SUPPLEMENTAL MATERIAL FOR:

Estimate of Undetected SARS-CoV-2 Infection in Acute Care Hospital Settings using an Individual-Based Microsimulation Model

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Introduction

The purpose of Modeling Infection Diseases in Healthcare Network (MInD-Healthcare) agent-based model (ABM) is to simulate agent movement to and from healthcare facilities. Originally built to model the natural history of *C. difficile* infection within a regional health system,[1] the ABM was adapted in 2020 to forecast hospitalizations for North Carolina during the COVID-19 pandemic. This supplement accompanies a manuscript detailing an analysis simulating the movement of people into acute care settings and SARS-CoV-2 infection rates to compare hospital testing policies over one month. Model scenarios were run under conditions reflective of North Carolina from December 15, 2021 to January 13, 2022 (Omicron [B.1.1.529 variant] dominant, high community-level transmission) under varying assumptions.

This supplement provides detailed information on modeling processes, parameter sources, calibration, and assumptions related to this analysis using NC MInD ABM. As the model is frequently updated and contains additional processes not included within this specific analysis, users can refer to a posted Overview, Design Concepts, and Details (ODD) protocol at https://arxiv.org/abs/2202.06853 for the NC MInD model in general and at https://arxiv.org/abs/2202.09243 for additional details on the COVID-19 submodel. Details on the model scenarios, analytic overview, sensitivity analyses, and output for the specific analysis are included within the manuscript.

Entities, State Variables, and Scales

The base model has two types of entities—agents and locations. Agents represent North Carolina residents as informed by a synthetic population of North Carolina. For this analysis, we modeled 5 million agents to represent the 10.6 million residents of North Carolina. Locations include over 100 nodes that are part of a geospatially explicit network. These nodes represent healthcare facilities where agents will seek healthcare during a model run and the community (**Table S1**). Agents moving between these nodes represent North Carolinians moving among healthcare facilities and the community. There are two location types: short-term acute care hospitals (STACHs) and the community. Data from the Cecil G. Sheps Center for Health Services Research, University of North Carolina at Chapel Hill was used to inform facility type, location, and bed count.[2–4]

Table S1. Location type and count of facilities in the ABM

Location Type	Description	Node Count
STACH	Short-term acute care hospitals[3,5]	104
Community	Everything outside of the healthcare facility types	1

Agent movement among households is not modeled, nor is agent interaction within a household. Agents located in the community node can be conceptualized to be anywhere in the community other than a modeled STACH. Healthcare facility locations (i.e., all noncommunity nodes) have static variables, including name, physical location (i.e., county and geocode), bed count, and a unique identifier (Facility ID) that is used throughout the ABM (**Table S2**). Agents who move to one of these locations are given a specific bed within the healthcare facility. At that time, an agent is added to the "Agents" attribute of the location node. STACH nodes have beds designated as intensive care unit (ICU) or non-ICU beds. Not all North Carolina counties have a modeled healthcare facility. Note that most variables are not relevant to the community node.

Table S2. Location node specific variables

Variable	Description	Dynamic	Type	Range
Bed Count	non-ICU and ICU	No	Integer	1-1000+
Name	Healthcare facility name	No	String	N/A
Category	Healthcare facility category	No	String	N/A
County	North Carolina county of the healthcare facility	No	String	1, 3, 5, … 201
Agents	Current agent IDs	Yes	List	N/A
Facility ID	Unique facility identifier	No	Integer	0-540

Each time step (i.e., 1 day), an agent's location state can be updated. The location state corresponds to the current location for that agent. An agent's life state is a binary variable (i.e., living or dead). Agents also have several demographic attributes (age, county of residence) based on the RTI SynthPop™ and attributes related to SARS-CoV-2 (COVID-19 disease state, vaccination) presented in **Table S3**. Throughout the model run, agents who change locations are assigned additional variables. An agent's LOS, leave healthcare facility day (model date on which the agent's LOS ends if they are at a facility node), previous location, other information may be added, updated, or removed throughout the model run.

Table S3. Agent state and demographic variables of the ABM

Variable	Description	Dynamic	Type	Range	Source
Unique ID	ID for the agent	No	Integer	0-10,600,822	n/a
Age Group	Age of the agent (<50 (0), 50-64 (1), 65+ (2))	No	Integer	0, 1, 2	RTI SynthPop™ 2017 dataset
County	Home county	No	Integer	1-201	RTI SynthPop™ 2017 dataset
Concurrent conditions (i.e., comorbidities)	Binary variable for presence of comorbidities	No	Integer	0, 1	Medicare Marketscan data 2016-2017
Location	Current location	Yes	Integer	0-540	RTI SynthPop™ 2017 dataset
Life	Life status	Yes	Integer	0, 1	n/a
COVID-19	COVID-19 state: Susceptible (1); Asymptomatic (2); Mild/moderate (3); Severe (4); Critical (5); Recovered (6)	Yes	Integer	1–6	North Carolina Department of Health & Human Services
Vaccination	Boolean for vaccination or not	No	Boolean	1, 2	North Carolina Department of Health & Human Services

Temporal and Spatial Resolution and Scales

The ABM is implemented with a 1-day time step, and there is no sense of daily time in the model. A 1-day time step was selected based on the assumption that an agent is primarily at one location each day. The number of daily time steps in the model is set by an input parameter. This analysis used 30 days for each model run.

Each facility in the model is geospatially explicit based on the GPS coordinates of the facility's address. Agents in the model are also geospatially explicit because they are from a specific North Carolina County. Each county is described by the coordinates at the county's centroid. This spatial resolution was chosen based on data availability and being able to move agents to locations based on the distance between an agent's home county and each facility.

Process Overview and Scheduling

For each time step, agents can go through several different updates, we will call these updates actions. Any action that was randomly selected to occur for the current model time, is placed in a list of actions for the model to execute. These actions contain the agent's unique ID and the type of action to execute. Examples of actions include an agent seeking hospitalization from the community, being transferred from one facility to another, or dying at a facility. Randomizing the updates before they are executed is important. Resources in the model (e.g., beds) may be limited. Randomizing the actions allows resources to be used in a more realistic manner. Randomization also helps maintain a realistic simulation of an agent's day.

Model Initialization

The model is currently parametrized to conditions from December 15, 2021 to January 13, 2022. Parameters linked to sources that change over time were taken from those sources as of the specified start date. Below we describe model initialization with respect to agent demographics, agent location, and hospitalization for non-COVID-19 indications. Initializing values for SARS-CoV-2 vaccination, COVID-19 hospitalizations, and community infection with SARS-CoV-2 are described within the "SARS-CoV-2 Infection" and "SARS-CoV-2 Vaccination" subsections.

Agent demographics

Agents for the ABM are created using demographic variables provided by RTI SynthPop™.[6] This synthetic population consists of one anonymized synthetic person per row, containing the synthetic person's home county; Federal Information Processing Standard code (corresponding to one of North Carolina's 100 counties); sex (female, male); and age in years. We completed two preprocessing steps on this file to prepare it for model input:

This baseline population is slightly smaller (~10m) than the estimated population of North Carolina for 2020 of 10,600,823.[7] Rows in the synthetic population are randomly selected and duplicated until we reach the population estimate of North Carolina for 2020. Only agent demographic information such as age, sex, and general location are used; duplicating agents is acceptable here because no household-specific attributes (e.g., household size) are used. We binned the age of the agents into age groups (<50, 50-64, ≥ 65).

A base model parameter sets the number of agents to include in the model (5 million). Using a smaller population reduces the amount of time it takes a model to complete, but also reduces the accuracy and consistency of the results. Based on this parameter, rows from the synthetic population are randomly selected and an agent is initiated with the values of that row. Each agent has the same probability of being selected. Unless selected to start in a facility, all agents initially start in the community.

Agents are assigned two additional variables outside of the variables in the synthetic population: Agents are given a unique ID. This value is used to track their movements and record any events that take place. Agents are randomly assigned concurrent conditions (i.e., comorbidities) (**Table S4**) based on their age group and data from Medicare Marketscan data from 2016-2017.

Table S4. Probability of concurrent condition assignment by age group

Age Group	Probability	Source
0 (<50)	0	Medicare Marketscan data 2016-2017
1 (50-64)	23.74%	
2 (65+)	54.97%	

Location Nodes

Location entities are created using input data that provide healthcare facility names, locations, bed counts, and other attributes based on hospital discharge and inpatient data from the Cecil G. Sheps Center for Health Services Research.[3] Each facility is assigned a specific number of beds based on the input data and the number of agents in the model. The number of beds for facility i, B_i^*, is equal to the number of beds multiplied by the ratio of agents in the model, n, to the population of North Carolina, p. Each facility must have at least one bed.

$$B_i^* = \max(1, B_i * \frac{n}{p})$$

To fill these beds, starting capacities are determined by input parameters (**Table S5**).[8]

Table S5. Parameters for starting capacities of STACH and LTACH facilities

Parameter	Description	Value	Source
Non-ICU fill	Proportion of non-ICU hospital beds filled at initiation	.65	Opinion
ICU fill	Proportion of ICU hospital beds filled at initiation	.50	Opinion

Each STACH is initiated with ICU and non-ICU agents to match starting capacity percentages specified by model parameters. Alternatively, in cases where individual hospital capacity data are available from another source, the model can initialize non-ICU and ICU capacities to the provided levels. Parameters control whether a global fill value is used or if real data are used. When using input parameters, STACHs will not all start at the same capacity level. Instead, they will start at capacities that reflect both their reported discharge data and the input parameter. On average, hospitals will start at capacities equivalent to the fill input parameters for non-ICU and ICU beds. The following is used to estimate hospital-specific starting capacities. Let H_{NB} be the number of non-ICU beds, H_{TB}be the total number of beds, H_{Tp}be the total number of discharged patients, and H_{LOS} be the mean LOS for hospital H. H_c is the average capacity for non-ICU beds of a facility based solely on discharge data.[2,3]

$$H_c = \frac{H_{NB}}{H_{TB}} * H_{TP} * \frac{H_{LOS}}{365}$$

Let R be the ratio of the input parameter, *non-ICU fill,* and the estimated average capacity of all hospitals. Then H_c^* , the actual starting capacity of hospital H for non-ICU beds given the discharge data and the input parameter, is $R * H_c$. A similar process is completed for ICU beds.

We do not model agents that are not North Carolina residents. However, several hospitals have large amounts of individuals from states other than North Carolina. Some hospital beds will be assigned *placeholder agents*. These placeholder agents represent agents at each facility that are not North Carolina residents. Placeholder agents do not move and do not have attributes and the total number at each facility remains constant for a model run. The number of placeholder agents is determined by multiplying the capacity of a facility by the proportion of discharges that were not North Carolina residents.

Agents are selected to fill hospital beds based on their home county and the discharge data for each hospital.[3] The probability that a bed will be filled by an agent from a specific county is equal to the number of discharges from that hospital and county divided by the total number of discharges from that hospital. After counties have been selected, agents within those counties are chosen based on their age (**Table S6**).[2]

Table S6. Probability of hospitalized agent being from a specific age group

Age Group	Probability
0 (<50)	40.99%
1 (50-64)	20.12%
2 (65+)	38.90%

All agents who were assigned a starting location other than the community are assigned a *remaining LOS* value. This value is drawn from a distribution created by aging facility-specific LOS distributions. This process is completed before ABM execution and is solely used to create

a *remaining LOS* distribution. This aging process consists of continuously pulling values from the normal LOS distribution as days are simulated. For each day that passes, 1 day is removed from the drawn values. After enough time has passed for the distribution to reach a steady state, whatever values remain that are greater than 0 are used as the remaining LOS distribution. These distributions are only used during model initialization.

Agent Movement

Movement from community to healthcare facility

Each agent in the community has a daily probability of leaving the community and going to an acute care setting for a non-COVID-19 indication or a COVID-19 indication. In the community movement step, the probabilities of movement for each agent are compared to random numbers to see if that agent will leave the community. When the action is executed, the agent will be assigned to a specific location and given an LOS. This "first-choice" location is based on an agent's home county and how often facilities admit patients from that county.

Movement from healthcare facility to community

Agents in healthcare facilities only leave that facility when their length-of-stay (LOS) ends. We use the location transition probabilities to determine the healthcare facility type of the agent's next destination or to determine if the agent dies. A random probability is generated, and this probability is compared to their transition probabilities. Most agents will move to the community upon discharge, but some are selected for a facility transfer. Once a healthcare facility type is determined, if a non-community node is selected, we compare a second random number to the facility transitions to determine the exact facility ID.

Anytime an agent moves to a new short-term acute care hospital (STACH), they have a probability of requiring an ICU bed. This probability is based on patient-level data previously used to calculated LOS distributions.[9] A logistic regression model was built using an agents age, concurrent conditions, and selected LOS, as well as the hospital's bed count to determine the probability of requiring an ICU bed. This probability is also controlled by an input parameter that can increase or decrease ICU stays. This input parameter was calibrated to create a steady state of ICU patients over the course of a 1-year model run.[9] For agents that arrive at an STACH, the agent is assigned an LOS based on facility-level distributions.

Healthcare facilities at capacity

It is possible that a facility will be at capacity when an agent tries to seek treatment. The following set of rules are applied when an agent goes to a facility that is at capacity:

- If the facility is a hospital, the agent will try to find any open bed, regardless of whether it is an ICU or non-ICU bed, and which type the agent initially sought.
- The agent will try to find a bed at all facilities located in their home county.
- The agent will try any additional North Carolina facilities located within a 200-mile radius of the centroid of the agent's home county; this value is controlled by an input parameter.

If the agent is turned away from their first-choice facility, that agent is added to a list of agents containing the date, location, and county. If the agent is turned away from all possible facilities, that agent is added to a list of agents who were completely turned away. Agents who are randomly selected to transfer from another healthcare facility will only try their first-choice facility. If this STACH is at capacity, the agent returns to the community. (**Table S7**).

Table S7. Distance Parameters

Parameters	Description	Value	Source
Max. Distance	The maximum number of miles a facility can be located from an agent's home county	200	Expert opinion

SARS-CoV-2 Infection

At model initiation, we assume that a certain percentage of agents are infected with SARS-CoV-2, and of those, a percentage are hospitalized for COVID-19. A percentage of agents are in the recovered state (i.e., SARS-CoV-2 infection in the last 90 days but not active infection). Susceptible-Infectious-Exposed-Recovered-Susceptible (SEIRS) compartmental models are used to generate cases of SARS-CoV-2 as model input for the ABM.

SARS-CoV-2 Infection within the SEIRS Compartmental Models

The ABM relies on daily SARS-CoV-2 infection projections. A SEIR model is a deterministic compartmental model used to simulate the spread of infectious disease. Because the ABM is being used to estimate infections during an ongoing pandemic, we altered the SEIRS approach to account for available historical data. Using a single effective reproductive number, we run an individual SEIRS model for each NC county using the following parameters (**Table S8**).

Table S8. SEIRS Parameters

Parameter	Value	Description	Source
Initial Case Multiplier	10 (02/01/20–06/01/20)	Multiplier representing unreported SARS-CoV-2 infections	Li et al., CDC, Rosenberg et al.[10–13]
Middle Case Multiplier	4 (10/01/20–12/15/21)	Multiplier representing unreported SARS-CoV-2 infections [10–13]	Li et al., CDC, Rosenberg et al.[10–13]
Current Case Multiplier	8 (12/15/21-present	Multiplier representing unreported SARS-CoV-2 infections	Assumed
Length of Infection	6 days	Average length of infectiousness	Hay et al.[14]
Time from exposure to symptom onset	5-7 days	Average number of days after exposure before someone has symptoms	Ferguson et al., Jansen et al.[15,16]
Immunity Length	90	Time after infection before moving from recovered to susceptible	CDC[17]
R_e	Varies	Effective reproductive number	Calibrated

Before running the SEIRS model to create 30-day case forecasts, we estimate the value of each compartment. These values are calculated based on the number of reported cases through the start date of the ABM using the following process:

- Case counts are smoothed using a 10-day rolling average. The smoothed cases are then scaled to ensure that the sum of the smoothed cases equals the sum of the reported cases.
- The smooth case counts are multiplied by case multipliers based on the reporting date. This multiplier represents the estimated ratio of reported cases to total infections (a majority of which are not reported).
- To estimate S_{ij} for day i and county j: we subtract the cumulative sum of infections up to that date from 1 and add back any infections that were > 200 days from day i.

$$S_{ij} = 1 - \sum_{d=1}^{d=i} Infections_d + \sum_{d=1}^{d=i-200} Infections_d$$

To estimate compartment E_{ij}: we divide the estimated infections for the next day by the population and model α.

$$E_{ij} = \frac{Infections_{i+i}}{population_j * \alpha};\ \alpha = \frac{1}{6}$$

To estimate compartment I_{ij}: we sum the previous 6 days of infections and divide by the county population.

$$I_{ij} = \sum_{i-6}^{i} \frac{Infections_i}{population_j}$$

To estimate compartment R_{ij}:

$$R_{ij} = 1 - S_{ij} - E_{Ij} - I_{ij}$$

Once each compartment has been estimated, the compartment model is run for 30 days. Each county has its own model. The final estimates of the SEIRS models produce the number of estimated infections for each county and day for 30 days after the start date. This output is used to drive new SARS-CoV-2 infections for the ABM. Vaccination status is not currently used in the SEIRS model but accounted for during the assignment of SARS-CoV-2 infection within the ABM.

Community Infection

The number of agents starting with a SARS-CoV-2 infection is determined by the start date of the model and the output of the SEIRS compartmental models. Each county will have an estimate for the proportion of infectious individuals on day 0 of the model. Random individuals from the community are selected to match a distribution of case severity. Agents are selected based on their age, using the age distribution for reported cases in North Carolina. Since severe and critical agents are initialized using known hospital case counts and are immediately assumed to be occupying a non-ICU (severe) or ICU (critical) bed, all other community cases are assumed to be asymptomatic or mild.[18]

COVID-19 Case Counts

The output of the SEIRS models provides forecasted cases to be created by the model for each county and each day of the model run. This forecasted number of cases is then inflated using a case multiplier to estimate infections. This parameter represents the underreporting of infections. Infections are further inflated to generate COVID-19 exposures for the model to create. The inflation of infections to exposures reflects the effectiveness and current level of vaccinations given the model's vaccination parameters. Vaccinated agents have a chance of being immune to COVID-19 based on the current estimation for vaccine effectiveness (further described in the subsection titled "SARS-CoV-2 Vaccination"). When an agent is selected to be exposed to COVID-19, but they are immune, the exposure is "blocked" and ignored in the model. Exposures that are not blocked become simulated COVID-19 cases. As an alternative to using SEIRS forecasts, models that simulate historical time periods can use actual COVID-19 case counts.

To inflate infections for a county, Inf_c, to potential cases for the ABM, PC_c, we use the county vaccination rate, $Vacc_c$, and the overall vaccine effectiveness, V_{eff}. When combined, we get an

estimate for the proportion of "blocked" cases. Estimated infections are inflated, so that after some cases are blocked, the number of estimated infections is created.

$$PC_c = \frac{Inf_c}{(1 - Vacc_c) + Vacc_c * (1 - V_{eff})}$$

The number of potential cases for each county, PC_c, will remain the same for each model run because the underlying county vaccination rate and underlying vaccine effectiveness do not change. However, the number of cases the model creates will change based on the scenario-specific county vaccination rate and vaccine effectiveness level.

COVID-19 Hospitalization

The base model will initialize agents in all healthcare facilities according to the process described above. Additional agents from the community are selected to start in hospitals based on input parameters specifying how many severe (non-ICU hospital bed) and critical (ICU hospital bed) COVID-19 infections at model initialization (**Table S9**).

Table S9: Count of Hospitalizations on Model Initiation by COVID Status

Agents	Description	Value
Severe	Agents are in an acute (non-ICU) hospital bed on 12/15/21	1,194 [19]
Critical	Agents start in an ICU hospital bed on 12/15/21	417 [19]

This information is not hospital-specific, and agents from the community are selected based on hospitalized COVID-19 cases by age for North Carolina (**Table S10**).[18]

Table S10: Proportion of Hospitalized COVID-19 Cases by Age

Age	Percentage of Hospitalized Cases
0–50	31%
50 < 65	25%
65+	44%

The purpose of this initialization is to have COVID-19 hospitalizations equal to the input parameters. Agents selected for COVID-19–related hospitalization are assigned a *remaining length of stay (LOS) value.* The process for creating this value is described in the original ODD. We use a COVID-19–specific LOS distribution when creating the *remaining LOS* distribution. [20(p19)]

SARS-CoV-2 Infection within the ABM

Each day several disease specific steps are taken within the ABM. Any update (action) that occurs will be added to the ABM's list of actions and placed in a random order before execution.

New SARS-CoV-2 Infection

The ABM will randomly choose individuals from the community who are susceptible to be given a COVID-19 infection. This choice is made using a weighted probability based on an agent's age, using the same distribution used for community infection initiation.

Infection severity (asymptomatic, mild/moderate, severe, or critical) is assigned according to an agent's age, vaccination status, and reported status (**Table S11-12**).

Table S11. Severity probability for reported cases (12.5% of cases)

Severity	Description	Not Vaccinated	Vaccinated
Asymptomatic	No symptoms	.05 [21]	.25 [21]
Mild/Moderate	Some symptoms; no hospitalization for COVID-19	Varies	.65
Severe	Hospitalization required	Calibrated to NC Data	Calibrated to NC Data
Critical	Hospitalization in ICU required	Calibrated to NC Data	Calibrated to NC Data

Table S12. Severity Probability for Nonreported Cases (87.5% of Cases)**

Severity	Description	Not Vaccinated	Vaccinated
Asymptomatic	See Table 5	.25	.5
Mild/Moderate	See Table 5	.75	.5

* A case multiple of 8 is used to estimate infections using reported case counts. Therefore, 12.5% of cases are reported and 87.5% of cases are not. We assume only reported cases can go to a hospital.
** There is a lack of literature for nonreported cases. We assume that vaccinated cases will be more asymptomatic because reported vaccinated cases are more asymptomatic.

If an agent is assigned an asymptomatic or mild/moderate case, their infection will last 7 days.[14] They are assigned a recovery day in the model, and their COVID-19 state will be set to "recovered" when the model reaches this day.

If an agent is assigned a severe (non-ICU hospital bed) or critical (ICU hospital bed) case, they will immediately go to a hospital. An LOS is assigned to them based on past COVID-19 hospitalizations (**Table S13**).[20]

Table S13. COVID-19–Related Hospitalization LOS Parameters

Parameter	Description	Value
LOS mean	Mean LOS: The average number of days that admitted COVID-19 agents spend in a hospital. Used in a truncated normal distribution for sampling agent LOS.	3
LOS std	Standard deviation of LOS: The standard deviation in number of days that admitted COVID-19 agents spend in a hospital. Used in a truncated normal distribution for sampling agent LOS.	5
LOS min	Minimum LOS: The minimum number of days that admitted COVID-19 agents spend in a hospital. Used in a truncated normal distribution for sampling agent LOS.	1
LOS max	Maximum LOS: The maximum number of days that admitted COVID-19 agents spend in a hospital. Used in a truncated normal distribution for sampling agent LOS.	50

Action 1: Recovery from SARS-CoV-2

Any agents whose recovery date for COVID-19 is the current date of the model will have their COVID-19 state set to "recovered." Recovered agents are assumed to be immune to infection for 200 days and half are assumed to test positively with polymerase chain reaction (PCR) testing.

SARS-CoV-2 Vaccination Status

Vaccination status is a binary (vaccinated/not vaccinated), time invariant agent state within the ABM. The model initializes with a set percentage of vaccinated agents based on input parameters (**Table S14**). This status does not change for the duration of the model run and no additional vaccinations are given. This decision is based on the short time horizon of the model (30 days). Vaccination rates for this analysis were based on reported rates at the end of the study period (e.g., Jan. 15, 2022) due to reporting delays.

Table S14. Vaccination Rates by Agent Group

Agents	Description	Value
Community (< 50)	All remaining agents (including agents in hospitals)	.47 [22]
Community (50 < 65)	All remaining agents (including agents in hospitals)	.74 [22]
Community (65+)	All remaining agents (including agents in hospitals)	.92 [22]

Agents receive vaccination assignments based on their ages and home counties. The probability of being assigned a vaccination at model initiation is p_{ac}, where a is an agent's age group and c is the home county. This value is based on the county's vaccination rate for a specific age group, CR_{ac}, the state's vaccination rate for a specific age group SR_a, and the input parameter for that age group, IP_a.

$$p_{ac} = \frac{IP_a}{SR_{ac}} * CR_{ac}$$

Vaccine effectiveness

Due to the heterogenous nature of vaccine immunity attributable to vaccine schedule and manufacturers, we implemented a single value for vaccine effectiveness intended as a population average. Vaccine effectiveness against infection was informed by the most recent data (January 27, 2022) published by the UK Health Security Agency, a pre-print from Ontario, Canada applying a test-negative design to provincial data, and a pre-print estimating vaccine effectiveness for patients receiving hemodialysis.[23–25] Due to lack of data, estimates for vaccine effectiveness against infection were informed by estimates of vaccine effectiveness against symptomatic disease.

Vaccine effectiveness against symptomatic disease caused by Omicron for recipients of two doses of Pfizer (BNT162b2) or Moderna (mRNA-1273) ranged from 25-70% at 0-3 months after last dose to 0-10% for 6 or more months since last dose.[23] Vaccine effectiveness for recipients of a booster dose of either Pfizer or Moderna ranged from 50-75% at 0-3 months after the last dose to 40-50% at 4-6 months after the last dose.[23] Buchan et al. reported that while receipt of a booster dose confers around 37% vaccine effectiveness against infection with the Omicron variant, increased waning immunity was seen for those without a booster (i.e., not up-to-date) so that by ten weeks after the last dose, there was no protection against infection.[26–29] Similarly, Spensley et al. reports a vaccine effectiveness against infection of 58% for patients receiving a booster and no protection against infection for those with two doses.[25]

Due to uncertainty around this parameter, we chose to average the vaccine effectiveness estimates reported for each group (2 doses vs. 3 doses) from the three studies (see **Table S15**). For the population vaccinated with two doses, we averaged reported vaccine effectiveness across timing (0-6+months) and settings (United Kingdom, Canada, United States) for an

average vaccine effectiveness of 7%. For the population vaccinated with three doses, the average vaccine effectiveness was 50%.

Table S15. Reported estimates for vaccine effectiveness against infection or symptomatic disease.

Number of doses	**United Kingdom Health Security Agency (all time periods)**[23]	**Buchan et al. (pre-print)**[24]	**Spensley et al. (pre-print)**[25]	**Average**
2 doses	23%	0%	0%	7%
3 doses	54%	37%	58%	50%

We did not model differing vaccine effectiveness dependent on type of vaccine, timing of doses or immunosuppression.

With data that 37% of the vaccinated North Carolina population had received a third dose by January 5, 2022, we created a weighted vaccine effectiveness of 24%.

Table S15. Reported estimates for vaccine effectiveness against infection or symptomatic disease.

Number of doses	**United Kingdom Health Security Agency (all time periods)**[23]	**Buchan et al. (pre-print)**[24]	**Spensley et al. (pre-print)**[25]	**Average**
2 doses	23%	0%	0%	7%
3 doses	54%	37%	58%	50%

We did not model differing vaccine effectiveness dependent on type of vaccine, timing of doses or immunosuppression.

SARS-CoV-2 Testing

Testing for SARS-CoV-2 infection was not simulated in the model but implemented using model output. We simulated hospital testing policies for patients admitted to short-term or long-term acute care hospitals with the following assumptions:

- Agents with severe and critical SARS-CoV-2 (i.e., requiring a non-ICU or ICU bed) were assumed to be known infections upon admission.
- Agents with mild SARS-CoV-2 infection were assumed to have answered positively to verbal screening procedures and to be known infections upon admission.
- Agents with asymptomatic SARS-CoV-2 infection were assumed to undergo testing either through rapid antigen or polymerase chain reaction (PCR) upon admission with the test sensitivity and specificity detailed below.

Rapid antigen test sensitivity and specificity

Rapid antigen tests are less sensitive for detecting the Omicron variant compared to the Delta variant in nasal samples, particularly in the first 1-2 days after infection.[30] A recent random-effects meta-analysis of the sensitivity of rapid antigen testing by the Ontario COVID-19 Science Advisory Table estimated a pooled sensitivity for the detection of Omicron infections was only 37.1%.[31] The studies cited range in estimates from 22.2% (Adamson) to 54.5% (Kanjilal 2022).[31] However, other studies have reported higher sensitivity during omicron including a preprint reporting on community testing in San Francisco and testing within a Spanish health department.[32,33] Significant heterogenicity in the performance of antigen testing may exist for detecting the Omicron variant[34] and this variance may be time varying with decreased sensitivity in the first 1-2 days of symptoms.[30] Estimated test sensitivity ranged from 37.1 to 97.6% (**Table S16**). Therefore, we used the middle of the range (67.4%) within our main analysis and decreased the sensitivity to 37% within a sensitivity. We assumed a test specificity of 98%, the negative percent agreement required for approval by the FDA for both antigen and PCR testing.[35]

Table S16. Reported estimates for rapid antigen test sensitivity for detecting omicron variant SARS-CoV-2 infection.

Source	**Setting**	**Test**	**Ct Threshold**	**Sensitivity**
Ontario COVID-19 Science Advisory Table[31]	Various settings	Various	<25	**37.1% (23.3-53.0%)**
Preprint: Goodall et al.[36]	Volunteer-led community testing site	Abbott Panbio	Not reported	**64.50% (95% CI: 52.1-75.3%)** for asymptomatic
Preprint: Schrom et al.[32]	San Francisco community testing site	BinaxNOW	<30	**89.8%** for asymptomatic; **97.6%** symptomatic
Preprint: de Michelena et al.[33]	Health Center in Spain	TaqPath COVID-19 Combo Kit	<30	**87.2%**

Drain	Summary of the literature	Not specific	Not specified	**36-82% for asymptomatic**

PCR sensitivity and specificity

PCR testing was assumed to have a test sensitivity of 77% for asymptomatic infection.[37,38] We assumed a test specificity of 98%, the negative percent agreement required for approval by the FDA for both antigen and PCR testing.[35] Studies report a range for the percent of individuals within the general hospitalized population who have persistent PCR positivity from 16.7% to 60%.[39,40] Increased age and comorbidities appear to increase the probability of persistent positivity.[40,41] We assumed that 30% of agents within the 'recovered' state (i.e., within 90 days post-infection) would test positive on PCR but negative on rapid antigen testing.

Key Data Sources for the Model

Our model was informed by the peer-reviewed literature, health department reports and data dashboards, hospital discharge data, and SARS-CoV-2 case counts from COVID ActNow. Severity of infection was informed by the peer-reviewed literature[15,42–45] as well as hospitalization data from North Carolina Department of Health and Human Services (NC DHHS).[46] To allow for replication of our analysis, below we describe the different data files used in the ABM. After the title of the file, we have provided the location in the code repository where the data file is located.

County-Distances (data/geography/…)
There are three geography files that must be included, one for each facility type. These files consist of the distance from each county center to the geocode for each facility in miles, and they are used to help select new facilities for agents. The code used to automatically create these files is available in the code repository.

Locations (data/locations/…)
To create appropriate facilities within the model, a file for each facility type is required. The hospital file (STACHs) consists of hospital name, location, and the count of ICU and non-ICU beds. It was extracted from an online list of North Carolina hospitals.[47] However, only hospitals that have information in the discharge data will be used. The nursing home file contains facility name, bed count, county, and geocode information. The nursing home facilities were taken from Centers for Medicare & Medicaid Services (CMS) data[8] and geocodes were programmatically added. The file for LTACHs was also derived from online data and contains the name, bed count, and geocode for each facility.[47]

Discharge Data (data/sheps_data/2018/…)
PDFs of the public North Carolina hospital data files are available in the repository. Data were automatically extracted from these PDFs and converted to the CSV files that the model reads as input. Code and instructions for converting PDFs to CSVs is in the code repository. There are three files:

> *Patient county of residence by hospital* provides the list of counties that agents came from for each hospital[3]
>
> *Short term acute care hospital patient characteristics* provides details on patient age group, home state of the patient, and patient disposition[2]
>
> *Short term acute care hospital discharge data* provides an LOS estimate for each facility[4]

Synthetic Population (data/synthetic_population/synthetic_population.parquet)
The synthetic population file provides agents for the model. It was provided by RTI International.[6]

COVID-19 Reported Cases (submodels/covid19/data/cases/covid19_cases.csv)
This file contains the number of confirmed COVID-19 cases by county and by day.[48] Instructions for downloading and cleaning these data are found in the repository.

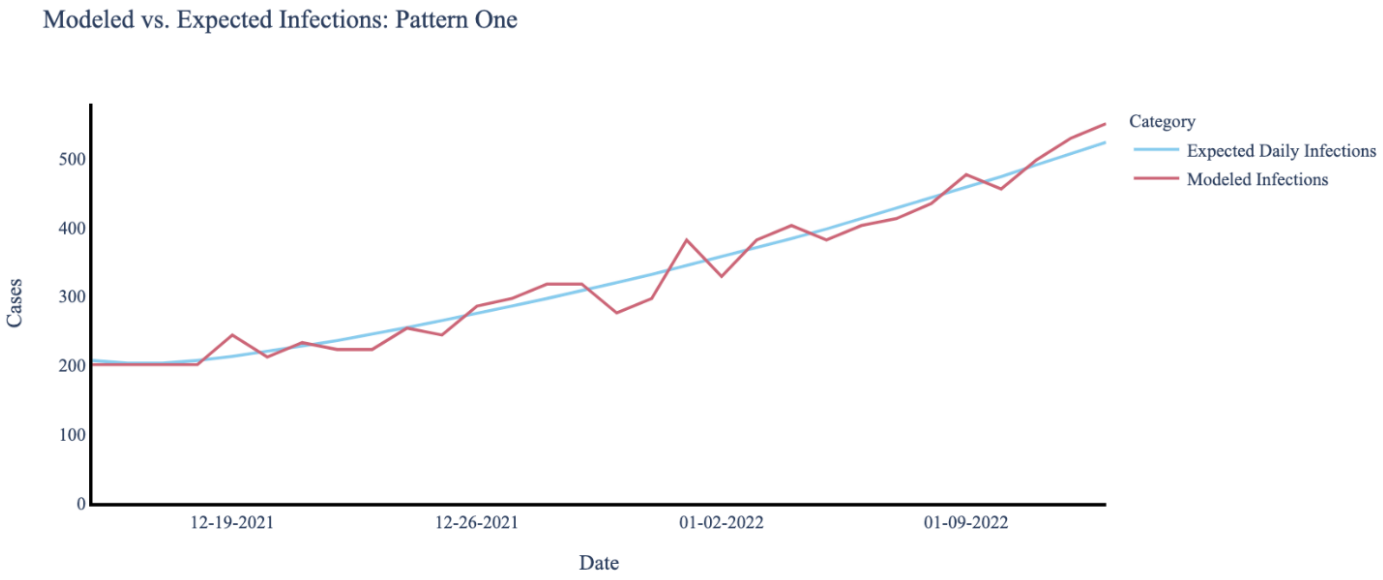
COVID-19 Vaccinations (submodels/covid19/data/vaccinations/vaccinations_by_age.csv)
This file contains the number of vaccinations by county and by age.[18] Instructions for downloading and cleaning these data are found in the repository.

Model Calibration

To calibrate the model, we evaluated the ABM by its ability to reproduce patterns related to SARS-CoV-2 case count infection severity levels, COVID-19 related hospitalizations, and additional purpose-specific patterns. We also calibrated the model to create realistic agent movement to and between all modeled healthcare facilities in North Carolina. To do so, we match known length-of-stay (LOS) values, individual facility capacities, transfers between different facility types, and agent demographics for agents in each type of facility. The example patterns below illustrate this calibration process.

Pattern 1: SARS-CoV-2 infections. We compared the daily number of forecasted SARS-CoV-2 infections by NC county to the number of SARS-CoV-2 infections produced in the model throughout the 30-day model run. **Figure S1** shows this pattern for one county.

Figure S1. Example output of modeled cases vs. expected cases for a 30-day run.



Pattern 2: COVID-19 Outcomes & Case Counts. We compared the proportion of COVID-19 case outcomes that occur in the model to the expected outcomes based on input parameters and known values. We specifically look at hospitalizations (**Table S17**) but have created a suite of additional unit tests that check additional outcomes. We test the following outcomes:

- Proportion of cases that get reported
- Proportion of cases that are post vaccination
- Modeled cases by age and vaccination match expected case counts
- Comparison of case outcomes by vaccination and reported status
- Proportion of vaccinated hospitalizations match reported values
- Proportion of vaccinated ICU hospitalizations match reported values
- Proportion of COVID-19 cases resulting in hospitalizations match reported values

Table S17 shows example output of the modeled cases by vaccination status, age group, and case outcome. The full table is available on the project repository. For this pattern, we are comparing the modeled outcome proportion to the target proportion.

Table S17: **Example COVID-19 case outcomes by vaccination status and age for reported cases**

Vaccination Status	Age	COVID State	Modeled Cases	Modeled Proportion	Target Proportion
Not Vaccinated	0	Asymptomatic	300	0.047	0.050
Not Vaccinated	0	Mild	5,919	0.936	0.935
Not Vaccinated	0	Severe	78	0.012	0.012
Not Vaccinated	0	Critical	24	0.004	0.003
Not Vaccinated	1	Asymptomatic	80	0.049	0.05
Not Vaccinated	1	Mild	1,464	0.904	0.904
Not Vaccinated	1	Severe	56	0.034	0.037
Not Vaccinated	1	Critical	19	0.012	0.009

Pattern 3: Length of stay. We compared length of stay (LOS) values assigned during a model run to the input LOS distribution for each facility. **Table S18** is the output for the four largest hospitals (by admissions) in the model. We show the modeled and expected value for admissions, average LOS, and the LOS standard deviation. Values for all facilities are available in the code repository. For this pattern, the modeled and expected values should be almost identical.

Table S18. Example model output for length of stay

Facility ID	365-day Admissions	Average LOS	Expected average LOS	Sd. LOS	Expected Sd. LOS
23	49,304	5.72	5.77	2.48	2.5
31	37,448	4.91	4.96	2.13	2.13
66	36,942	6.02	6.07	2.66	2.64
89	36,151	7.21	7.29	3.21	3.21

Pattern 4: Average capacity. We compared the average capacity value for each facility over the duration of a model run to the average capacity specified as input for each facility (**Table S19**). We also check that average capacity is consistent over the model run and does not steadily increase or decrease over time for each facility. For this pattern, we expect all large facilities to be within 5% of the expected value.

Table S19. Example model output for average capacity

Facility ID	Average Capacity	Min	Max	Sd.	Expected Capacity
23	885.14	809	960	25	894
36	740.18	677	713	25	738
89	738.26	678	799	23	723
62	639.72	578	692	21	629

Pattern 5: Agent movement between healthcare locations. We aggregate agent movement between different facility types and compare these values to aggregate North Carolina discharge data.[2] To do this, the number of all movements from one location type to another is

recorded and compared to the expected number of movements for those two location types (**Table S20**). Movement between certain location types (e.g., community to community) is not possible. For this pattern, we expected all larger targets to be within 5%.

Table S20. Example model output for agent movement between healthcare locations

Location Type	New Location Type	Target	Modeled Value
Community	Community	0	0
Community	Hospital	825,150	815,414

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