Predicting the effects of waning vaccine immunity against COVID-19 through high-resolution agent-based modeling

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Abstract

The COVID-19 pandemic is yet again on the verge of escalating, despite a hopeful case decrease recorded during spring and summer 2021, due to successful vaccination roll-outs. Together with the emergence of new variants, the potential waning of the vaccination immunity could pose threats to public health. It is tenable that the timing of such a gradual drop in the immunity of most of the vaccinated population would synchronize with the near-complete restoration of normalcy. Should also testing be relaxed, we might witness a potentially disastrous COVID-19 wave in winter 2021/2022. In response to this risk, many countries, including the U.S., are opting for the administration of a third vaccine dose, the booster shot. Here, in a projected study with an outlook of six months, we explore the interplay between the rate at which boosters are distributed and the extent to which testing practices are implemented. Projections are based on a highly granular agent-based model that provides a close, one-to-one digital reproduction of a real, medium-sized U.S. town. Focusing on the dominant Delta variant, we contemplate the waning immunity provided by the locally available Johnson&Johnson, Pfizer, and Moderna vaccines. Theoretical projections indicate that the administration of boosters at the rate at which the vaccine is currently administered could yield a severe resurgence of the pandemic, even worse than the first wave experienced in spring and summer 2020. Our projections suggest that the peak levels of mid spring 2021 in the vaccination rate may prevent the occurrence of such a scenario. Our study highlights the importance of testing, especially to detect infection of asymptomatic individuals in the very near future, as the release of the booster reaches full speed.

Winter and spring 2021 marked a long-awaited massive vaccination campaign against COVID-19, starting approximately one year after the inception of the outbreak. As of the mid-September 2021, 42.6% of the World and 63.8% of the U.S. population took at least one dose of the vaccine, while 30.8% and 54.5%, respectively, are fully vaccinated [1]. However, approaching fall 2021 brings to light a new unknown: the possibility of waning vaccination immunity and the consequent need for a third dose of vaccine —the booster shot [2]. There is evidence that the booster shot would not only restore the original protection, but would also enhance people's immunity against the most recent variants, including the widely dominant and highly transmittable Delta variant [3, 4]. Many countries, including the U.S., are starting their re-

vaccination campaigns, in an attempt to prevent new outbreaks accompanied by socially and economically disastrous restrictions [3, 5, 6].

In the next few weeks (tentatively, starting September 20$^{\text{th}}$, 2021), booster shots will become available to all the adults in the U.S. eight months after they took their second vaccine dose, with plans for expansion to people taking the one-dose Johnson&Johnson vaccine [2]. At the same time, despite a surge in new infection cases [7] and the nationwide dominance of the Delta variant [8], non-pharmaceutical interventions (NPIs) are gradually being relaxed [9], and preparations for a return to full-time in-person education and work are underway [1,10,11]. Following mass vaccinations, COVID-19 testing is continuously reduced [1], with the enforcement of mandatory testing slowly abandoned by public health authorities [12] and contact-tracing quarantine no longer required for fully vaccinated individuals [9, 13]; not to mention the ongoing trend in encouraging indoor gatherings (e.g., restaurants, bars, gyms) for the fully vaccinated. In this evolving scenario, scientifically backed policy-making is of paramount importance.

Mathematical modeling has played a key role in assisting public health authorities to combat the COVID-19 pandemic [14, 15]. Since COVID-19 onset, mathematical models are being routinely used to forecast the course of the pandemic and guide policymakers' decisions on several chief issues, including the enforcing of NPIs [16–20], the design of testing policies [21, 22], the implementation of contact tracing [23–26], and the implementation of vaccination campaigns in light of the concurrent uplifting of NPIs [27–34].

Mathematical modeling can also play a critical role in the present scenario, where vaccine-induced immunity seems to be waning, testing coverage is being lowered, and a booster shot campaign is going to be implemented. The interplay of these critical issues has received only limited attention so far. Layton et al. [4] have simulated the emergence of new virus strains, including hypothetical deadlier variants in Ontario, Canada, in light of realistic vaccination and booster campaigns implemented in the region. Their results, projected until the end of 2021, point out the need of vigilance and readiness to reinstate severe NPIs, as well as the possible importance of a large-scale campaign of booster shots. Over longer time horizons, other studies have been carried out to evaluate the potential benefits of annual re-vaccination campaigns against COVID-19. In particular, Song et al. [35] have simulated different scenarios in the loss of immunity, spanning until 2029. Their findings indicate that an annual re-vaccination campaign could avoid future COVID-19 outbreaks if the vaccine is sufficiently efficacious and provides at least

six months of protection. Sandmann et al. [36] have compared the economic burden of introducing a regular vaccination program in the U.K. to the cost associated with implementing social distancing measures for the next decade. Their work highlights the benefits of re-vaccination schemes, evidencing that they would allow to avoid large outbreaks and consequent restrictions. Lastly, Li et al. [37] have compared different re-vaccination strategies in 15 countries over the next 20 years in terms of long-term efficacy. Their findings identify a public health benefit in alternating re-vaccination between fragile older strata and highly active portions of the population, who habitually generate a high number of contacts.

All of these studies evidence that re-vaccination campaigns are key to reduce potential COVID-19 upsurges. However, none of these efforts provide detailed insight into the short-term roll-out of booster shots, which is rapidly turning into a dire issue as fall is approaching and the immunity of many people is waning. Moreover, the long-term predictions of most of these studies are limited to coarse-grained considerations, which cannot take into account granular details of the population.

Here, we fill in this gap by providing a systematic study of the effectiveness of a re-vaccination campaign in the upcoming 2021–2022 fall/winter season, considering as key factors the rate of administration of booster shots and the population coverage of testing policies implemented during this phase. We perform our study by means of a high-resolution agent-based model (ABM), which faithfully provides a one-to-one digital reproduction of a real, medium-sized U.S. town. As a test case, we simulate COVID-19 spreading in the town of New Rochelle, NY, for the next six months, expanding on our previous efforts [22, 33]. The digital town closely mirrors the geography and demographics of the actual one, including household distribution, lifestyles, and mobility patterns of its residents. The progression model is expanded to incorporate salient features of the predominant Delta variant [8], booster shot campaign, and co-existence of three vaccines (Johnson&Johnson, Pfizer, and Moderna) providing different levels of protection over time. The level of detail in the model allows us to closely study the combined effect of booster shot administration and testing practices in this stage of the pandemic.

Materials and Methods

Our computational framework consists of two components: a detailed database of the town of New Rochelle, NY, and a high-resolution ABM that reproduces the spread of COVID-19 at a one-to-one granularity level that includes mobility patterns among households, schools, workplaces, and non-essential locations (including leisure locations).

The database of the town contains geographical coordinates of every building, residential and public. It includes any workplace and non-essential location, identified using SafeGraph [38], explicitly distinguishing schools, retirement homes, and hospitals. Town population is recreated using U.S. Census data on residents age, household and family structure, education, and employment characteristics. Residents can work and gather in New Rochelle, and in its vicinity, including New York City. They commute to work via common means such as public transit, cars, or carpools, and visit each other in private.

Each resident of New Rochelle is mapped into an agent in the ABM. In the ABM, agents are characterized by a health state that can change according to a disease progression model detailed in the following, and they can take two types of tests — safe, contact-less car tests, and more risky ones performed in a hospital. If infected, agents may undergo three types of treatment — home isolation, routine hospitalization, and hospitalization in intensive care unit (ICU). The ABM was originally proposed in Truszkowska et al. [22], while a later extension of the work incorporated a simplified version of the vaccination campaign [33].

For this projective study, we tailored the ABM to capture the scenario as of fall 2021, thereby introducing realistic and time-dependent vaccination effects, booster shots, increased mobility of fully vaccinated agents, and CDC-compliant contact-tracing measures [13, 39, 40]. In the following, we detail these new features. For details on the other features of the model, the reader should refer to our previous publications [22, 33]. Figure 1 schematically illustrates major components of our computational framework.

COVID-19 progression model

In our model, all the agents who are not infected, with exception of those recently recovered, are susceptible to COVID-19. Once infected, agents can undergo testing and treatment. Agents who are not symptomatic can get

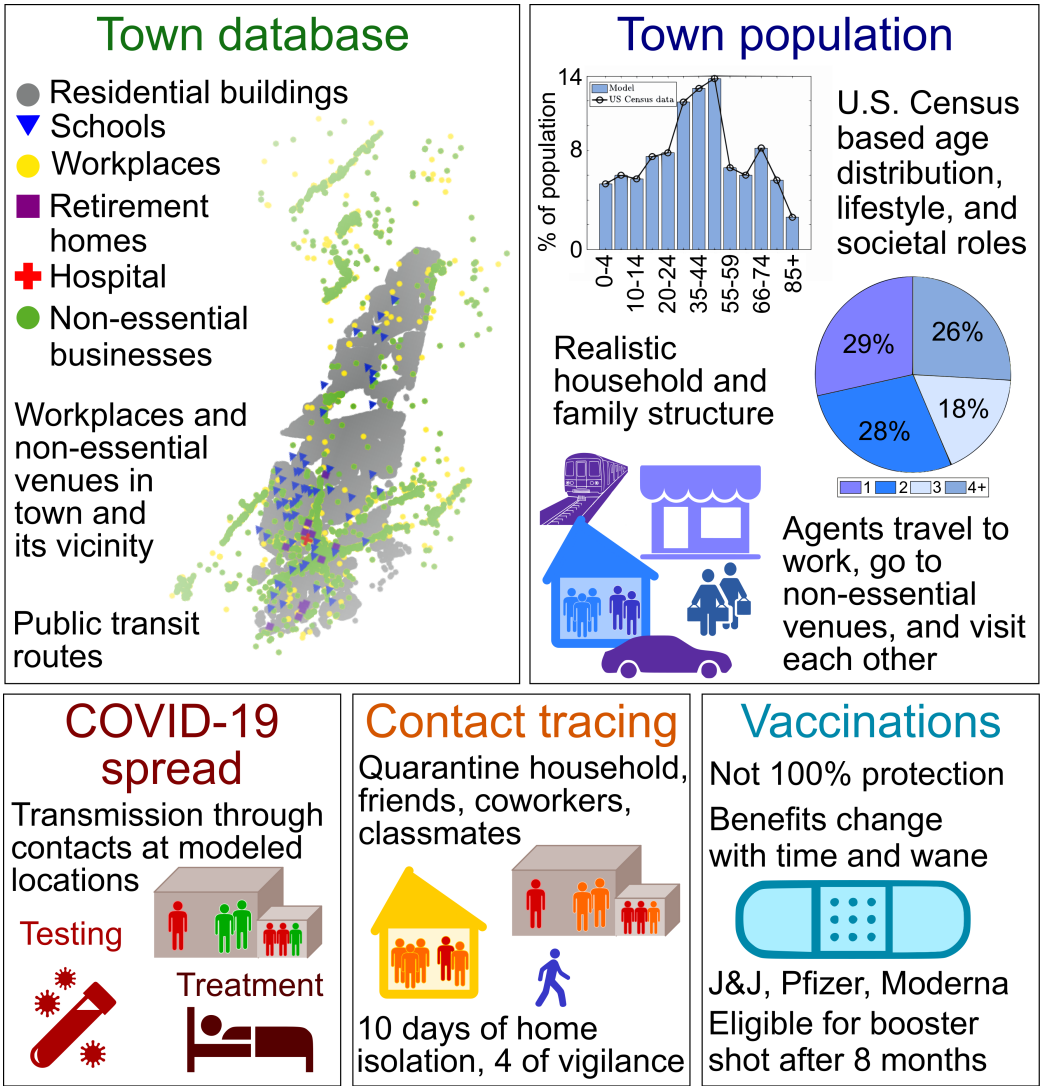

Fig 1. Schematic outline of the ABM computational framework. The database of New Rochelle, NY, includes geographical information of every residential and public building in the town. It also incorporates workplaces and non-essential venues in the area as many town residents work outside of town and some frequent non-essential locations locations in its vicinity. Each resident is represented as an agent. The population faithfully mirrors the sociodemographic profile of the actual one. The top-right panel shows the age distribution of agents, as registered in the U.S. Census data. The pie chart represents the percentage of households with the indicated size, also in close agreement with the Census (values omitted for clarity). COVID-19 spreads through contacts at different locations associated with the agents, and infected agents can be tested and treated. Positive test result triggers contact tracing, resulting in CDC-compliant quarantine of potentially exposed individuals. Finally, the platform models imperfect, realistic vaccines, which grant a number of benefits, and wane with time. After 8 months, vaccinated agents become eligible for a third vaccine dose, the booster shot.

vaccinated, and anyone can be contact-traced and quarantined.

The progression model is shown in Fig 2. A susceptible agent (S) can be vaccinated (S_v), may be home isolated, irrespective of their vaccination status, as a result of a quarantine order due to a contact with an agent with a confirmed COVID-19 infection (I_{CT}). Isolation may also be triggered if a susceptible agent has COVID-19-like symptoms due to some other disease, such as seasonal influenza (I_{Hm}). Agents can be tested, via one of the two available testing types, in a car (T_c) or in a hospital (T_{Hs}). The former type is considered contact-less and safe, while the latter carries infection risks.

Upon infection, a susceptible agent becomes exposed (E), not showing symptoms of the disease. The exposed agent can also get vaccinated (E_v) as long as their infection status is not known. Even without any symptom, exposed agents can be tested and home isolated. Agents can either recover after being asymptomatic (R), or develop symptoms after the latency period and transition to the symptomatic state (Sy). Symptomatic agents cannot get vaccinated, which is also the case for agents with symptoms similar to COVID-19 due to another disease. However, vaccinated agents can become symptomatic as a result of an infection (Sy_v), potentially leading to milder symptoms.

Agents with symptoms can test and subsequently receive treatment through home isolation (I_{Hm}), normal hospitalization (H_N), or hospitalization in an intensive care unit, ICU (H_{ICU}). Agents can either recover or die (D). Symptomatic and exposed agents can also get contact traced, and home isolated on that account. A contact-traced symptomatic agent will undergo treatment regardless of their testing status. Recovered agents are temporarily immune to COVID-19 and, after a certain period of time, they can also be vaccinated. Once their natural immunity is lost, these agents transition to the vaccinated susceptible category (S_v).

Contact-traced agents cannot be vaccinated, and even if susceptible, they become vaccine-eligible only after some period of time. These restrictions hold for the booster shots as well. The booster shot, modeled as a third vaccine dose, becomes available to agents starting from the day they are supposed to be subject to immunity waning. Present policies suggests that, on average, individuals are in this status after eight months from vaccination [2]. An agent receiving a booster shot follows the same progression as any vaccinated agent.

All the parameters that characterize the transitions in the COVID-19 progression model are listed in Table 4. An explicit expression of the contagion

probability for each agent i, $p_i(t)$, depending on the agent's characteristics (including lifestyle, workplace or school, household in which they live) can be found in Truszkowska et al. [33]. The main elements of novelty of the present modeling extension include realistic treatments of the effect of vaccination and contact tracing and are detailed in the following.

Vaccinations

An agent can get vaccinated with one of the three vaccine types distributed in the area according to their availability. We considered one vaccine mirroring the one-dose Johnson&Johnson (abbreviated as J), and two vaccines with the characteristics of the two-dose Pfizer and Moderna vaccines (abbreviated as P and M, respectively). The probability of being administered a given vaccine type was computed based on data collected manually on actual vaccine offer in the town, as of late July 2021, see Table 5 [41].

Once agent i is vaccinated, five of the model parameters related to the individual are modified accordingly. Specifically, four quantities decrease upon vaccination: (1) the probability of being infected by COVID-19, (2) the transmission rate if infected, (3) the probability of requiring hospitalization, and (4) of dying if infected. Conversely, (5) the probability of being asymptomatic when infected increases upon vaccination.

To model such a temporal effect, for each vaccine $\alpha = J, P, M$ and for each model parameter $k = 1, \ldots, 5$, we introduce a function $\gamma_{\alpha,k}(s)$, which models the effect of vaccine α on parameter k as a multiplicative coefficient, s time steps after vaccine administration. As an example, the probability of COVID-19 infection $p_i^v(t)$ for agent i vaccinated with vaccine α at time t_i is reduced compared to the original probability in the absence of vaccination $p_i(t)$ to

$$p_i^v(t) := \gamma_{\alpha,1}(t - t_i)\, p_i(t)\,. \tag{1}$$

Similar expressions can be written for the other four properties (see S1 Appendix for more details).

The shape of these functions is estimated from efficacy data on vaccines. Specifically, they are all defined as piece-wise linear functions. For the one-dose vaccine, they increase up to their most favorable values two weeks after the shot (smaller than one for property $k = 1, \ldots, 4$ and greater than 1 for property 5). In case of two-dose vaccines, the functions linearly interpolate efficacy values collected at the time of the first shot, of the second one, and at

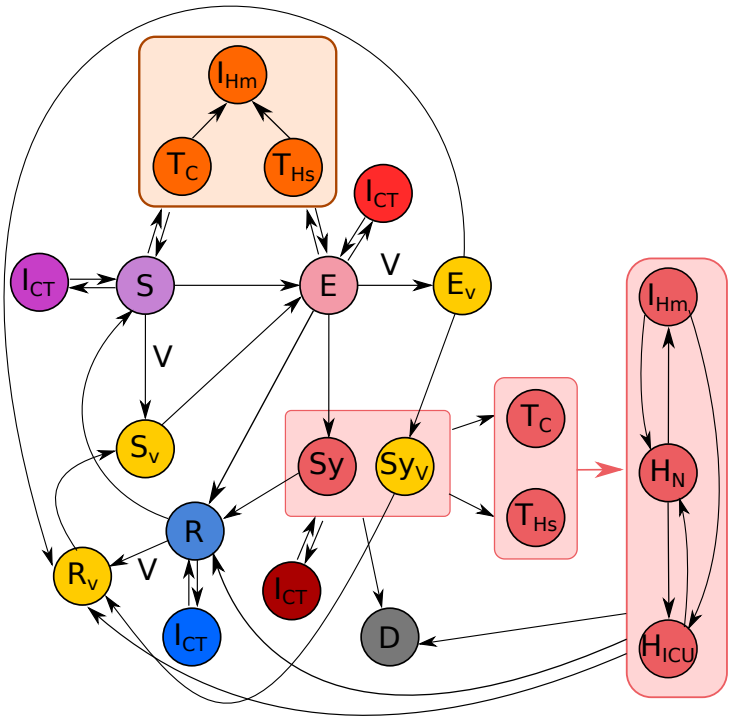

Fig 2. Diagram of the COVID-19 epidemic progression. Agents' health states are susceptible (S), exposed (E), and symptomatic (Sy). Since a vaccination does not grant 100% immunity, and exposed agents can be vaccinated, the progression distinguishes those three health states in their vaccination version, S_v, E_v, and Sy_v. Susceptible and exposed agents can be tested and home isolated (I_{Hm}). Testing can take place in a contact-less form in a car (T_c) or in a hospital (T_{Hs}). All the agents can be subject to contact tracing and subsequent quarantine (I_{CT}). Exposed agent may recover without ever developing symptoms (R), or become symptomatic after a latency period. Symptomatic agents can undergo testing and subsequent treatment through home isolation (I_{Hm}), normal hospitalization (H_N), or hospitalization in an intensive care unit, ICU (H_{ICU}). They can either recover or die (D). A recovered agent, if not already vaccinated, can vaccinate as well (R_v). Recovered agents are temporarily immune to the disease and after some period of time they become susceptible again, regardless of their vaccination status.

the attainment of full immunity. The second dose is always contemplated in the model, following local vaccination campaign that sets the appointment for the second shot at the time the first shot is administered, one month later [42]. The peak benefits for all three vaccine types last for an eight-month period following CDC booster shots recommendations [2]. In this period, the functions have a constant value. Once that period is over, the benefits linearly drop toward 1, assuming full loss of immunity over the course of six months. We assume that the booster restores peak vaccination benefits in 24 hours after its administration and that that they remain constant for a period that is longer than the simulation horizon (that is, six months). The exact expressions of all these functions and all the details on their estimations are reported in S1 Appendix.

Agents 12 years and older can vaccinate. We model local vaccine hesitancy through an upper bound on vaccination coverage in the town. An agent is considered fully vaccinated two weeks after their shot of a one-dose vaccine, or two weeks after the second shot of a two-dose vaccine. A fully vaccinated agent is more socially active, and is more likely to visit other agents or non-essential venues, as detailed in Table 4.

Contact tracing

Contact tracing implemented in the model is compliant with local guidelines [13, 39, 40] following their stricter version from winter 2021. When an agent is tested positive to COVID-19 (we contemplated a realistic quota of false positives), their household members and frequent/recent contacts are quarantined. This is modeled through targeting a predetermined number of coworkers and agents with whom they carpool, in case this is their transit mode to work.

Contact tracing of a retirement home employee results in quarantining a fixed number of residents in addition to coworkers. Conversely, a confirmed positive resident leads to a quarantine of some other residents and employees.

With respect to schools, the granularity of our model was set to the single school. Hence, contact tracing of a student who tested positive is modeled by quarantining a predetermined number of other students of same age from that agent's school, plus one teacher. This logic applies upon tracing a teacher, with a random choice of a number of same-aged students to quarantine.

Finally, since agents visit each other in private, we model contact tracing imposing a quarantine on the entire households visited by a COVID-19

positive agent during the course of 14 days, according to local policies. Due to the limited supervision on restrictions to private visits, we accounted for reduced compliance, estimating such a parameter from the literature, see Table 4. The quarantine in the model placed an agent in a home isolation for a period of 10 days. Afterwards, the agent continues to monitor themselves for COVID-19 symptoms for a duration of 4 days, reflecting the guidelines. If during this two-week period the agent develops COVID-19 symptoms, they are selected a treatment regardless their testing status. Finally, following the stricter guidelines fully vaccinated agents still have to quarantine, and negative test results do not shorten the quarantine duration.

Simulation setup

Simulations are initialized with a predetermined number of COVID-19 infected agents in the two phases of the disease, that is, exposed or symptomatic, to mimic real conditions in the town. These initial cases can be in different testing stages and undergo treatment. A certain initial number of vaccinated agents is also contemplated, based on the data collected from the vaccination campaign put in place between January 2021 and the start of the simulation. We assume a random distribution of vaccination times in the past, so that these vaccinated agents have different level of immunity at the beginning of the simulations.

Model parameters related to vaccinations and contact tracing are based on the literature and official releases from the CDC [43]. The duration of immunity is based on the CDC recommendation to sign up for the booster shot eight months after achieving peak vaccination benefits [2]. The characteristics of different vaccine types are based on official CDC and Food and Drug Administration (FDA) releases [44–49] and are outlined in detail in S1 Appendix. As indicated therein, in the absence of confirmed values, we either interpolated between the known benefit levels, or we used them for scaling. The parameters used in our contact tracing practices are also listed in Table 4, where our assumptions on the number of contacts each agent has in their workplaces, schools, and other visited locations, are detailed. The complete parameter set and all the modeling assumptions are detailed in Table 4.

The complete computational framework, including code needed to reproduce the study is available through our GitHub repository. The database is accessible through `https://github.com/Dynamical-Systems-Laboratory/`

NR-population-revac and the agent-based model through https://github.com/Dynamical-Systems-Laboratory/ABM-COVID-revac.

Results

Our simulations projected COVID-19 spreading over a time span of six months starting from September 7$^{\text{th}}$ 2021. At this time, we assumed that most of the town residents eligible for a vaccine had received their vaccination earlier in the year. As the first dose was administered in January 2021, during the six-month simulation window many of the vaccinated residents would lose their immunity. The types of the vaccines and their effects mirrored those that were distributed in the area and included the two double-dose vaccines (Moderna and Pfizer) and one single-dose vaccine (Johnson&Johnson), see Table 5. Per CDC guidelines, an agent was set to start losing their immunity at approximately eight months after they become fully vaccinated [2]. At this time, they become eligible for a booster shot, which would restore their peak resistance to the virus, thereby immunizing again the population at the rate set by the administration. The same vaccination rate was used to immunize those who were not vaccinated, including vaccine hesitancy that would prevent complete immunity of the town population.

Curbing an upcoming wave requires a vaccination rate at least equal to the rate in spring 2021

To quantify the impact of the vaccination rate on the spread of COVID-19, we performed simulations with two different rates: 0.58% and 0.11% of the total population per day. These two values correspond to the maximum vaccination rates attained at the beginning of April 2021 and the rate registered in early September 2021, respectively [50].

In our simulations, whose outcome is illustrated in Fig. 3, we assumed that effective testing practices were enacted during the entire period. In particular, we hypothesized that each symptomatic agent was tested with probability equal to 80%, while such a probability was reduced to 40% for asymptomatic agents. These parameters are representative of testing practices enacted during spring 2021 [51].

We compared the prevalence (total number of infections) and death toll for the two vaccination rates for six months starting from September 7$^{\text{th}}$, 2021.

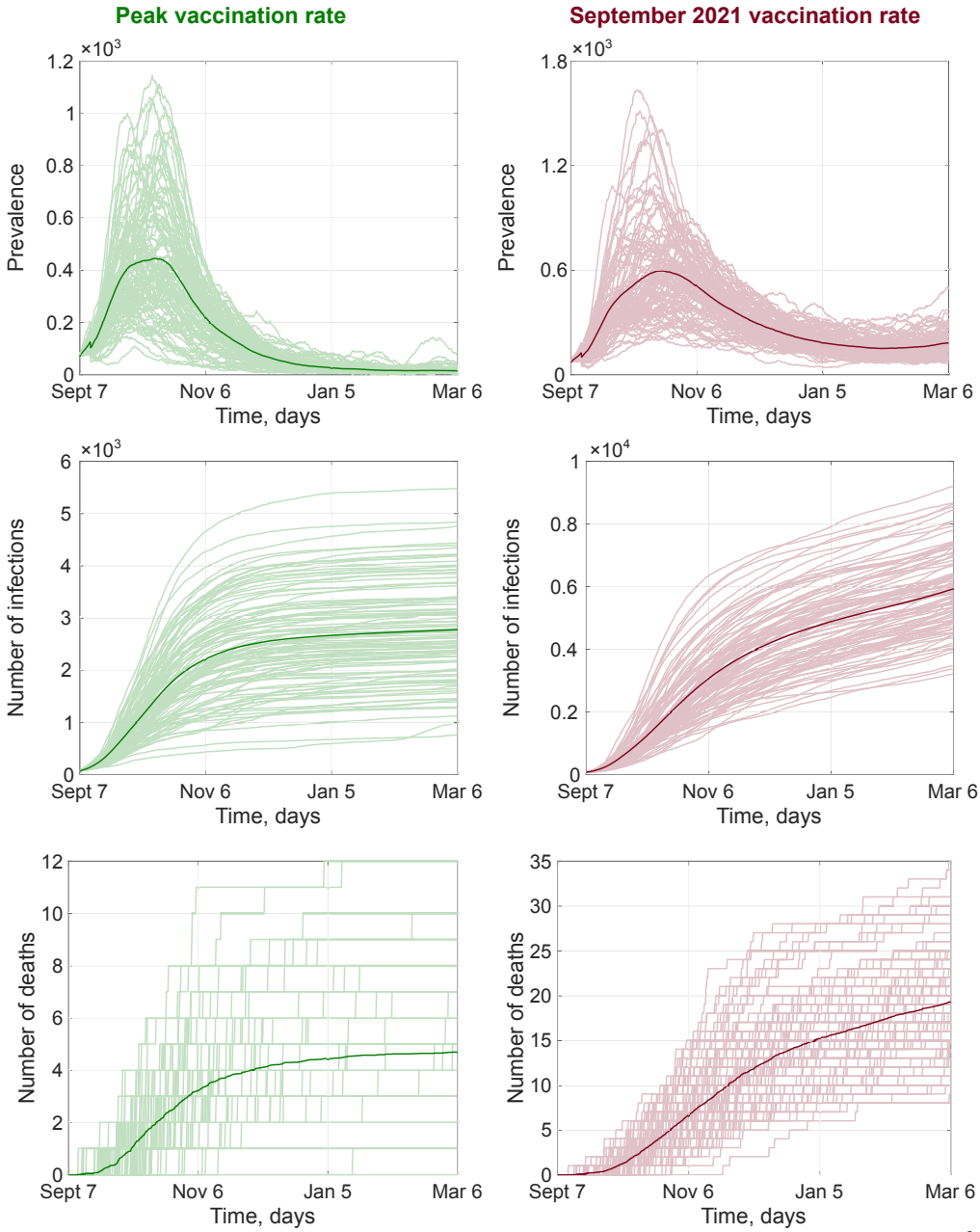

Fig 3. COVID-19 spreading over six months from September 7$^{\text{th}}$ 2021, amid two different vaccination campaigns. Prevalence, total number of infections, and total deaths for the next six months at either peak vaccination rate of 0.58% (green) or present vaccination rate of 0.11% (red). For each scenario, 100 independent realizations are shown and their average is highlighted.

Results from Fig. 3 show that, for the higher vaccination rate (green curves), the average prevalence should increase, reaching its maximum around mid-October. The average peak of prevalence should exceed 400 active cases per day, and then it should quickly drop in few weeks, potentially reaching the end of the outbreak at the beginning of 2022. On the contrary, the current vaccination rate (red curves) would lead to a 50% increase in the peak number of cases per day. Even more alarming is the projection that it would not be sufficient to eradicate the disease, leading to a possible slow rise in number of cases during winter 2022. These results indicate the need to maintain a fast pace during the booster campaign toward curbing potential upcoming waves and quickly eradicating the disease.

Testing is still needed, even with high high vaccination rates

We also investigated the role of testing and contact tracing implemented during the booster shot campaign, toward elucidating the impact of these practices, their interplay with the vaccination rate, and, ultimately, to understand whether massive testing campaigns are still needed in this phase.

We conducted a parametric study by varying the vaccination rate and the overall efficacy of testing practices over a two-dimensional grid. Specifically, we considered re-vaccination rates ranging between 0.01–5% of the population per day. These two extreme values represent scenarios in which the entire re-vaccination campaign would last more than 20 years or just 20 days. For context, the peak vaccination rate was 0.58% during April 2021 and the lowest rate was 0.027% in mid-summer 2021 [50]. The efficacy of the testing practices was encapsulated by a global parameter, termed "testing efficacy," which measures the probability that a symptomatic agent is tested. In the simulations, we varied such a parameter from 10% to 100%, representing scattered to ideal testing.

We performed these parametric studies within three different detection scenarios, according to the ability of detecting pre-symptomatic and asymptomatic agents (hereby, referred to as exposed): high detection (in which exposed agents are tested with the same probability of symptomatic ones), medium detection (in which the probability for an exposed individual to be tested is reduced by 50% with respect to the one of a symptomatic agent), and low detection (in which exposed agents reduce the probability of being

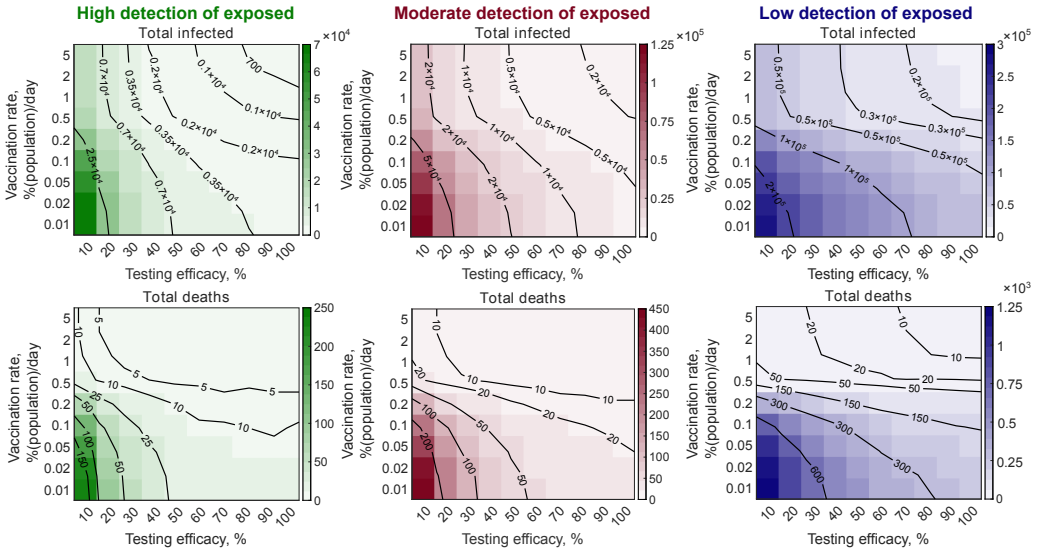

Fig 4. Interplay between re-vaccination rates and testing efficacy. Two-dimensional heat-maps showing the combined effect of vaccination rate and testing efficacy on the total number of infected and deaths over a period of six months starting from September 7$^{\text{th}}$ 2021. Three different detection levels of exposed agents capture a range of contact tracing efforts.

tested to 10% of the one of symptomatic agents). While high detection of exposed is ideal —but likely unrealistic, since asymptomatic infections are more difficult to be detected without a massive implementation of testing practices and contact tracing— medium and low detection are representative of testing practices seen since the onset of the pandemic [51].

Our results, shown in Fig 4, highlight the need to continue testing during the upcoming booster shot campaign. In particular, for all the examined detection scenarios, testing less than 20–30% of symptomatic agents always resulted in a dramatic increase of infections and deaths. To overcome the ensuing surge it would necessary to apply unprecedentedly high vaccination rates of 1–5% of the total population per day, likely beyond the capacity of the healthcare system that we have seen in spring 2021.

Our results also emphasize that detecting pre-symptomatic and asymptomatic agents is a critical issue. In fact, for all combinations of re-vaccination rate and testing efficacy, reduced detection of such agents results in a many-fold increase of total number of infections and deaths. For example, with low detection of exposed agents (third scenario, in blue in Fig. 4), the number of

deaths may exceed over 600 (that is, approximately 0.8% of the population of the town), reaching peaks of more than 1,000 deaths in the worst case scenarios of both low testing efficacy and low re-vaccination rates.

Discussion

The chief goal of this work was to systematically analyze the spread of COVID-19 in the upcoming 2021 fall/winter season, as immunity gained due to vaccination wanes over the year and testing practices change. Toward this aim, we extended a mathematical model designed in our previous efforts [22, 33], a high-resolution ABM of a medium-sized U.S. town faithfully reproducing spatial layout, demographics, and lifestyles of urban areas, to quantify the effects of a range of vaccination and testing efforts. As in our previous studies, we focused on the town of New Rochelle, NY, which was the location of one of the first COVID-19 outbreaks in the U.S., and is representative of many towns in the country [52].

Complementing our earlier efforts, we enhanced the capabilities of the computational framework along three main directions. First, we considered realistic types and administration of vaccines, as well as time-varying vaccination benefits, including waning immunity after an eight-month period and adminstration of a booster shot [2]. Second, immunity achieved through recovery was also considered to be no longer permanent [53]. Third, we modeled contact tracing, consistent with the CDC and local health department guidelines [13, 39, 40]. Overall, the current model is a highly realistic and detailed digital representation of the town and its residents, with the resolution of a single individual, thus allowing for reliable "what-if" analyses of the epidemic during the upcoming fall/winter season. Equipped with a new parameter set tuned on the now-dominant Delta variant, we studied the local outcome of the interplay between the rate of vaccination and efficacy of testing practices.

Predictably, we found that low testing efficacy may lead to a disastrous increase in both infections and deaths, irrespective of vaccination efforts of any intensity. In fact, low testing efficacy seems to hamper any benefits that would be offered by realistic re-vaccination campaigns. The final count of cases and casualties would be substantially independent of vaccination rates, unless booster shots were administered to more than 1% population per day (an unrealistic scenario, since it is almost twice as much as the peak

vaccination rate during spring 2021). For low-to-moderate testing efficacy, vaccination rates below 0.5% consistently lead to a case and death toll comparable with those experienced during the first wave [22].

These results, in agreement with other studies on testing practices during previous phases of the COVID-19 pandemic [26,54], highlight the central role of testing, contact tracing, and quarantining in the fight against COVID-19 and echo the "Path out of the Pandemic," presented by the U.S. Government on September 10^{th}, 2021, as part of "President Biden's COVID-19 Plan" [55].

To contain COVID-19 mortality below the level of the first wave, we predict that at least 0.5% of population per day should be immunized/re-immunized, as testing and contact tracing are carried out with moderate efficacy. Such a 0.5% vaccination rate is not unreasonable, given that the local vaccination rate during spring 2021 measured 0.57% of town population [50]. Vaccination rates below 0.5% might lead to scenarios that are worse than those recorded in spring 2020 [1]. In particular, using a vaccination rate equal to the vaccination rate adopted in September 2021 would lead to a potentially disastrous rise in the number of infections around the beginning of 2022. While the number of deaths projected in this scenario are still lower than those in the first wave, likely due to reduced mortality rates of vaccinated individuals, the steep increase portends that this number would ultimately overcome first wave figures.

These projections emphasize the importance for a booster shot, in line with the "President Biden's COVID-19 Plan" [55] that highlights the need of "further protecting the vaccinated" (with the booster shot). To efficiently combat the spread, the booster shot campaign should be conducted on a scale close to the one implemented during the peak immunization efforts in spring 2021. Similar conclusions have been drawn by other authors. For example, Layton et al. [4] report doubling of deaths by late December 2021 in Ontario, Canada, as a consequence of reducing the baseline vaccination rate by 20%. Sandmann et al. [36] predict the occurrence of up to two annual COVID-19 waves in the UK, whose magnitudes are strictly tied to vaccine efficacy and active NPIs. In the worst case scenario, it is expected that there will be a new wave this fall, with a magnitude comparable, or even higher, than the one observed during 2020. Similarly, Song et al. [35] indicate reoccurring new surges in the worst cases of vaccination efficacy and immunity duration, and a constant, but non-zero COVID-19 incidence in the best scenarios, starting from mid-2021.

Testing of symptomatic individuals plays a key role in controlling the

spread, especially when it is accompanied by moderate contact tracing efforts. Seen from another perspective, testing a mere 40% of the symptomatic individuals with moderate contact tracing efforts should avoid exceeding mortality rates of the first wave. Beyond a 60% testing efficacy, the effect of increased testing is diluted and higher vaccination rates are needed to bring down mortality rates. While testing levels of 40% or above are achievable [51], lower levels might be afforded by reducing delays in testing and contact tracing [25, 26].

Likewise, the detection of asymptomatic individuals is of paramount importance to combat the spreading. In particular, going from high- to low-detection of such individuals more than doubles the number of cases and deaths. This finding is consistent with the literature, whereby efficacious tracking of the asymptomatic individuals has been shown to arrest the progression of the spread of the virus [56,57]. High detection rates can be realized with aggressive contact tracing strategies that can identify stranger contacts in addition to close contacts [58]. At the same time, while it is reasonable that most people who develop symptoms or are informed of exposure to an infected individual will isolate, and possibly test, detecting asymptomatic individuals could become progressively more difficult, especially with general decline in social distancing practices and lifting of mandatory testing by many employers and institutions [1, 12].

While insightful, our results are not free from limitations. Though calibrated in real data, the high granularity of our model comes at a cost of a series of assumptions. Importantly, immunity due to vaccination was modeled based on educated guesses due to limited data availability. Except for waning immunity benefits from vaccination, all the parameters in our simulations were time-invariant; in real settings factors such as NPIs or testing coverage are likely to change in response to emerging situations [59, 60] and, likewise, vaccination rates to dynamically change. Moreover, we tested the general, uninfected population in a non-random fashion, and contact tracing guidelines within our model were more conservative than those currently in-place.

The need to administer booster shots must also be put in context with respect to medical, social, and moral concerns [3, 61]. First, the waning of immunity is still not confirmed with certainty, and the health effects of a third dose remain, to some extent, unexplored [3]. It cannot be excluded that a third dose may only selectively boost the efficacy for individuals who are immunocompromised or whose initial vaccination had low efficacy [62]. Also,

any adverse effects of the third dose may have a negative impact ok vaccine acceptance [62]. Second, with less than 5% of the populations in low income countries being fully vaccinated, the World Health Organization has deemed every booster shot as "ethically questionable" and warned that unmitigated COVID-19 pandemic in those areas will continue yielding new variants [61,63]. Despite these concerns, countries have already started their booster shot campaigns in an attempt to curb the risk of new surges and restrictions [64]. These decisions are likely driven by the Delta variant, which dilutes the herd-immunity thresholds estimated for the wild-type strain [65–68].

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S1 Appendix

Here, we detail additional information on the model, building in our previous work [22, 33]. We refer to these two publications for details about the framework; here, we focus the presentation on the new elements introduced in this study and changes with respect to the previous implementations (such as those due to the Delta variant).

Vaccination

In the following, we expand the corresponding subsection in the Materials and Methods with details on modeling the effects of vaccinations on COVID-19 progression. Specifically, once an agent i is vaccinated, five parameters in the original model [22] related to that individual are modified: (1) the probability of being infected by COVID-19, (2) the transmission rate, (3) the probability of requiring hospitalization, (4) the probability of dying, and (5) the probability of being asymptomatic.

The extent to which these five parameters are impacted for an agent i depends on the vaccine type $\alpha \in \{J, P, M\}$ and the time elapsed t_i since the vaccine was administered. Specifically, a parameter (or function) $k = \{1, 2, \ldots, 5\}$ is modified by vaccine α, s time-steps after the first dose is administered through a function $\gamma_{\alpha,k}(s)$. The functions corresponding to the five parameters are detailed next.

The probability of being infected by COVID-19 for a susceptible unvaccinated agent i is denoted by $p_i^v(t)$. Upon being vaccinated vaccine α at time

t_i this probability is reduced to

$$p_i^v(t) := \gamma_{\alpha,1}\,(t - t_i)\,p_i\,(t)\,. \tag{2}$$

Along the same lines, once an agent i gets infected with COVID-19, their transmission rate becomes

$$\beta_i^v(t) := \gamma_{\alpha,2}\,(t - t_i)\,\beta_i\,(t)\,, \tag{3}$$

where $\beta_i(t)$ is the transmission rate for an unvaccinated agent. The probability of requiring hospitalization is similarly reduced compared to its base value χ_i to

$$\chi_i^v(t) := \gamma_{\alpha,3}\,(t - t_i)\,\chi_i, \tag{4}$$

and the probability of dying decreases from that for an unvaccinated agent at μ_i to

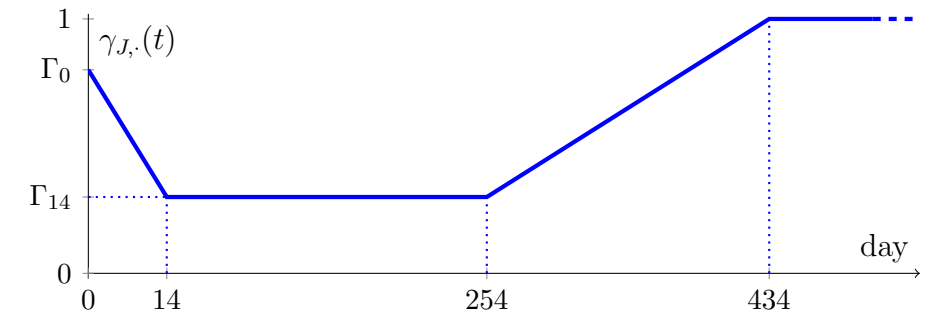
$$\mu_i^v(t) := \gamma_{\alpha,4}\,(t - t_i)\,\mu_i. \tag{5}$$

Finally, the probability of becoming asymptomatic for a vaccinated agent increases from σ_i according to

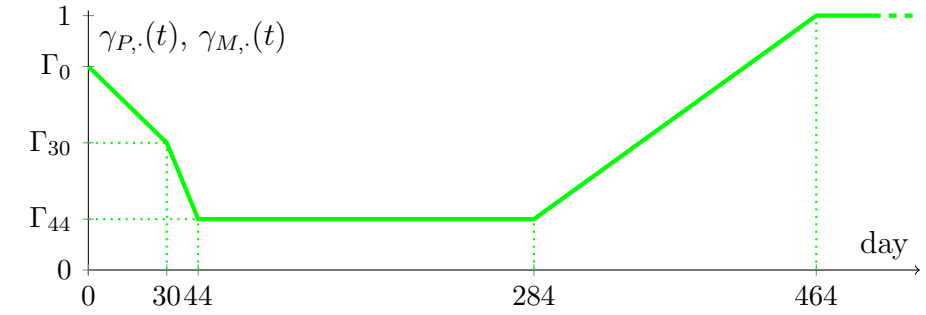
$$\sigma_i^v(t) := \gamma_{\alpha,5}\,(t - t_i)\,\sigma_i. \tag{6}$$

For unvaccinated agents, the probabilities of hospitalization χ_i, dying μ_i, and becoming asymptomatic σ_i depend only on testing practices and age, and are therefore independent of t. Instead they depend on time for vaccinated agents, as illustrated in Eqs. (4)–(6).

The functions $\gamma_{\alpha,k}(s)$ have a piece-wise linear form, controlled by k and α. Specifically, the functions are designed to reach a peak value in 14 days after the single shot of Johnson&Johnson, and in 44 days for the two-dose vaccines. Functions decrease for parameters $k = 1, \ldots, 4$ and increase for parameter $k = 5$. Since, the peak benefits from vaccines last for an eight-month period (following CDC recommendations for when a booster shot should be taken [2]), the functions are designed to attain a constant value in this window. Once the corresponding 254 day period after the vaccination is over, the benefits linearly interpolate to 1 over the course of six months (that is, until day 434), beyond which they remain at 1. Hence, the curve is fully determined by two parameters: the value of the function immediately following vaccination (Γ_0) and the peak value (Γ_{14}), as illustrated in Fig. 5a. These values are reported in Table 1.



(a)



(b)

Fig 5. Shape of the functions γ for a) a one-dose vaccine (in blue) and for b) a two-dose vaccine (in green).

In case of two-dose vaccines, the functions have two discontinuities as the linearly change to a peak value: one at the moment when the second shot is administrated one month after the first shot (day 30), and second two weeks (day 44) after the second shot. Similar to the one-dose vaccine, the peak benefits are then kept constant for an eight-month period [2]. Once that period is over (that is, from day 284), the benefits linearly go to 1, losing them over the course of six months (day 464). Hence, here the curve is fully determined by three parameters: the value of the function immediately following the first shot (Γ_0), the value at the moment of the second shot (Γ_{30}), and the peak value (Γ_{44}), as illustrated in Fig. 5b. These values are reported in Table 2 and Table 3 for the Pfizer and Moderna vaccine, respectively.

The characteristics of vaccination effects were based on the data officially distributed by CDC [44–46] and the Food and Drug Administration [47–49]. If the data for all the modeled time points was not available, we uniformly interpolated between the known values. In cases where there was only one or two datapoints, we scaled the parameter relative to one with most reported datapoints. For example, we assumed that the increase in probability of never developing symptoms, when unknown, changed proportionally to the established vaccine efficacy (that is $1 - \gamma_{\cdot,1}(s)$). If no data was available, we guessed the value based on the parameter type and its relation with other vaccine benefits. In particular, we let the transmission reduction follow the drop in infection probability. We also used this relationship to extrapolate the reduction in hospitalization likelihood for the Moderna vaccine ($\gamma_{M,3}$).

We assumed that the booster shot restores peak vaccination benefits in 24 hours after its administration and retains such benefits for a period that is longer than the simulation horizon (that is, six months). Hence, if an agent i receives the booster shot at time $\tilde{t}_i$, then all the five parameters that are affected by the vaccinations detailed in the above take their peak values, that is, we set $\gamma_{J,\cdot}(t) = \Gamma_{14,\cdot}$, $\gamma_{P,\cdot}(t) = \Gamma_{44,\cdot}$, and $\gamma_{M,\cdot}(t) = \Gamma_{44,\cdot}$, for all $t > \tilde{t}_i$.

Table 1. Values of the functions γ from the one-dose Johnson&Johnson vaccine at different times. The known (reported) values are indicated in bold.

	Function	Γ_0	Γ_{14}
Infection	$\gamma_{J,1}(s)$	**0.405**	**0.337**
Transmission	$\gamma_{J,2}(s)$	0.405	0.337
Hospitalization	$\gamma_{J,3}(s)$	**0.233**[1]	**0.146**
Death	$\gamma_{J,4}(s)$	0	**0**
Asymptomatic	$\gamma_{J,5}(s)$	1.19	1.326

[1]This value was reported after a 14 day period, but since it is lower than the peak value we use it at the moment of the vaccination.

Table 2. Values of the functions γ from the two-dose Pfeizer vaccine at different times. The known (reported) values are indicated in bold.

	Function	Γ_0	Γ_{30}	Γ_{44}
Infection	$\gamma_{P,1}(s)$	**0.476**	**0.095**	**0.05**
Transmission	$\gamma_{P,2}(s)$	0.476	0.095	0.05
Hospitalization	$\gamma_{P,3}(s)$	0	**0**	**0**
Death	$\gamma_{P,4}(s)$	0	**0**	**0**
Asymptomatic	$\gamma_{P,5}(s)$	1	1.524	1.6

Table 3. Values of the functions γ from the two-dose Moderna vaccine at different times. The known (reported) values are indicated in bold.

	Function	Γ_0	Γ_{30}	Γ_{44}
Infection	$\gamma_{M,1}(s)$	**0.25**	0.154	**0.059**
Transmission	$\gamma_{M,2}(s)$	0.25	0.154	0.059
Hospitalization	$\gamma_{M,3}(s)$	**0.25**	0.154	**0**
Death	$\gamma_{M,4}(s)$	0	**0**	**0**
Asymptomatic	$\gamma_{M,5}(s)$	1.5	1.83	1.882

Out-of town non-essential locations

As detailed in [33], the agents in the model can visit various non-essential locations, such as grocery stores and leisure locations. Human-to-human interactions made at these places, termed non-essential locations, contribute to the spread of the disease. In [33], we only modeled the non-essential locations that were within the administrative limits of the town of New Rochelle. However, with the current uplifting of the lockdown measures, many residents of New Rochelle have started again visiting leisure and non-essential locations that are outside the town. To address this, in our new implementation of the model, we extended the database to include popular venues outside of town limits, as indicated by the SafeGraph data [38].

In our model, the risk of infection at a location is proportional to the number of infected agents therein [22]. For in-town locations, such a quantity can be exactly determined, as the model provides a one-to-one reproduction of the entire population of the town (see [33] for more details). However, this is not possible for places outside New Rochelle as it would require explicit accounting for all the people in town vicinity. Thus, we approximated the risk of infection in a out-of-town non-essential location based on the estimates on the contagion in the area in which it is located.

Following the notation from [33] and referring the reader therein for the complete mathematical model, the infectiousness of an out-of-town non-essential location λ_{N} is defined as,

$$\lambda_{\mathrm{NO}} = \beta_{\mathrm{N}} \chi_I \,, \tag{7}$$

where β_{N} is the transmission rate at a generic non-essential location, and χ_I is the COVID-19 prevalence reported for the geographic region around the town [69–71].

Delta variant

To adapt the spreading to the locally dominant Delta variant, we increased transmissibility of COVID-19 by a factor of 1.6 [72]. We also reduced the average latency period to 3.7 days [73]. All these changes are detailed in Table 4.

Changes in the behavior of symptomatic agents

Infected agents with symptoms can no longer visit non-essential locations. This also holds for agents with COVID-19 like symptoms due to other diseases such as seasonal influenza. Infected agents with symptoms no longer contribute to the infection risks in public transit or carpools, which reflects their complete avoidance of other community members.

Higher education

The age of agents who can attend higher education institutions changed to 18-24 (previously it was 18-21).

Table 4. Other parameters of the ABM. [1] Scaled down to town size and time-step. [2] Scaled down to town size, time-step, and doubled following calibrated percentage of asymptomatic adults in Ref. [22], used as a proxy for underdetection. [3] Scaled down to town size, time-step, and doubled following calibrated percentage of asymptomatic adults in Ref. [22], used as a proxy for underdetection; this is the total number of cases recovering from COVID-19 during an average recovery period used in Ref. [22] and scaled with the new latency duration.

	Value	**Reference**
Increase of all COVID-19 transmission rates due to Delta variant	1.6	[72]
Fraction of the population that is estimated to be infected in the area at a time-step	0.0003	[69–71]
Infectiousness in a out-of-town workplace	0.000318	[69–71]
Infectiousness in a out-of-town leisure location	0.00010944	[69–71]
Current capacity of public transit compared to its maximum capacity	0.66	[74] for public transit
Fraction of susceptible agents with COVID-19-like symptoms	1e-6	[75]
Latency period	log-normal distribution with 1.225 mean and 0.418 standard deviation, days	[73, 76]
Fraction of the nominal transmission rate at workplaces, public transit, carpools, and leisure locations associated with current reopening efforts	0.2	[74] for workplaces
Fraction of agents going to leisure locations at each time-step	0.5	Assumption
Fraction of fully vaccinated agents going to leisure locations at each time-step	0.75	Assumption

Initial number of vaccinated agents	51,342	[50][1]
Maximum number of agents that can be vaccinated	64,364	Assumption
Time before recovery and vaccination eligibility	21 days	Assumption
Duration of natural immunity after recovery	180 days	Assumption
Compliance to home isolation after potential exposure from a house guest (contact tracing)	0.109	[77]
Maximum number of quarantined coworkers, students, or retirement home residents	10	Assumption
Duration of the quarantine	10 days	[13, 39, 40]
Duration of the after-quarantine awareness	4 days	[13, 39, 40]
Number of initially infected agents in the town	4	[69]
Number of agents that are initially active COVID-19 cases	66	[1][3]

Table 5. Parameters related to vaccinations and booster campaign.

	Value	**Reference**
Fraction of people taking Johnson&Johnson vaccine	20%	[78]
Fraction of people taking Pfeizer vaccine	45%	[78]
Fraction of people taking Moderna vaccine	35%	[78]
Minimum vaccination age	12 years old	[79]
Start of the vaccination campaign	January 1st 2021	Assumption
Time for the booster to restore the peak benefits	1 day after the shot	Assumption
Duration of booster effects	240 days after the shot	Assumption
Complete end of booster effects	420 days after the shot	Assumption