission of a lockdown. This effective value was found consistent with the herd immunity value drawn from a reproductive number analysis.

Additionally, the data processing method to extract infections at large from the total cases was clarified. These infections at large \( W(t) \) are a decisive index to estimate the end of the pandemic when \( W(t) \) becomes zero, occurring behind the time when daily new cases become zero and yielding a conservative measure to plan public health prevention and control the pandemic.

A previous study [8] reported that the herd immunity level is evaluated as \( 1 - 1/aT = 1 - 1/(0.117 \times 14) = 0.39 \). Figure 2 indicates the herd immunity level is established on 13 February 2021. Therefore, a CVE of 0.4 is found to be adequate in Israel to suppress infections.

The transmission rate \( a_0 \) obtained should be discussed. The Israeli third-wave COVID-19 pandemic is compared with that in Tokyo, with a similar population size of 14 million to Israel’s 9.8 million. The prevalent strain in the fourth-wave pandemic in Tokyo was an alpha strain, a finding similar to the third-wave pandemic in Israel.

\( a_0 \) was evaluated to be 0.09 in Tokyo using the same approach, that is ATLM with \( T = 14 \) [25] but 0.117 in Israel. It may come
from the difference in pandemics with and without vaccination. Anyway, the difference between the two is not large, and thus, the currently obtained α₀ is reasonable. For more information, the conventional strain during the first wave of the pandemic and the delta strain in the fifth-wave pandemic both observed in Tokyo have 0.164 [8] and 0.121 [25], respectively.

In the present study, ATLM did not include the asymptomatic patient. Nonetheless, the prediction succeeded in explaining the profile of various observed data trends within a tolerable range of errors, especially for the number of isolated individuals and infections at large. This fact suggests that most symptomatic patients if any might have been non-infectious in Israel.

**Limitations and future work**

Limitations of the present method are as follows: First, the present vaccination model presumed the random order of receiving vaccines based on age and sex in a community in concern; however, senior citizens received vaccines on a priority basis and then middle-aged and younger generations follow in Israel. This might have increased the positive number more than the present numerical results because the active generation is likely infected due to their higher human contact.

Secondly, we assumed no waning of vaccination immunity. This assumption is proper if the vaccine injection rate is sufficiently rapid to induce a waning of immunity.

No available data have been established on the waning characteristics for the alpha variant currently under consideration. However, noting that herd immunity seems to have been established in 3 months, the above assumption is proper in the present calculation. However, this assumption cannot be applied to the omicron strain because the waning is faster than ever. Therefore, our future work should develop a method to evaluate the effectiveness in a community with the waning of immunity after considering the vaccination.

Thirdly, the present ATLM is a homogeneous model for average individuals and disregards their differences among generations. The associated parameters are the transmission rate, virtual collective population, characteristics of vaccine-waning immunity and order of vaccine injection by age.

| Variable | Unit | Value     |
|----------|------|-----------|
| T        | (day) | 16 15 14 12 10 |
| α₀       | (1/day) | 0.0995 0.104 0.108 0.119 0.135 |
| M₀       | (–) | 2 000 000 1 850 000 1 670 000 1 440 000 1 350 000 |
| x(0)     | (–) | 1705 1600 1520 1315 1080 |
| (dy/dt)_{t=20.5} | (1/day) | 251 251 251 251 251 |
| α₀T      | (–) | 1.592 1.560 1.512 1.428 1.35 |
| (dy/dt)_{peak} | (%) | 104 102 100 100 98 |
Considering the difference between generations, a heterogeneous model is needed, which is composed of generation-wise equations with relevant parameter values, which will be again our future task.

The present vaccination model is established based on the efficacy data of the BNT162b2 mRNA COVID-19 vaccine (Pfizer-BioNTech COVID-19 vaccine). It should be extended to accommodate other COVID-19 virus strains, variants and vaccines.

Fourthly, generally, deterministic approaches including the ATLM assume a homogeneous model to calculate the spread of infection. Namely susceptible as well as infectious people are supposed to be well mixed in a society at any time. In the real world, however, infection begins spreading at a specific time and place in the society and majority people move along their routine courses in daily life. Then, in a community with small size population, the routine courses may reach all through the community and the infection can spread throughout the community. To the contrary, in a community with large size population and/or area, the infection spread will not reach throughout and tends to be localized because infectious period of the virus is limited. Such population heterogeneity would limit the magnitude of infection spread. In another words, ordinary persons move around in a limited portion of the community and the possibility of encounter with those who live far away is quite small. Then, the effective size of population in a community M in terms of infection spread may be much smaller than real population size. Unfortunately, there are no good models yet to evaluate the size of M. Therefore, we estimated M empirically based on the observed infection data in a growing phase of the pandemic of interest.

In summary, this is the first study of a full simulation during the third wave of the COVID-19 pandemic in Israel accompanied by a mass vaccination campaign and simultaneous lockdown. Existing data and policymaking elsewhere would be aided by including the present model. Potential users of the present model are advised to reassess the values of delayed constants \( T, H, V \) and \( \xi \) in the model when the application to other countries is attempted because they are influenced by the difference in medical regulations or practices.

**Conclusion**

A simple numerical epidemic model ATLM was extended to simulate an entire trend of various infection-related variables by considering the vaccination campaign and simultaneous lockdown. The model is described by a single discrete DDE with explicit inclusion of the time lag of infection isolation. It provides a full simulation of various infection variables in an entire period from the initial infection through the end-point with a small number of fitting parameters. The time series data of both vaccine dose ratio and lockdown period were used in this model. The model was examined within 15% of errors compared with Israel’s various COVID-19 pandemic trend data such as daily new cases, the number of isolated people and infections at large and effective reproductive number. Moreover, parameter survey calculations for several scenarios have clarified that a synergy effect exists between vaccination and lockdown. In particular, Israel’s success in the avoidance of the onset of the rebound lies in a
high-dose rate in mass vaccination campaign so that herd immunity can be achieved before recission of the lockdown.

**Data availability**

We used time-series data of COVID-19 from 8 November 2020 to 31 March 2021, in Israel [9, 10].

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**Author contributions**

M.U. developed and verified the epidemiological model. S.K. developed the parameter identification method. M.K. examined calculation results in an alternative solution algorithm. All authors have read and agreed to the published version of the article.

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**Conflict of interest**

The authors declare that they have no conflict of interest related to this report or the study it describes.

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Appendix 1

Calculation of the first approximation of $M$ and $\alpha$

In ATLM, the infection rate (number of newly infected persons) $\frac{dx(t)}{dt}$ is given by the following equation by the susceptible population $M$ and the infection coefficient $\alpha$.

$$\frac{dx(t)}{dt} = \alpha \{x(t) - x(t - T)u(t - T)\} \left(1 - \frac{x(t)}{M}\right) \quad (A.1)$$

Here, $x(t)$: cumulative number of infected persons, $T$: number of days from infection to quarantine, $u$: the step function.

Since the data on the number of newly infected persons vary widely, an integral is used to smooth the data.

The intervals $[t_1, t_2], [t_3, t_4] (0 < t_1 < t_2 < t_3 < t_4)$ are used as those of interest.

The following equation is obtained from the integral of Equation (A.1) in the interval $[t_1, t_2]$.

$$\int_{t_1}^{t_2} \frac{dx(t)}{dt} dt = \left\{ \int_{t_1}^{t_2} \{x(t) - x(t - T)\} dt - \frac{\int_{t_1}^{t_2} \{x(t) - x(t - T)\}x(t) dt}{M} \right\}$$

(A.2)

Normally, $T < t_1$. For this reason, we set the step function $u = 1$.

Equation (A.2) is modified to obtain Equation (A.3).

$$\frac{\int_{t_1}^{t_2} \{x(t) - x(t - T)\}x(t) dt}{M \int_{t_1}^{t_2} \{x(t) - x(t - T)\} dt} + \frac{\alpha \int_{t_1}^{t_2} \{x(t) - x(t - T)\}x(t) dt}{M} = 1$$

(A.3)

Similarly, Equation (A.4) is obtained in the interval $[t_3, t_4]$.

$$\frac{\int_{t_3}^{t_4} \{x(t) - x(t - T)\}x(t) dt}{M \int_{t_3}^{t_4} \{x(t) - x(t - T)\} dt} + \frac{\alpha \int_{t_3}^{t_4} \{x(t) - x(t - T)\}x(t) dt}{M} = 1$$

(A.4)

Equations (A.3) and (A.4) are linear equations of $\frac{1}{x}$ and $\frac{1}{y}$. Then $M$ and $\alpha$ are calculated.

Usually, the following inequality holds owing to monotony of $x(t)$.

$$\frac{\int_{t_1}^{t_2} \{x(t) - x(t - T)\}x(t) dt}{\int_{t_1}^{t_2} \{x(t) - x(t - T)\} dt} < \frac{\int_{t_3}^{t_4} \{x(t) - x(t - T)\}x(t) dt}{\int_{t_3}^{t_4} \{x(t) - x(t - T)\} dt}$$

The condition (A.5) is sufficient for $M$ and $\alpha$ to be positive.

$$\frac{\int_{t_1}^{t_2} \{x(t) - x(t - T)\}x(t) dt}{\int_{t_1}^{t_2} \{x(t) - x(t - T)\} dt} < \frac{\int_{t_3}^{t_4} \{x(t) - x(t - T)\}x(t) dt}{\int_{t_3}^{t_4} \{x(t) - x(t - T)\} dt} \quad (A.5)$$

Example of Israel

The source of the number of newly infected persons is as follows.

Israel COVID: 836,926 Cases and 6,334 Deaths—Worldometer (worldometers.info)

The intervals were 29 November 2020 to 12 December 2020 (14 days) and 13 December 2020 – 26 December 2020 (14 days) before the lockdown. The number of days from infection to quarantine was $T = 14$ days. Therefore, the measured number of newly infected persons $\frac{dx(t)}{dt}$ on day $t$ was used as the data of the number of newly infected persons $T = 14$ days ago.

The cumulative number $x(t)$ of infected persons was accumulated from the minimum number of newly infected persons on 25 October.

Setting $1/M \to x$ and $1/\alpha \to y$,

we obtained the following two linear equations.

$$\begin{align*}
\frac{x}{0.00001729} + \frac{y}{9.886} &= 1 \\
\frac{x}{0.00000765} + \frac{y}{10.3176} &= 1
\end{align*}$$

From this equation, $M = 1.66714 \times 10^6$ and $\alpha = 0.104788$ were obtained. These values are the first approximations.

All integrals were calculated with the trapezoidal formula. Also, it was used for the data on the number of newly infected people $\frac{dx(t)}{dt}$. Therefore, numerically, $\int_{t_1}^{t_2} \frac{dx(t)}{dt} dt \neq x(t_2) - x(t_1)$

If the number of newly infected persons is accumulated from 15 November, almost the same $M$ and $\alpha$ are obtained.

If necessary, these are graphically tuned such that they are consistent with the measurement.