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## SARS-CoV-2 transmission in opposition-controlled Northwest Syria: modeling pandemic responses during political conflict

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### ABSTRACT

**Introduction:** Ten years of conflict has displaced more than half of Northwest Syria's (NWS) population and decimated the health system, water and sanitation, and public health infrastructure vital for infectious disease control. The first NWS COVID-19 case was declared on July 9, 2020, but impact estimations in this region are minimal. With the rollout of vaccination and emergence of the B.1.617.2 (Delta) variant, we aimed to estimate the COVID-19 trajectory in NWS and the potential effects of vaccine coverage and hospital occupancy.

**Methods:** We conducted a mixed-method study, primarily including modeling projections of COVID-19 transmission scenarios with vaccination strategies using an age-structured, compartmental susceptible-exposed-infectious-recovered (SEIR) model, supported by data from 20 semi-structured interviews with frontline health workers to help contextualize interpretation of modeling results.

**Results:** Modeling suggested that existing low stringency non-pharmaceutical interventions (NPIs) minimally affected COVID-19 transmission. Maintaining existing NPIs after the Delta variant introduction is predicted to result in a second COVID-19 wave, overwhelming hospital capacity and resulting in a four-fold increased death toll. Simulations with up to 60% vaccination coverage by June 2022 predict that a second wave is not preventable with current NPIs. However, 60% vaccination coverage by June 2022 combined with 50% coverage of mask-wearing and handwashing should reduce the number of hospital beds and ventilators needed below current capacity levels. In the worst-case scenario of a more transmissible and lethal variant emerging by January 2022, the third wave is predicted.

**Conclusion:** Total COVID-19 attributable deaths are expected to remain relatively low owing largely to a young population. Given the negative socioeconomic consequences of restrictive NPIs, such as border

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or school closures for an already deeply challenged population and their relative ineffectiveness in this context, policymakers and international partners should instead focus on increasing COVID-19 vaccination coverage as rapidly as possible and encouraging mask-wearing.

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## INTRODUCTION

### *Syrian conflict and COVID-19 in Northwest Syria*

Ten years into Syria's protracted and violent conflict, more than half of the 22 million prewar population has been displaced and more than half a million civilians have been killed, including more than 900 health workers (UNOCHA, 2020; Fouad et al., 2017). The conflict has decimated the health system, water and sanitation infrastructure, and public health infrastructure crucial for managing infectious diseases. Northwest Syria (NWS), a 2,460 square-kilometer territory bordered by Türkiye on one side and government-controlled areas on the other, has an estimated population of 4.2 million. This includes 2.6 million internally-displaced people, around 1.2 million of whom live in displacement camps (Global Shelter Cluster, 2021). The average population density is 800 per square kilometer but exceeds 5,100 per square kilometer in the Al Dana displacement camp, increasing the risk of infectious disease transmission (REACH, 2020). On July 9, 2020, the Assistance Coordination Unit/Early Warning Alert and Response Network (ACU/EWARN) announced the first confirmed COVID-19 case in NWS, a doctor aged 39 years, with July 4, 2020, reported as the date of onset (WHO, 2021a). As of May 26, 2021, EWARN confirmed 23,072 cases and 83 deaths, both of which have increased in subsequent months (ACU, 2021).

Of the many COVID-19 transmission and response risks in NWS, the greatest may be fragmented health system governance and policymaking, which means no single institution can enforce COVID-19 mitigation measures (Douedari and Howard, 2019). Four key actors help coordinate the COVID-19 response in NWS, including the World Health Organization (WHO)-led COVID-19 Taskforce, the Syrian Interim Government (SIG)-led COVID-19 National Response Team, de-facto authorities in Idlib, and Turkish-supported local councils in northern Aleppo. This affects COVID-19 response coordination and the implementation of non-pharmaceutical interventions (NPIs) in NWS. Although age is a major risk factor for COVID-19, its impact on severity and mortality in Syria may be lower given the relatively young population. Other risks in NWS that likely affect the local epidemic trajectory, include (i) transmission risks owing to high population densities and overcrowding in displacement settings, where large multi-generational households are common; (ii) poor water, sanitation, and hygiene (WASH) infrastructure in NWS's 43 sub-districts; and (iii) limited treatment owing to poor health system capacity, with total numbers of hospital beds, Intensive Care Unit (ICU) beds, and ventilators of 370, 137, and 131, respectively. This is 3 times fewer than the minimum Sphere guidelines requirement of 6.1 inpatient beds per 10,000 persons (Sphere, 2018). In May 2021, the AstraZeneca vaccine was rolled out in NWS through COVAX to initially cover 2% and then 20% of the population, primarily health workers and those with comorbidities (WHO, 2021b; Sphere, 2018; World Health Organization, 2021a; Health Cluster Turkey Hub, 2021; World Health Organization, 2021b).

### *SARS-CoV-2 surveillance and epidemiology in NWS*

ACU/EWARN expanded surveillance to include COVID-19, providing daily and weekly reports. During initial pandemic preparations in spring 2020, ACU/EWARN had only 1 testing machine with a limited daily capacity of approximately 180 tests. Testing capacity expansion in May 2020–September 2020 included 3 laboratories equipped with a total of 4 PCR machines, more staff trained in laboratory testing, and resources allocated to purchasing diagnostics, providing a total capacity of over 1,500 tests daily. WHO case definitions were used, combining clinical, epidemiological, and laboratory criteria (UNOCHA, 2021). Laboratory positivity rates varied from approximately 3% in the early stages of the pandemic to 40% at the peak of the first wave. ACU/EWARN commenced contact tracing from the first COVID-19 case on July 9, 2020, to help contain circulation and initiate isolation of cases and contacts. Although this helped limit the number of cases from the first detected cluster, other clusters appeared and the situation quickly changed from multiple clusters to community transmission. Thus, COVID-19 transmission and relevant mitigation initiatives should be considered within NWS socioeconomic realities and health system capacities (Douedari et al., 2020).

### *Objectives*

This study aimed to model 5 COVID-19 trajectory scenarios in NWS and explore potential explanations for the relatively low numbers of reported cases and deaths during the first wave. Objectives were to (i) estimate numbers of cases, hospital occupancy, and deaths if 4 of current NPIs were released for 12 months without the emergence or introduction of a variant of concern (VOC); (ii) explore interpretation and contextualization of modeling results through interviewing frontline health workers; and (iii) estimate numbers of cases, hospital occupancy, and deaths after the SARS-CoV-2 B.1.617.2 (Delta) variant emerges, and varying vaccination coverages are achieved.

## METHODS

### *Study design*

We conducted a mixed-method study, with modeling projections of COVID-19 transmission scenarios supported by semi-structured interviews with frontline health workers.

### *Modeling data collection and fitting*

#### *Model and data source*

We used an age-structured, compartmental susceptible-exposed-infectious-recovered (SEIR) model, developed by the COVID-19 International Modeling (CoMo) Consortium, and a participatory approach in engaging local policymakers throughout the modeling process (Aguas et al., 2020; Adib et al., 2021). EWARN/ACU provided the epidemiological dataset on April 4, 2021, which included daily case data (i.e. people tested positive),

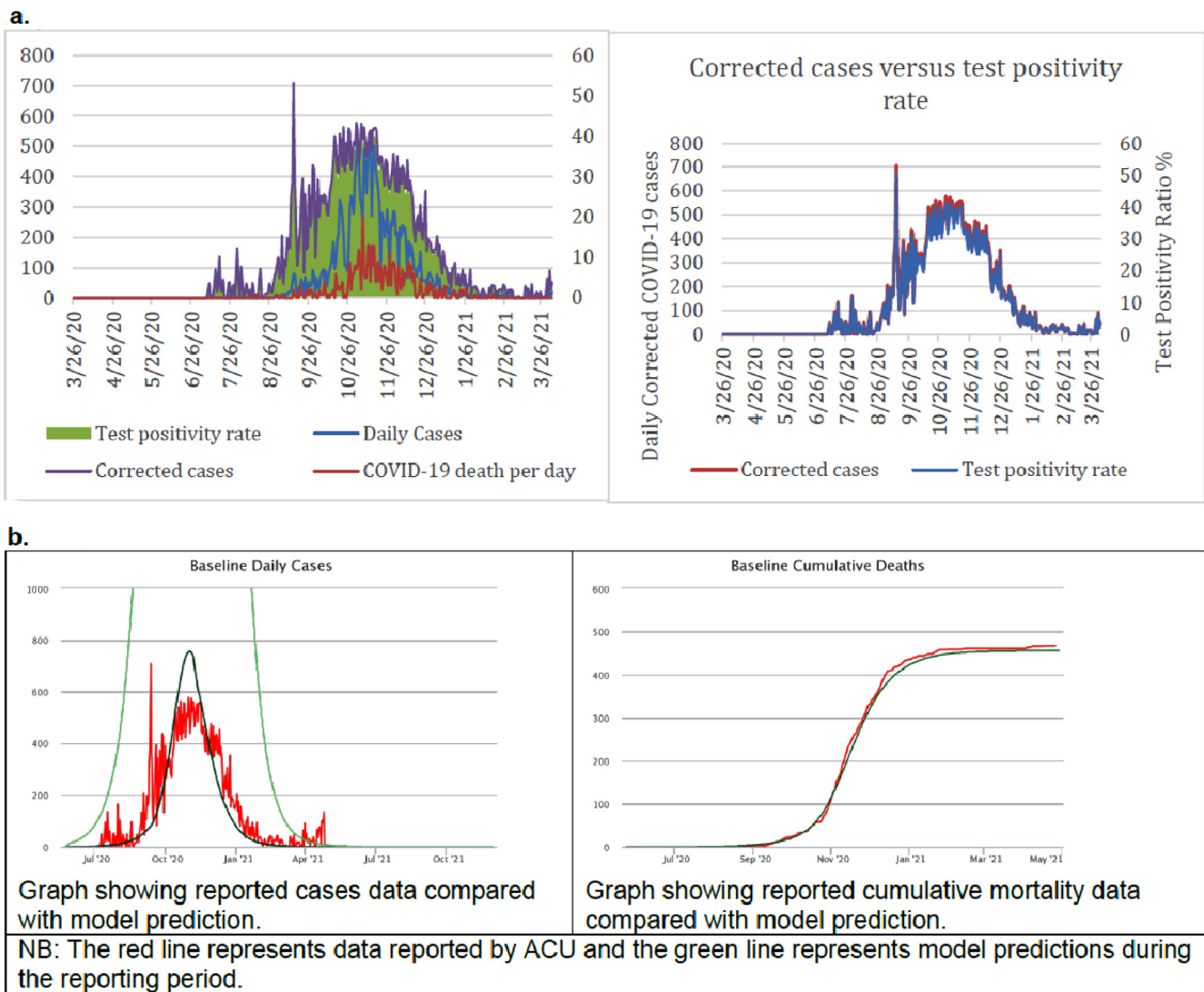


Figure 1. Model corrections and fitting.

daily deaths (i.e. deaths within 28 days of a positive test by date of death), and polymerase chain reaction (PCR) test performance (i.e. daily number of people receiving a PCR test).

Correction of COVID-19 cases

Figure 1 shows a clear reliance of reported daily cases on underlying testing efforts, which distorted the relative severity of the first wave. First, we control for the effect of daily testing capacity variation and testing effort changes in NWS on the reported daily case data by applying a testing effort correction factor consisting of the number of people PCR tested per day at the peak of the first wave in November 2020, that is, 1,400 tests per day. Each day (i) we have:  $corrected\_cases_i = (reported\_cases_i * 1400) / PCR\_tests_i$ . Then, we generated a time series of corrected case data (Figure 1a, right). The raw case series showed no time delay between peaks in cases and deaths, indicating potential under-reporting of cases when testing was low, whereas the corrected case series generated a more accurate mirroring of test positivity data.

Model fitting

Parameter estimation was performed using a particle-filtering approach through the ‘pomp’ R package and assuming the reported case and death data can be accurately described by a Poisson process. We tried to reproduce the dynamics of COVID-19 transmission in NWS by estimating the set of parameters  $q$  that maximizes

the log-likelihood (LL) of observing the daily numbers of reported deaths  $D$  and cases  $C$ ,

$$LLd(\theta|D) = - \sum_{k=1}^n yd(k, \theta) + \left( \sum_{k=1}^n \tilde{y}d(k) \ln(yd(k, \theta)) \right) - \sum_{k=1}^n \ln(\tilde{y}d(k))!$$

$$LLc(\theta|C) = - \sum_{k=1}^n yc(k, \theta) + \left( \sum_{k=1}^n \tilde{y}c(k) \ln(yc(k, \theta)) \right) - \sum_{k=1}^n \ln(\tilde{y}c(k))!$$

in which  $yd(k, \theta)$  is the simulated model output number of COVID-19 deaths at day  $k$ ,  $yc(k, \theta)$  is the simulated model output number of COVID-19 cases at day  $k$ ,  $n$  is the total number of days included in the analysis, and  $\theta = \{p; st; I_0; sc\}$  is the set of parameters to estimate, including (p) probability of infection given contact, (st) start date of simulation, ( $I_0$ ) number of infected individuals on the first day of simulation, and (sc) scaling factor for infection hospitalization rate. Two measurements, that is, daily mortality count (LLd) and daily case incidence count (LLc), are included in a weighted global function evaluating the model’s probability density function:  $LL = LLd + LLc(\max(\tilde{y}d) / \max(\tilde{y}c))$ . The last term weighs the case incidence likelihood to have the same importance for the overall likelihood as the death incidence likelihood and depends on the ratio between observed peak number of cases and observed peak number of deaths.

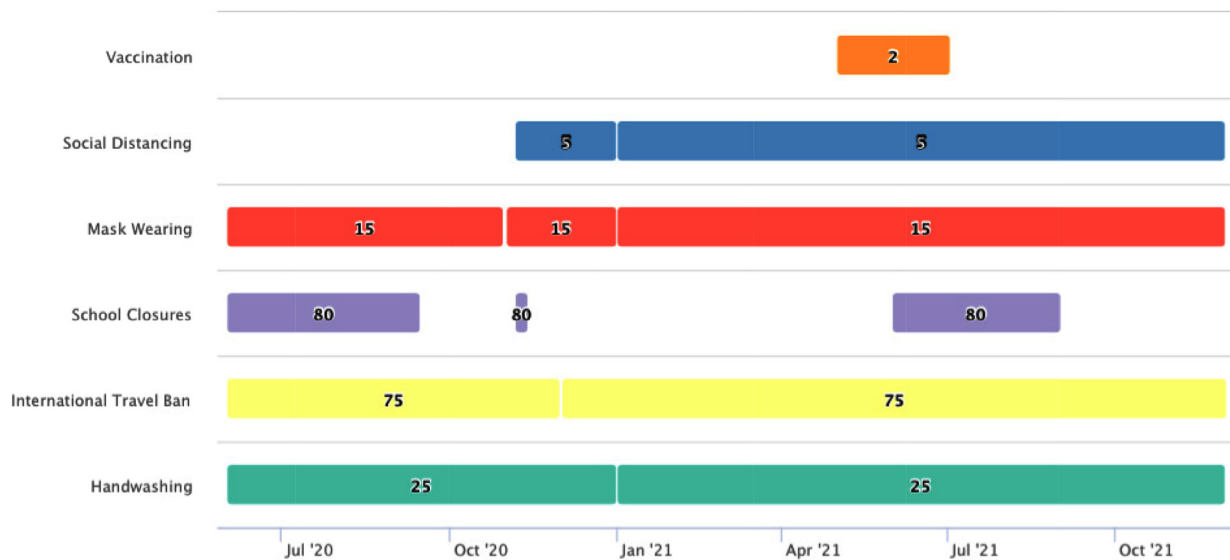


Figure 2. Timeline and coverage of non-pharmaceutical interventions in NWS.

The remaining model parameters were taken from the literature whenever possible or customized to fit the NWS context using expert opinion and local data, including population profile, hospitalization parameters, and efficacy and coverage of selected NPIs for each scenario. Apart from relevant peer-reviewed literature, parameters were based on Relief Experts Association (UDER) surveys and expertise of Syrian public health professionals and policymakers, including Idleb Health Directorate, NWS Health Information System Unit, EWAR/ACU, NWS Syria Corona Awareness Team, NWS COVID-19 Taskforce, and COVID-19 National Response Team for NWS.

Figure 1b shows results of model fitting for our baseline scenario using the following parameters: (i) estimated start date of simulation at June 1, 2020; (ii) assumed simulation end date of June 30, 2022; (iii) estimated probability of infection giving contact at 0.0127; (iv) assumed mean infection migrant per day of 0.01; (v) assumed percentage all asymptomatic infection reported at 0%; (vi) assumed percentage all symptomatic infection reported at 17%; (vii) estimated scaling factor for infection hospitalization rate (IHR) at 2.102; and (viii) average duration of immunity at 1.5 years, as there is growing evidence suggesting previous exposure to SARS-CoV-2 does not guarantee total immunity (Tillett et al., 2021). We calculated uncertainties by running the model 100 times with a 10% Gaussian noise on parameter values and depict the 95% credible intervals.

#### NPIs included in transmission scenarios

For scenario modeling, we defined *coverage* as “the proportion of people in the population adhering to interventions” and *efficacy* as “the relative change in risk of infection if adhering to the intervention.” NPIs implemented in NWS are an international travel ban, handwashing, mask-wearing, safe-distancing, and school closures. Figure 2 and Table 1 show the change of coverage in each scenario. We added vaccination as rollout began in May 2021.

1 *International travel ban*: movement was estimated at 5% pre-pandemic rates, as NWS international borders have been closed since March 2020, except for limited movement including official crossings, such as humanitarian and medical staff, traders, Turkish officials and military staff, and low-level smuggling activities between NWS and Northeast Syria or government-controlled Syria (Relief Experts Association, 2020).

- Handwashing*: coverage was estimated at 25%, based on an UDER survey of WASH access and handwashing practices in NWS and assumptions of improved hygiene practices owing to COVID-19, such as frequent 20-second handwashing with water and soap and avoiding handshaking or touching mouth, nose, and eyes (Relief Experts Association, 2020).
- Mask-wearing*: coverage was estimated at 15%, based on an UDER survey of facemask use in NWS showing approximately 10% of the population reported mask-wearing in public and other data suggesting actual rates were nearer 5% (Relief Experts Association, 2020).
- Safe-distancing*: coverage was estimated at 5%, in discussion with local decision-makers, as they estimated no more than 5% of the population adhered to restrictions on local gatherings and celebrations.
- School closures*: coverage was 80% in summer 2020, based on an UDER survey of community leaders, who postponed reopening for 2 weeks in September. Schools were then reopened with some modest interventions that rapidly reverted to normal practice (Relief Experts Association, 2020).
- Vaccination*: we assumed that AstraZeneca remains the main vaccine provided in NWS starting May 2021, with an observed efficacy of 74%, duration of the efficacious period of 1.5 years, and vaccine coverage of 2% by September 2021, and 20% or 60% by June 2022 in accordance with NWS’s approved application for COVAX support and discussion with NWS policymakers (WHO, 2021b).

#### Modeling transmission scenarios

The baseline (current) scenario predicts the impact on the COVID-19 trajectory of extending low coverage NPIs for 12 months with no VOC and 2% vaccination coverage.

Scenario 1 predicts the impact on the COVID-19 trajectory of ending 4 existing NPIs (i.e. international travel ban, handwashing, mask-wearing, safe-distancing) with no COVID-19 VOC introduced for the next 12 months alongside 20% vaccination coverage. School closures were only for a week in November 2020 and 3 months June–August 2021, whereas vaccination coverage was assumed to be 2% by May 2021 and 20% by June 2022 (i.e. in accordance with planned vaccine rollout in NWS). The remaining parameters are kept the same as in the baseline scenario.

**Table 1**  
Coverage parameters for non-pharmaceutical interventions.

Parameters	From	To	Scenario 1	Scenario 2A	Scenario 2B	Scenario 2C	Scenario 2D
Handwashing	01/06/2020	31/12/2020	25	25	25	25	25
Handwashing	01/01/2021	30/06/2022	0	25	0	50	25
International travel ban	01/06/2020	30/11/2020	75	75	75	75	75
School closures	01/06/2020	14/09/2020	80	80	80	80	80
Mask-wearing	01/06/2020	30/10/2020	15	15	15	15	15
Mask-wearing	01/11/2020	31/12/2020	15	15	15	15	15
Mask-wearing	01/01/2021	30/06/2022	0	15	0	50	15
School closures	06/11/2020	12/11/2020	80	80	80	80	80
School closures	01/06/2021	01/09/2021	80	80	80	80	80
International travel ban	01/12/2020	30/06/2022	0	30	0	30	30
Safe-distancing	06/11/2020	31/12/2020	5	5	5	5	5
Safe-distancing	01/01/2021	30/06/2022	0	5	0	5	5
Vaccination	01/05/2021	30/06/2022	20	20	20	60	20

**Table 2**  
Variant related parameters for each modeled scenario.

Virus Parameters	Duration	Transmissibility	Lethality	Breakthrough infection probability	Average duration of immunity
<b>Scenario 1</b>	01/06/2020 - 30/06/2021	1	1	0	1.5 year
	01/07/2021 - 30/06/2022	1	1	0	1.5 year
<b>Scenario 2B</b>	01/06/2020 - 30/06/2021	1	1	0	1.5 year
	01/07/2021 - 30/06/2022	1.6	1	20	1.5 year
<b>Scenario 2C</b>	01/06/2020 - 30/06/2021	1	1	0	1.5 year
	01/07/2021 - 30/06/2022	1.6	1	20	1.5 year
<b>Scenario 2D</b>	01/06/2020 - 30/06/2021	1	1	0	1.5 year
	01/07/2021 - 31/12/2021	1.6	1	20	1.5 year
	01/01/2022 - 30/06/2022	2	2	30	1.5 year

Scenario 2 predicts the impact on the COVID-19 trajectory of introducing the SARS-CoV-2 B.1.617.2 (Delta) in July 2021. This has been done by adjusting 4 parameters: virus transmissibility, lethality, breakthrough infection probability, and coverage of international travel ban. The latter was changed from 75 to 30 to allow for the entry of a new variant. Table 2 shows the coverage and duration of each of these parameters. The remaining calibration parameters were the same as for Scenario 1 with the same NPIs until June 30, 2022. We also included a worst-case scenario (2D) that enables some examination of the sensitivity of our model given limited evidence on the transmissibility, lethality, and breakthrough infection probability of the next VOC. We considered the worst-case scenario by increasing virus transmissibility, lethality, and breakthrough infection probability to 2, 2, and 30, respectively.

*Interview data collection and analysis*

To aid interpretation, OAA and YD conducted 20 interviews with purposively recruited frontline health workers at health facilities and COVID-19 treatment centers (Table 3). Inclusion criteria were (i) living in NWS and involved in COVID-19 response, (ii) aged over 21 years, and (iii) being able to speak Arabic or English. OAA and YD conducted interviews in Arabic using Zoom (Zoom Video Communications, Inc) or WhatsApp applications between March 2020 and May 2021. After providing informed consent, interviewees were asked about COVID-19 cases, responses, and issues. We analyzed data thematically, using deductive and inductive manual coding as described by Braun & Clarke (Braun et al., 2019).

*Patient and public engagement*

We used a participatory approach in modeling by engaging NWS policymakers and practitioners from the start of this study. They contributed to study design, identifying relevant research questions and scenarios, analysis, and interpretation of data. Four who have been particularly active are included as co-authors.

**Table 3**  
Interviewee characteristics.

ID	Professional Role	Sector	Gender
HCW1	Programme director	COVID-19 health center	Male
HCW2	Internal medicine specialist	Hospital	Male
HCW3	Internal medicine specialist	COVID-19 health center	Male
HCW4	Internal medicine specialist	Hospital	Male
HCW5	Internal medicine resident	COVID-19 health center	Male
HCW6	Internal medicine specialist	Hospital	Male
HO1	Field manager	NGO	Male
HO2	Manager	NGO	Male
HO3	Private health worker	Private clinic	Male
HO4	Manager	Local health authority	Male
HO5	Orthopedic resident	Hospital	Male
R1-01	Manager	Local health authority	Male
R1-03	Head of department	Hospital	Female
R2-02	Trauma Specialist	Hospital	Male
R2-03	Head of department	Hospital	Female
R2-04	Team leader	NGO	Female
R3-01	Manager	Local health authority	Male
R3-02	Trauma Specialist	Hospital	Male
R3-03	Head of department	Hospital	Female
R3-04	Team leader	NGO	Female

**RESULTS**

*Predicted COVID-19 underreporting, transmission, and case fatality rates*

Case correction and model fitting provided relatively low reporting, transmission, and case fatality rate estimates. Modeling estimated 47.5% of the NWS population would have been infected with SARS-CoV-2, with approximately 538 deaths, between June 1, 2020, and May 26, 2021. Only 1.2% population infection was reported to EWARN during the same period, though this only included symptomatic cases with no serology data available.

Modeling indicated the effective reproductive number (*Rt*) remained just below 1.5 during the first wave in July 2020 to Novem-

**Table 4**  
Summary of key modeling results.

Parameter	Baseline	Scenario 1	Scenario 2A	Scenario 2B	Scenario 2C	Scenario 2D
Simulation period	01/06/2020- 30/06/2022	01/06/2020- 30/06/2022	01/06/2020- 30/06/2022	01/06/2020- 30/06/2022	01/06/2020- 30/06/2022	01/06/2020- 30/06/2022
Total COVID-19 cases at peak	NA	NA	1,051	1,084	567	1,051
Reported and unreported cases at 2 <sup>nd</sup> peak	NA	NA	47,201	48,323	35,673	47,201
Reported and unreported cases at 3 <sup>rd</sup> peak	NA	NA	NA	NA	NA	NA
Peak date	NA	NA	Sep-21	Sep-21	Dec-21	Sep-21 (2nd Wave), March 2022 (3rd wave)
Total COVID-19 deaths	541	539	2,133	2,360	2,031	3,312
Minimum required hospital beds at peak	NA	NA	543	582	360	606
Minimum required ICU beds at peak	NA	NA	79	79	79	79
Minimum required ventilators at peak	NA	NA	133	133	132	133

NB: Baseline scenario (current situation) = extending low coverage NPIs for 12 months without any VOC and 2% vaccination coverage. Scenario 1 = Releasing low coverage NPIs without any VOC and 20% vaccination coverage. Scenario 2A = Extending low coverage NPIs for 12 months with Delta variant and 20% vaccination coverage. Scenario 2B = Releasing low coverage NPIs with Delta variant and 20% vaccination coverage. Scenario 2C = Increasing coverage of 4 NPIs with Delta variant and 60% vaccination coverage. Scenario 2D = Extending low coverage NPIs for 12 months with more transmissible variants than Delta and 20% vaccination coverage.

ber 2020, declined below 1 in December 2020, and increased to 1 by October 2021 (Figure 3a). Modeling also indicated a relatively low overall COVID-19 fatality rate, with a very low infection fatality rate (IFR) for people aged younger than 45 years and a much higher IFR for older people. Figure 3b shows reported and predicted hazard ratios by the NWS age group in years, indicating increased predicted fatality rates from people aged 35 years with the most significant increases in both predicted and reported rates from people aged 65 years.

*Qualitative explanations on under-reporting*

To explore the lower reported than predicted death rates, we asked frontline health workers for their perspectives. Most health workers suggested some under-reporting of COVID-19 deaths was owing to limited testing capacity, poor data management, and lack of coordination between public and private health sectors in NWS.

*‘There are many cases that have been treated in private hospitals, which consider out of the NWS health system coverage and do not share its health records.’ (HCW4)*

Others reported that patients with severe symptoms were hesitant to be admitted to hospitals, preferring to be treated at home, and so were never registered or included in case data.

*‘The majority of people with severe cases refused the hospitalization and demanded to be treated at home. This might be diminished the probability of being exposed to secondary hospital infections by antibiotic-resistant bacteria and decrease the case fatality rate.’ (HCW2)*

*Qualitative perspectives on low transmission*

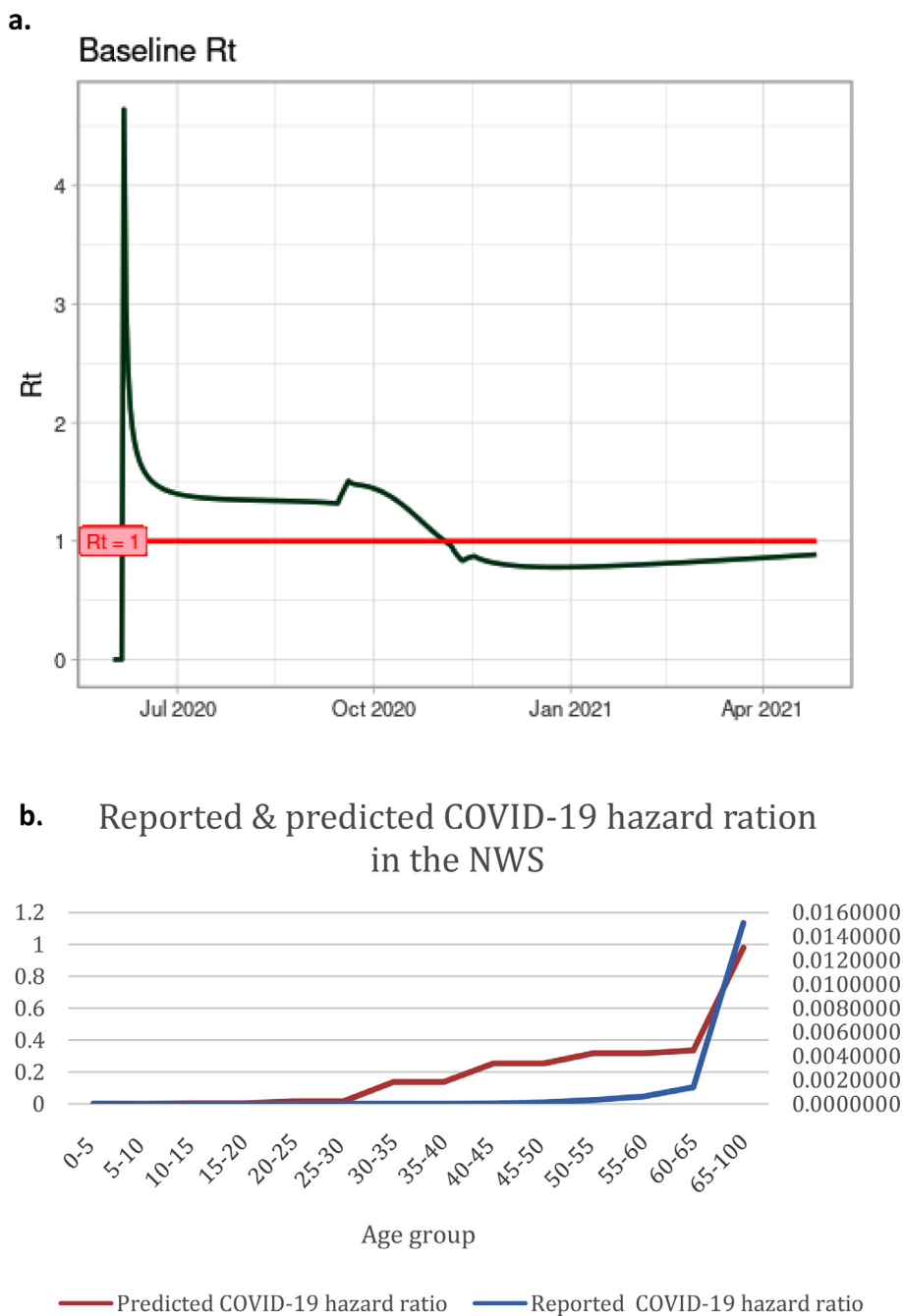
Health workers proposed several theories for the relatively low COVID-19 transmission noted in NWS. A common theory was that so many had died already that those left were more able to resist infection. Another related it to the lack of insulated shelter for internally displaced families, representing over half the NWS population, which may have had a positive unintended consequence of allowing constant airflow.

*‘The low infection rate in the camps might be explained by the nature of the tents that are torn and always open to the airflow. Furthermore, the desperate uninhabitable condition except for youth, in which elderly die due to NCDs [non-communicable diseases].’ (HCW6)*

Another theory was that relatively low COVID-19 transmission during winter could be related to communal behavior in NWS, given few public activities and constant electricity cuts had imposed an informal form of curfew that may have reduced transmission temporarily.

*‘Unlike other countries, the winter season has had a relatively positive role regarding COVID-19 pandemic in NWS. Due to the lack of electricity and the early sunset, something comparable to the curfew happens every day for 14 hours until morning, as well as a significant reduction in socialising. However, this shifting is relative. The next morning, overcrowding in schools, markets, bakeries and camps is noticed.’ (HCW2)*

Some interviewees highlighted increased public adherence to prevention measures after confirmation of the first COVID-19 case in the area and the potential effects this had on reducing transmission. In addition, one interviewee suggested women were more protected from COVID-19 in public spaces because of the conservative NWS social norms many women wore niqabs, which covered their mouth and nose.



**Figure 3.** Baseline scenario. (a). Baseline effective reproductive number in NWS July 2020-May 2021. (b). Predicted and reported age-based hazard ratios (%) in NWS.

*'Patterns of the veil of women in NWS might have an essential role similar to the face-masks. Almost 30% of women wear the niqab as a religious habit.'* (HCW1)

**Qualitative suggestions on the low case fatality rate**

Health workers suggested that low case fatality rates could be owing to natural or cross-immunity from other infections or vaccination.

*'NWS population might have unique characteristics such as low median age, strong immunity due to previous infections since childhood, multiple vaccines administered, vegetable diet, and rural lifestyle in general.'* (HCW5)

**COVID-19 transmission scenarios**

**Scenario 1. Ending low-coverage NPIs with no VOC and 20% vaccination coverage**

This transmission scenario predicted 48.9% of the NWS population would be infected with SARS-CoV-2 by June 30, 2022, with 550 cumulative attributable deaths, and Rt remained below 1 between November 2020 and August 2021, then reached 1 by August 2021 and remained around 1 until June 30, 2022 (Figure 4). This scenario further predicted no second COVID-19 wave, as the herd immunity threshold was reached during the first wave (Table 4), and indicated limited NPI effectiveness and adherence since the start of the pandemic in NWS. As a health worker reported:



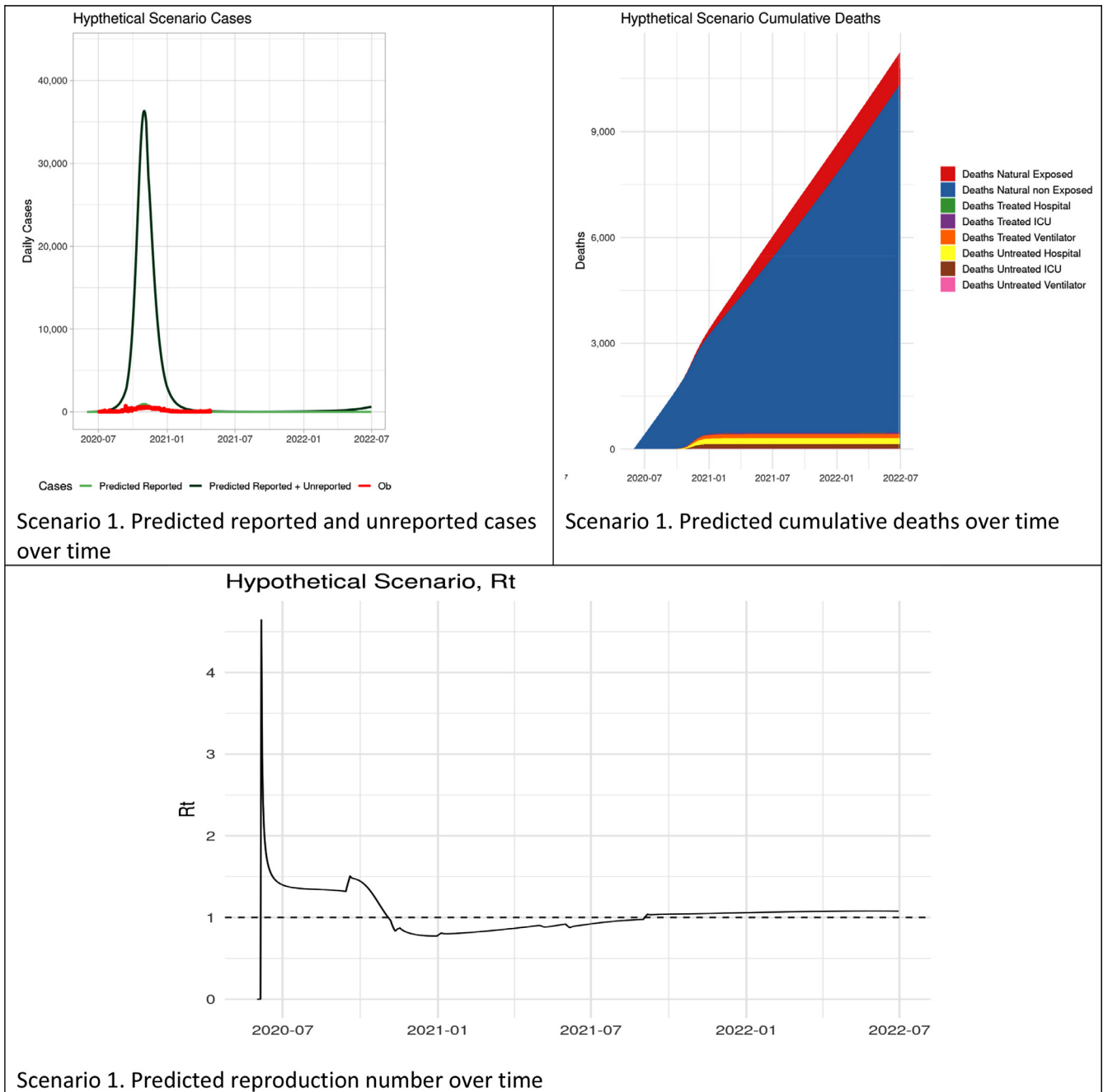


Figure 4. Scenario 1 Predictions of cases, deaths, and reproduction number.

'NPIs have little impact on the ground, and few people adhere to them. Despite the small number of interventions implemented, such as facemasks and hygiene practices, nothing seems to have significant impact except partial travel and border restrictions.' (HCW2)

**Scenario 2. Introducing variants**

This transmission scenario predicted that the introduction of a new variant in NWS would result in a second wave of infections, with hospital bed needs exceeding existing capacity unless NPIs are increased (Table 4).

**Scenario 2A. Extending NPIs for 12 months and introducing the Delta variant with 20% vaccination coverage**

This scenario predicted that the introduction of the SARS-CoV-2 Delta variant at the end of June 2021 would result in a second wave around December 2021, with 47,201 symptomatic and asymptomatic daily cases at its peak and 2,133 total deaths (i.e. a fourfold increase). It further estimated the numbers of hospital beds, ICU beds, and ventilators required at the peak of the second wave would be 543, 79, and 133, respectively.  $R_t$  was predicted to be above 1 between January 2022 and June 2022, reducing to 1 by June 2022 (Figure 5, Scenario 2A)

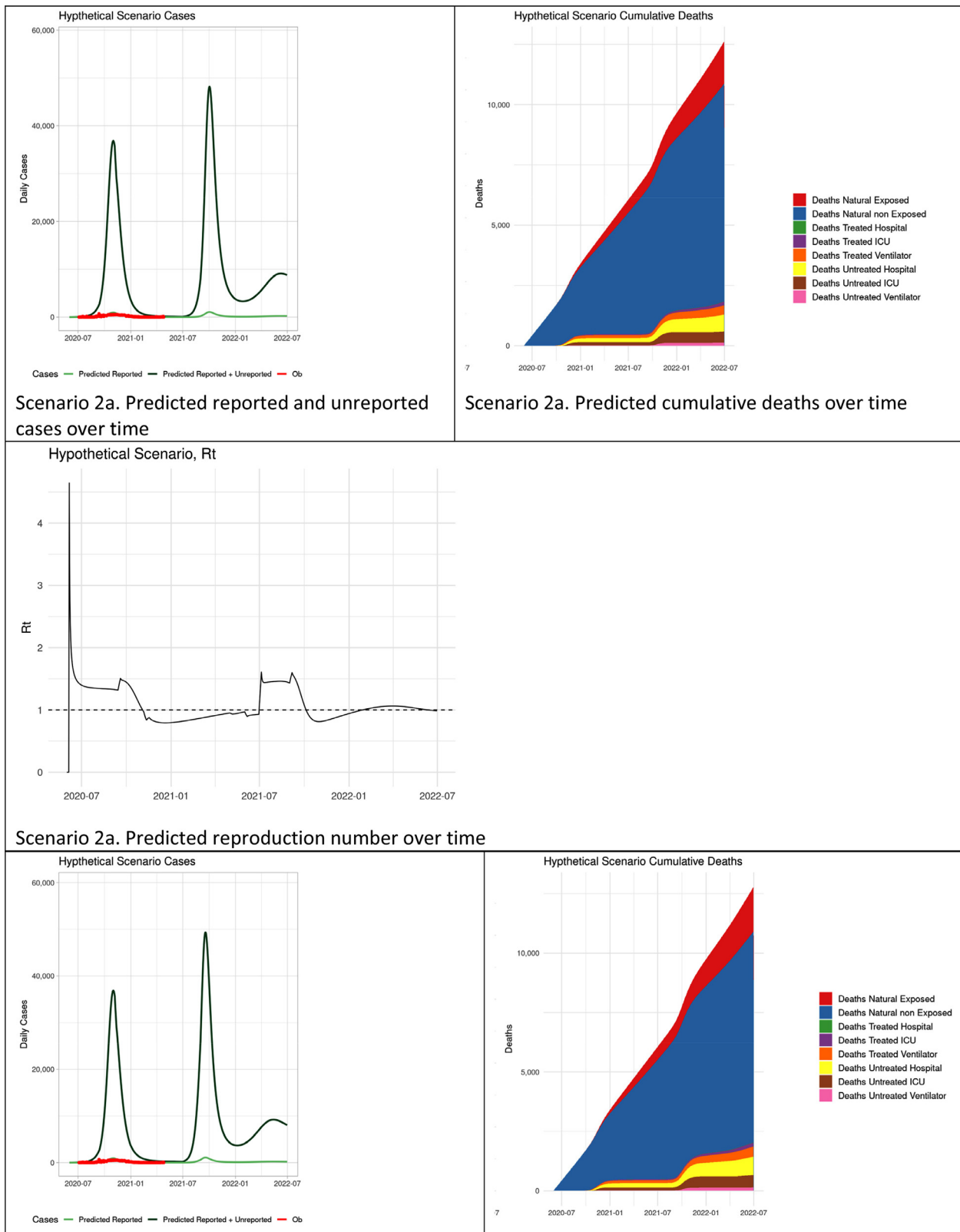


Figure 5. Scenario 2A-D predictions of death, cases, and R number with vaccination coverage of 20%, and 60%.

Scenario 2B. Ending NPIs and introducing Delta variant with 20% vaccination coverage

This transmission scenario, similarly to Scenario 2A, predicted the introduction of the Delta variant would result in a second wave around September 2021, with 48,323 daily cases

at its peak and 2,360 related deaths. It estimated the numbers of hospital beds, ICU beds, and ventilators required at the peak of the second wave would be 582, 79, and 133, respectively. *Rt* was predicted to be above 1 between January

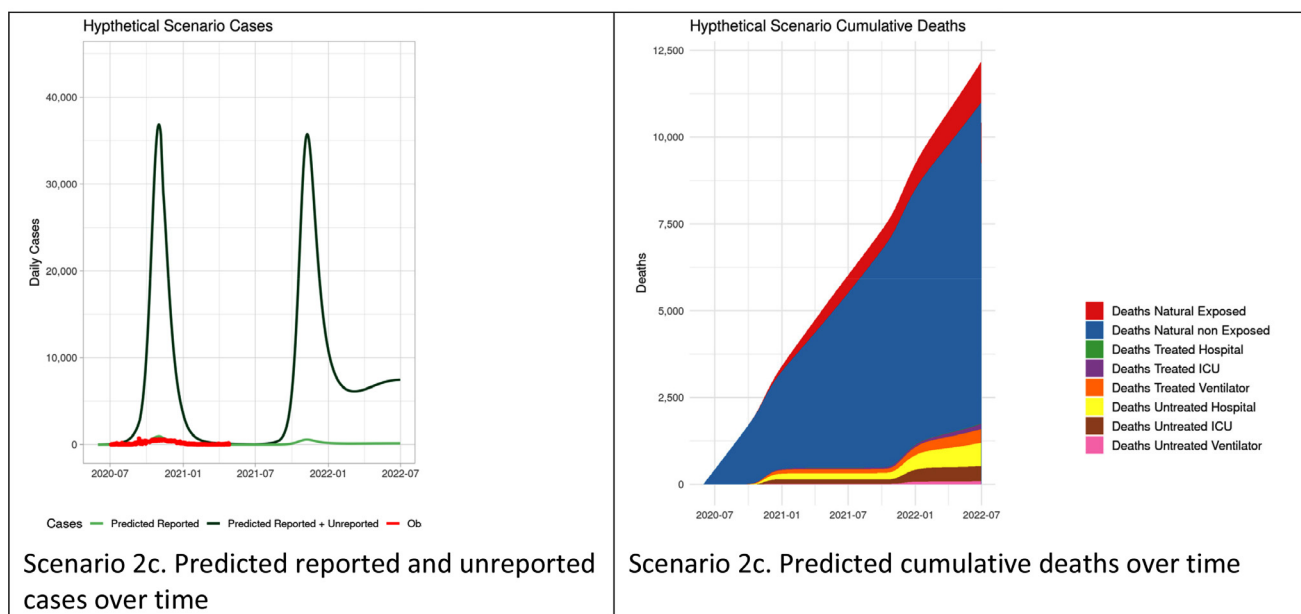
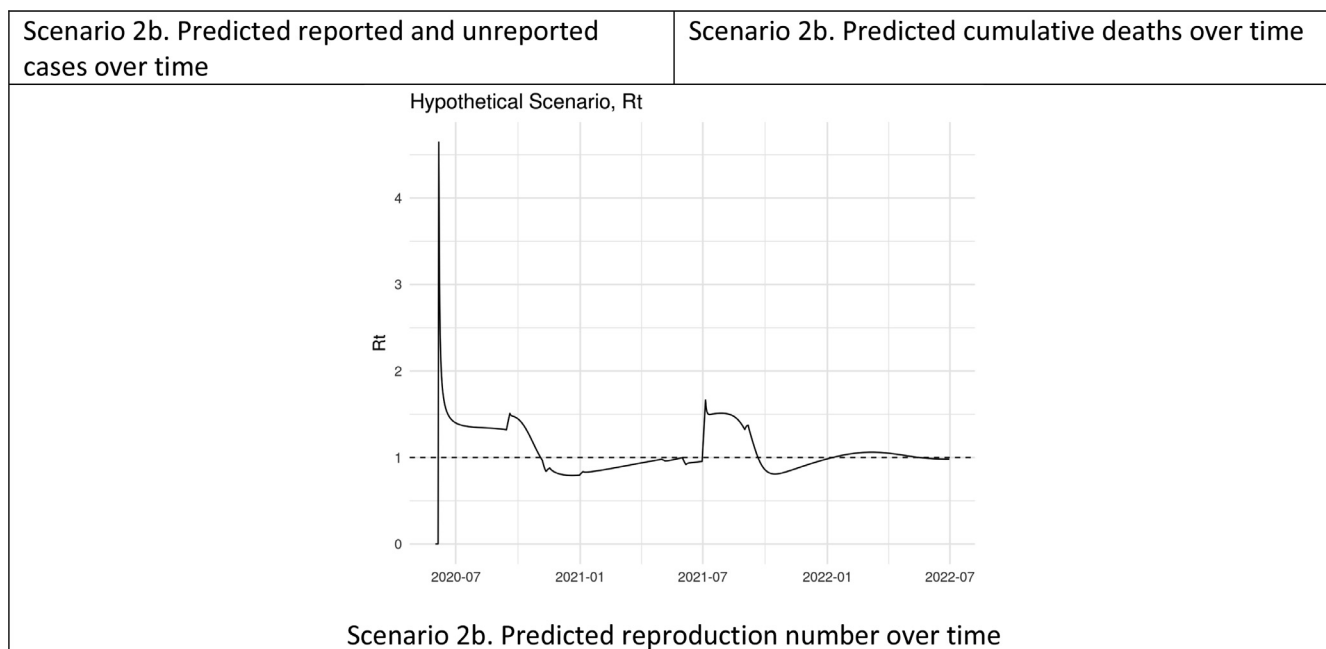


Figure 5. Continued

2022 and June 2022, and reach 1 by June 2022 (Figure 5, Scenario 2B)

**Scenario 2C. Increasing coverage of 2 NPIs with Delta variant and 60% vaccination coverage**

This transmission scenario, which modeled increasing COVID-19 vaccination coverage to 60% and 2 NPIs (i.e. mask-wearing, handwashing) to 50% coverage, predicted a delayed second wave in November 2022, with 35,673 daily cases at its peak and 2,031 total deaths. It estimated that hospital occupancy would remain within a manageable threshold, with numbers of hospital beds, ICU beds, and ventilators required at the peak as 360, 79, and 132, respectively. Rt was predicted to hover just around 1 between January 2022 and June 2022 (Figure 5, Scenario 2C)

**Scenario 2D. Extending NPIs for 12 months while introducing a more transmissible and lethal variant than Delta with 20% vaccination coverage (worst case scenario)**

In this scenario, we increased variant parameters for transmissibility, lethality, and breakthrough infection probability to 2, 2, and 30, respectively. This scenario predicted that introducing a more transmissible variant with a higher capacity to evade immunity and greater lethality by January 2022 would result in the third wave around March 2022, with a lower peak than the second wave, with 17,946 symptomatic and asymptomatic cases daily at its peak and 3,484 total deaths (i.e. around a sixfold increase). It estimated that the numbers of hospital beds, ICU beds, and ventilators required at the peak of the second wave would be 543, 79, and 133, respectively. Rt was predicted to increase over 1 between

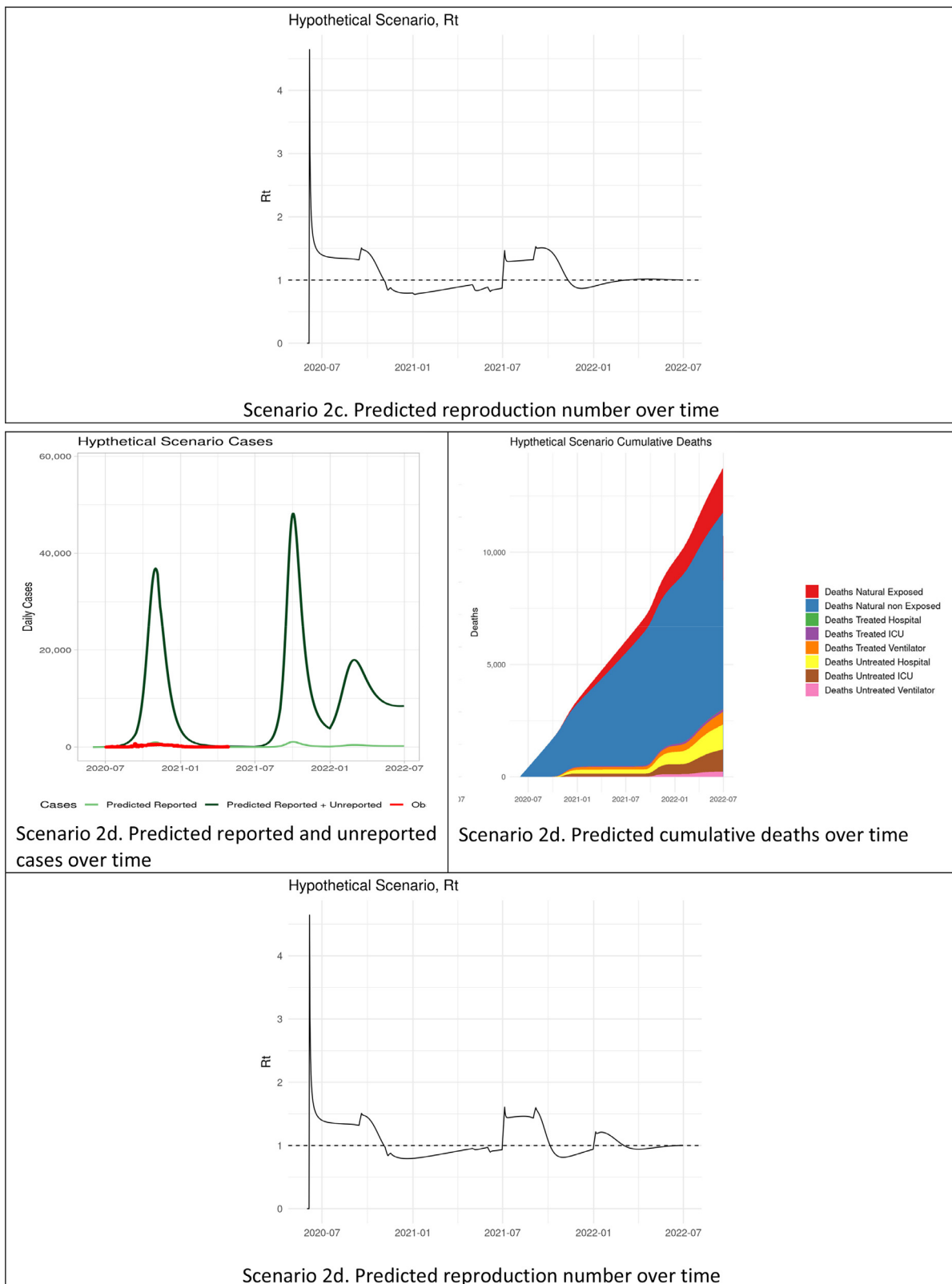


Figure 5. Continued

January 2022 and March 2022, then decrease to below 1 between March 2022 and June 2022.

## DISCUSSION

### Key findings

This is a first effort to model COVID-19 trajectories for NWS, a conflict-affected and opposition-controlled region of Syria characterized by a fragmented health system governance and mass forced displacement, using a participatory tailored approach to selecting model parameters and scenarios. As such, it is both particularly challenging to model pandemic trajectories in this area and particularly necessary to document collaborative attempts to do so. The inclusion of semi-structured interviews, in addition, helped generate possible explanations for model findings related to under-reporting and potential herd immunity.

This study simulated multiple COVID-19 trajectory scenarios in NWS:

- (1) predicting COVID-19 transmission when releasing 4 of the existing NPIs (i.e. handwashing, mask-wearing, safe-distancing, international travel ban) and no variant;
- (2A) predicting COVID-19 transmission with the Delta variant, 20% vaccination coverage by June 2022, and continuation of low coverage of existing NPIs;
- (2B) predicting COVID-19 transmission with the Delta variant, 20% vaccination coverage by June 2022, and ending existing NPIs;
- (2C) predicting COVID-19 transmission with the Delta variant, with an increased vaccination coverage to 60% by June 2022 combined with higher coverage of mask-wearing/handwashing;
- (2D) predicting COVID-19 transmission with a more lethal and transmissible variant than the Delta variant as of January 2022, 20% vaccination coverage by June 2022, and extending existing NPIs.

These scenarios were chosen as most relevant by NWS policy-makers. The no-variant scenarios, predicting around 47.5% population infection by June 2022 and no second wave, supports the theory that herd immunity was reached during the first wave in November 2020 in line with our interviewees' assumptions that most of the population was already infected or had cross-immunity from similar SARS viruses such as the 2012 MERS epidemic in the region (CDC, 2021b). The Delta scenarios, predicting tripling of the death toll, exceeding the ventilator threshold, and the second wave if the Delta variant emerges in NWS without increases in vaccination coverage, appears a likely concern without more rapid vaccine rollout given the rapid global spread of the Delta variant. In May 2021, COVAX began rolling out the AstraZeneca vaccine in NWS, yet reports of delayed shipments, and concerns about cross-border negotiations that would further hinder vaccine implementation, are ongoing (World vision, 2021a; World vision, 2021b).

Scenario 2C indicated that increasing vaccination coverage to 60% by June 2022 coupled with increased coverage of mask-wearing/handwashing would delay the second wave for 2 months, and reduce hospital occupancy to below the threshold of concern. These notable reductions could be because the NWS population is young, and 2% coverage targeting the most vulnerable, as required by COVAX, would already cover most older people.

Further research is needed into reasons for relative low case and death numbers (Statista, 2021; Our world in data, 2021). In the absence of serology data, it is difficult to explain the underlying causes of the relatively low COVID-19 attributable death rates compared with other low-income or conflict-affected settings or validate estimates of the population infected (Our world

in data, 2021). The relatively young population is likely one factor, as only 4% is aged over 65 years. Another likely factor is under-reporting, as modeling predicted 47.5% of the NWS population would have been infected by May 2021 but only 1.2% were reported, and interviews also highlighted under-reporting. This study highlighted the need for serology data in NWS, to improve modeling estimation of numbers infected over time and track infections missed through lack of healthcare access or who were treated or died within the community, which are likely higher than reported (CDC, 2021a). The literature supports potentially high under-reporting rates in a range of settings with weak reporting or fragmented infrastructure. For example, post-mortem surveillance in Ghana showed COVID-19 mortality under-reporting was higher in communities than health facilities (Mwananyanda et al., 2020), at 73% of total COVID-19 deaths. We triangulated model estimates with qualitative interview data to explore COVID-19 under-reporting and lower than expected transmission and case fatality rates. Health worker theories were supported by an UDER community survey identifying fears of hospital infection or being isolated in community treatment centers and preferring the care and support of their family when ill as barriers to seeking COVID-19 diagnosis and treatment (Relief Experts Association, 2020). Both health workers and surveys reinforced findings by Douedari et al that displaced families were more worried by daily challenges than COVID-19 and might not prioritize care-seeking (Douedari et al., 2020).

Overall, our modeling indicates that implementing NPIs other than vaccination in NWS is relatively ineffective, and increasing their coverage would likely provide limited benefit concerning the hardship caused unless there are radical changes in the virus. Current low-coverage NPIs appeared to mitigate the local epidemic trajectory somewhat. Even introducing a new variant such as B.1.617, low population age provides some protection, which combined with vaccination of 60% of the population should be sufficient to decrease COVID-19 transmission in NWS and reduce deaths to 2,031. Therefore, responses should be balanced with negative impacts on the economy and psychosocial well-being of an already traumatized population (e.g. further school and religious facility closures could do more harm than good for child development/protection and social cohesion) (Roberton et al., 2020).

### Limitations

Several limitations should be considered. First, model uncertainties include the following: (i) COVID-19 is a novel disease and knowledge on transmission dynamics is evolving, so model assumptions will also evolve; and (ii) simulations will change with new data and interventions, such as widespread PCR testing, vaccination rollout, and potential treatments. Second, the CoMo model is age-structured and does not account for other transmission-relevant factors in NWS such as population density, displacement, poor housing, comorbidities, and COVID-19 protection measures in health facilities which may increase COVID-19 transmission. Third, unreliable morbidity and mortality data owing to (i) ongoing conflict; (ii) historically poor data management systems and inconsistent case identification in Syria; and (iii) predominantly manual health information systems across Syria. Fourth, fragmented COVID-19 response governance could affect NPI implementation and vaccine rollout.

### Conclusions

This study used a contextualized CoMo model to support COVID-19 response decision-making in NWS. Modeling indicated that NPIs minimally affected COVID-19 transmission, with herd immunity potentially reached during the first wave in November

2020. The likely introduction of a new variant with only existing NPIs would result in a second COVID-19 wave that would quadruple attributable deaths and exceed hospital capacity. Vaccination coverage of 20% is expected to reduce transmission, whereas vaccination coverage of 60% combined with 50% coverage of mask-wearing and handwashing is predicted to decrease hospital beds and ventilators occupancy to 227 and 130, respectively, which is below the existing threshold. However, introducing a new variant with higher transmissibility and immunity evasion capacity in January 2022 would result in the third wave around March 2022. Total COVID-19 attributable deaths are expected to remain relatively low, probably owing to a young population. Thus, policymakers should increase vaccination coverage as quickly as possible rather than emphasizing NPIs in this context, given potential negative socio-economic consequences of NPIs for an already challenged population.

### Conflict of interests

All authors declare no conflicts of interest.

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### Author contributions

MM conceived the study. MH and NA collected epidemiological data and HT and HR provided data for coverage parameters. MM, OAA, and WO conducted modeling with support from RA, BG, and HEC. OAA and YD collected and analyzed qualitative data, with support from NH. MM and OAA drafted the manuscript with help from HEC, AA, and NH. NH critically revised for content. All authors contributed to interpretation and approved the version for submission.

### Ethics

The Saw Swee Hock School of Public Health Departmental Ethics Review Committee in Singapore (reference SSHSPH-052) and London School of Hygiene & Tropical Medicine Observational Research Ethics Committee in the United Kingdom (reference 17360) provided ethics approval.

### Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijid.2022.01.062.

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