ACTaccelerator
ACCESS TO COVID-19 TOOLS

Expanded use case analysis for

Rapid antigen diagnostics for SARS-CoV-2 mitigation

PHASE 2 RESULTS FROM THE ACT-ACCELERATOR SARS-COV-2 RAPID ANTIGEN TESTING MODELLING CONSORTIUM

CONTENTS

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EXECUTIVE SUMMARY

Diagnostic testing for SARS-CoV-2 remains an important tool in the COVID-19 pandemic response by allowing for the timely detection and isolation of infectious cases, reducing the potential for further transmission. Antigen-detecting rapid diagnostic tests (Ag-RDTs) can be performed at the point of care, cost less than RT-PCR testing and provide quick results. There is therefore particular **interest in the use of Ag-RDTs for the scale up of diagnostic testing in limited resource settings** where RT-PCR testing capacity is constrained and **to support COVID-19 surveillance or response efforts** where RT-PCR testing is more readily accessible.

THE ACT-ACCELERATOR RAPID ANTIGEN TESTING MODELLING CONSORTIUM IS WORKING TO IDENTIFY THE USE CASES IN WHICH AG-RDTS CAN BE BEST UTILIZED TO CREATE THE LARGEST REDUCTIONS IN ONWARD TRANSMISSION OF SARS-COV-2.

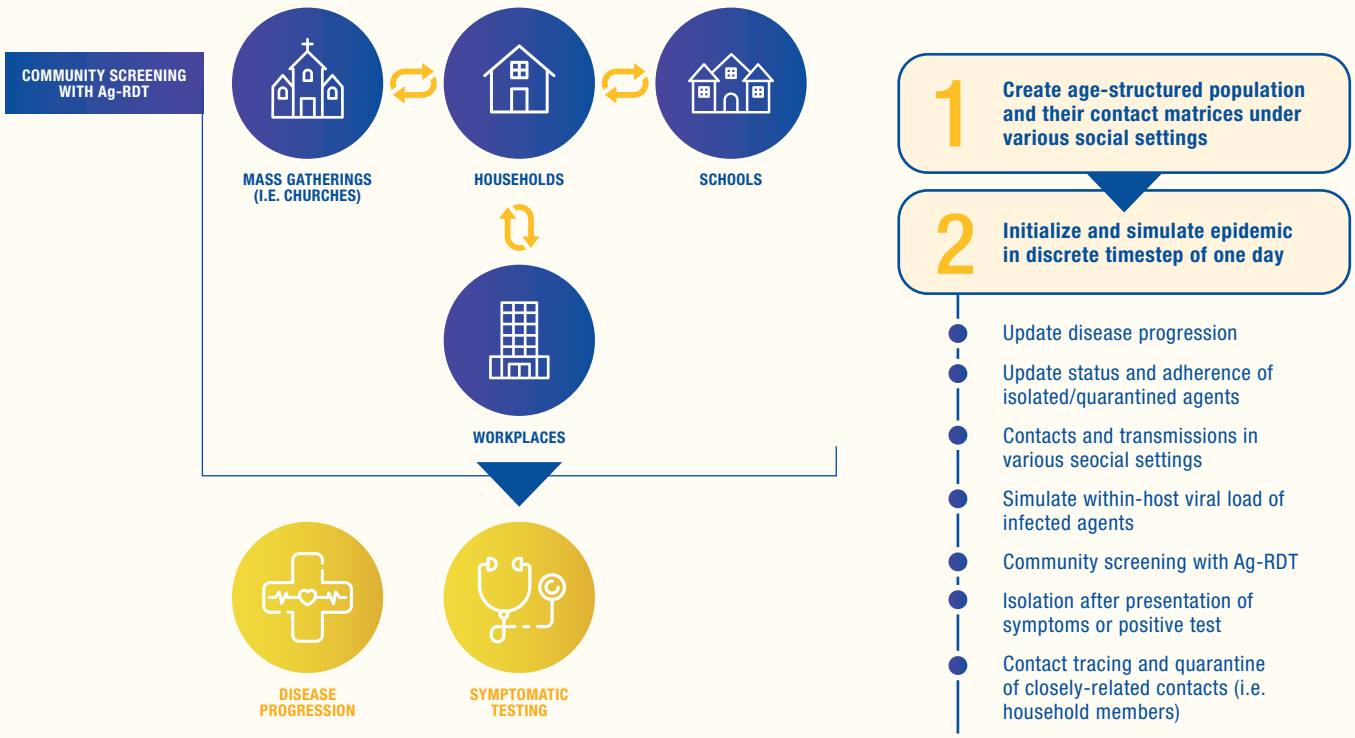
In Phase 1 of our use case analysis, we identified a range of scenarios across various sectors of society where Ag-RDT screening for SARS-CoV-2 would be appropriate and the optimal testing strategies for these settings.

MODELLING CONSORTIUM PHASE 2 APPROACH

IN PHASE 2 OF OUR ANALYSIS, WE DEVELOPED AN AGENT-BASED MODELLING FRAMEWORK (PATAT) TO INVESTIGATE THE IMPACT OF TESTING WITH AG-RDTS ON REDUCING SARS-COV-2 TRANSMISSION IN A LOW- AND MIDDLE-INCOME COUNTRY ARCHETYPE.

Using this modelling framework and the use cases identified in Phase 1, we investigated the effectiveness of using Ag-RDTs for symptomatic testing, both with and without the combination of asymptomatic community testing, on onward disease transmission according to different Ag-RDT allocation strategies and availability in four social settings: households, schools, formal workplaces and churches.

Figure 1. Schematic of the Propelling Action for Testing And Treatment (PATAT) simulation model



MAIN FINDINGS FROM PHASE 2

1. **Testing of symptomatic individuals yields greater benefits than all asymptomatic community testing strategies** until the vast majority of symptomatic individuals who are likely to seek testing at healthcare facilities have been tested.

2. **Testing demand at healthcare facilities is likely to be largely shaped by non-SARS-CoV-2 infected individuals** because of the overlap of SARS-CoV-2 infection symptoms with other respiratory tract infections. Hence, a very large number of tests are likely to be required to saturate demand.

3. **The utility of testing for averting infections relies entirely on people changing their behaviour to reduce contacts following a positive test.** Encouraging and incentivizing these changes of behaviour are essential for the effectiveness of testing.

4. **Testing has the potential to be most effective at reducing transmission when $R_0 \leq 1.5$ (i.e. equivalent to initial instantaneous reproduction number (R_t) ≤ ~1.6).** Because SARS-CoV-2 outbreaks can have R_0 values appreciably above 1.5, testing can be made more effective by combining it with other measures to reduce R_0, such as masking, social distancing, and other non-pharmaceutical interventions.

5. **If R_0 is below ~1.5, or can be reduced to that point through public health interventions, increasing testing from 100 tests per 100 000 people per day** (current minimum testing rate target set by the ACT-A Diagnostics Pillar) **to 200–400 tests per 100 000 people per day provides the greatest marginal increases in testing utility** (i.e. infections averted per test performed). Again, the greatest utility of these tests is only achieved if they are dedicated to symptomatic testing.

6. **The current minimum testing rate target by the ACT-A Diagnostics Pillar of 100 tests per 100,000 people per day is likely insufficient to saturate symptomatic testing demand.** In turn, the much lower recommended testing rate by the World Health Organization of 100 tests per 100,000 people per week (i.e. 14 tests per 100,000 people per day) is not sufficient as well.

7. **After saturating testing demand from symptomatic individuals who sought testing at healthcare facilities, any additional tests allocated for asymptomatic community testing should be prioritized for distributions across households.** Relative to schools, formal workplaces and regular mass religious gatherings, community testing through households yields greater reduction in transmissions. However, this is only possible after symptomatic testing demand has been largely satisfied.

SUMMARY AND NEXT STEPS

In Phase 2, we identified that **community testing** will only achieve high levels of infection reduction **after symptomatic testing demand is saturated.** As expected, this demand rapidly increases with R0. Importantly, the current minimum testing rate target by the ACT-A Diagnostics Pillar of providing 100 tests per 100 000 persons per day is likely to fall far short of meeting this demand. In other words, even before facilitating any form of asymptomatic community testing, **the current greatest priority should be to increase investments in testing availability to meet symptomatic testing demand.** Testing can potentially be increased through implementations of new innovations at healthcare-provided testing facilities such as the integration of self-testing at these facilities.

The next phase of our work will focus on how the accumulation of immunity over the first two years of the pandemic and the distribution of antiviral therapeutics could impact testing utility, how community structures in different countries as well as alternative testing strategies such as self-testing could impact the effectiveness of testing programs. We will also update our results simulating epidemics of more recent variants-of-concern (i.e. Delta and Omicron) that have shorter generation intervals.

MAIN REPORT

INTRODUCTION

DIAGNOSTIC TESTING FOR SARS-COV-2 REMAINS AN IMPORTANT TOOL IN THE COVID-19 PANDEMIC RESPONSE BY ALLOWING FOR THE TIMELY DETECTION AND ISOLATION OF INFECTIOUS CASES, REDUCING THE POTENTIAL FOR FURTHER TRANSMISSION.

Real-time reverse transcription polymerase chain reaction (RT-PCR) tests remain the gold standard for COVID-19 diagnostic testing with higher test sensitivity (>95%) than antigen-detecting rapid diagnostic tests (Ag-RDTs), but they require sophisticated laboratory infrastructure, sample transport, skilled personnel and can be plagued by long turnaround times. While Ag-RDTs may have lower test sensitivity (>80%), they can be performed at the point-of-care and provide results within 10 to 30 minutes. Ag-RDTs can be utilized for both the scale up of diagnostic testing in resource-limited settings where RT-PCR testing capacity is constrained and to support surveillance or response efforts where RT-PCR testing is more readily accessible.

Ag-RDTs also have the potential to be of substantial utility in a range of scenarios and settings for the control and mitigation of the COVID-19 pandemic, especially in resource-limited settings. Identifying the use cases in which Ag-RDTs can best be utilized to support the largest reductions in onward transmission is important for decision-making and resource allocation efforts, particularly during the heightened demand when SARS-CoV-2 transmission is high. The aim of the Phase 1 use case analysis was to identify a range of scenarios across the various sectors of society where Ag-RDT screening for COVID-19 would be appropriate for use: community testing, schools and universities, sporting events, concerts and places of worship, and for exiting quarantine and isolation periods. Phase 1 leveraged mathematical models from multiple modelling groups to address use-case specific questions. The different use case settings presented in the Phase 1 report required different testing strategies to most efficiently and effectively reduce infections across a range of epidemic conditions. In particular, Phase 1 found that the speed and frequency of antigen rapid testing to identify SARS-CoV-2 cases outweighed the benefit of higher test sensitivity of RT-PCR, making Ag-RDTs a valuable tool for case detection, outbreak investigation and contact tracing. The results from these use cases provide the beginning of an evidence base for the use of Ag-RDTs in various settings and quantify the value of expanding access to Ag-RDTs.

The results presented for the use cases in Phase 1 only quantified the effectiveness of testing strategies on reducing transmissions within each use case. They did not offer any information on the impact of each use case on the broader community or the effects these testing strategies could have on onward community transmission. Importantly, the results of each use case from Phase 1 cannot be directly compared with one another because of differences in the underlying modelling frameworks and the lack of explicit consideration of the proportion of any population that might be captured within any particular use case. Further, while these findings emphasized the value of widespread, high frequency Ag-RDT use, they acknowledged that health systems in resource-limited settings may have difficulty scaling up testing to this extent; thus, it is **imperative to determine the optimal testing strategy that balances trade-offs between feasibility, costs, and reduction in infections.**

The aim of this phase of the work was to develop and use an agent-based modelling framework to investigate the relative potential effectiveness of combining use cases for a representative low- and middle-income country (LMIC) archetype (representative defined in terms of demographic profile, urban/rural geography, mixing patterns, and level of public health resources). Using this modelling framework, we investigated the potential impact of using Ag-RDTs for testing of individuals with COVID-19 symptoms (symptomatic testing), both with and without the combination of asymptomatic community testing, on onward disease transmission according to different Ag-RDT allocation strategies and availability in four social settings: households, schools, formal workplaces and churches.

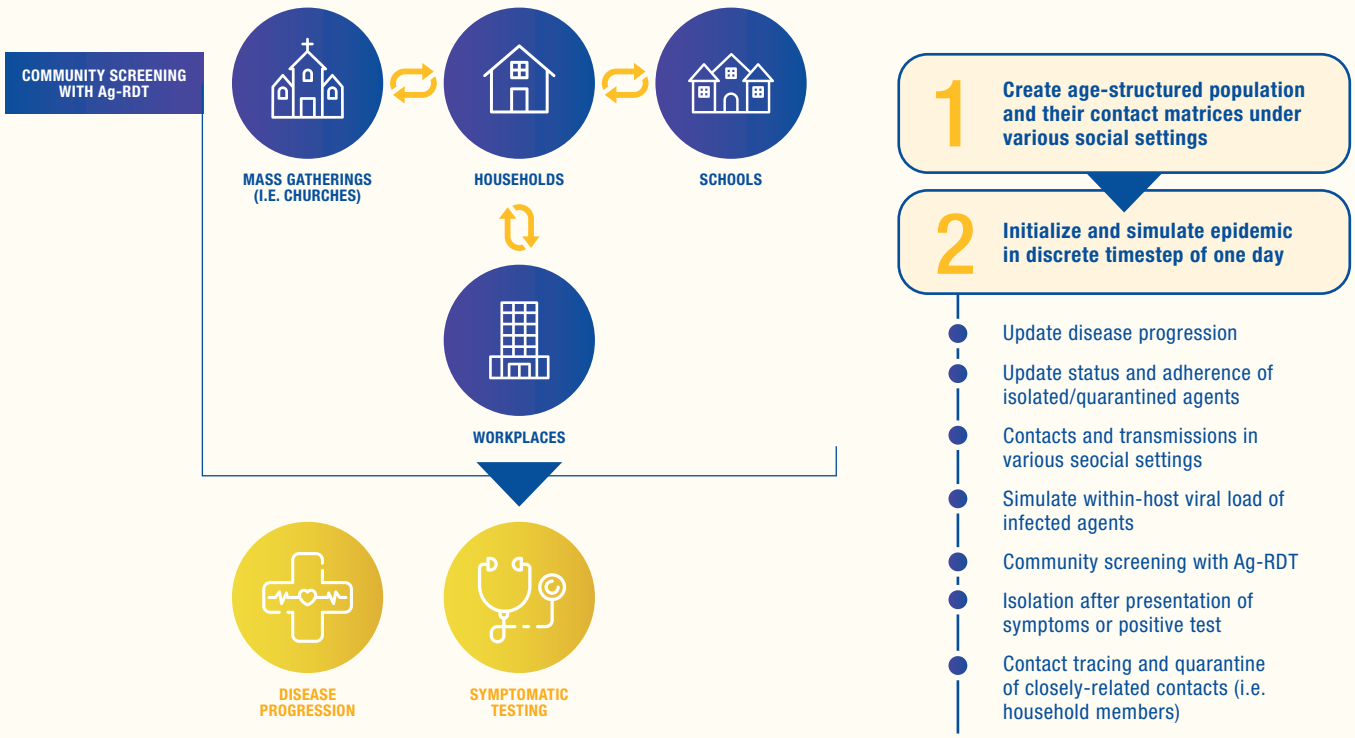
METHODS

PROPELLING ACTION FOR TESTING AND TREATMENT (PATAT)

PATAT is a stochastic agent-based model that is designed to investigate the impact of professional-use Ag-RDTs provided in healthcare clinics to symptomatic individuals, as well as asymptomatic community testing during COVID-19 outbreaks in LMICs (**Figure 1**). This model is similar to Covasim[1] (a widely used agent-based modelling framework for studying the epidemiology of SARS-CoV-2), but is importantly different in terms of its structure which can more closely mirror the SARS-CoV-2 epidemic in LMICs. In each PATAT simulation, an age-structured population of individuals (agents) is first created within contact networks in households, schools, workplaces and churches (i.e. mass gatherings) based on realistic demographic data. Additionally, healthcare clinics where agents seek symptomatic testing are also distributed within the simulated population based on a given healthcare clinic-to-population ratio. Although PATAT does not model the geolocation of agents explicitly, households, schools, churches and healthcare clinics are ordered to implicitly approximate a neighborhood (localized community) structure. The movements of each agent within the community are recorded daily.

The simulation starts by seeding a proportion of agents with SARS-CoV-2 infection. Given that the sensitivity of Ag-RDTs depends on the viral loads of individuals at the point of testing,[2] PATAT generates a within-host viral load trajectory for each infected agent during the course of their infection by randomly drawing from a distribution of known within-host viral load trajectories using previously developed methods[3]. We used incubation and viral shedding periods reported for wild-type SARS-CoV-2 in this work. Owing to the lack of robust data for asymptomatic infected people, we conservatively assumed their viral load trajectories are drawn from similar distributions. PATAT then simulates the epidemic by iterating over a given period of time with each time step corresponding to one day. For each day, the simulation first updates the disease progression of infected individuals based on the SEIRD (Susceptible-Exposed-Infectious-Recovered /Death) epidemic model, further stratifying infected agents based on symptom presentation (i.e. asymptomatic, mild or severe). Depending on the proximity from their homes, symptomatic agents may seek symptomatic testing at the nearest healthcare clinics after a random delay since symptom onset (drawn from a lognormal distribution of mean 1 day; s.d. = 0.5 day). PATAT then updates the status of agents who are isolated/quarantined, including simulating agents who stop adhering to these restrictions prior to the stipulated isolation/quarantine period. Community testing for SARS-CoV-2 by Ag-RDT may then be applied according to allocation strategies and availability. Finally, PATAT computes transmission events within different contact networks over the course of the day.

Figure 1. Schematic of the Propelling Action for Testing And Treatment (PATAT) simulation model



DISTRIBUTION OF HEALTHCARE-PROVIDED COMMUNITY TESTS

We investigated performing community testing in four social settings: households, schools, formal workplaces and churches. These settings were chosen because of their fixed nature and potential accessibility for implementing testing programmes.

For each setting, we simulated two ways in which the community test stocks may be distributed:

1. **An even distribution to as many entities as possible once per week.** For example, if we have 10 tests available for 10 households per week, then one member of each household would get a test.

2. **A concentrated distribution to test every individual in selected entities twice a week and the same individuals in the same selected entities will be tested every week.** For example, if we have 10 tests available for 10 households per week but only one of which house five members, then all 10 tests will be distributed to this selected household of five for testing on Monday and Thursday of every week while the remaining nine other households will not be tested.

In terms of dividing test stocks between symptomatic and community testing, we considered two approaches: (1) strictly allocate 15% of all available tests per week to healthcare clinics for symptomatic testing, with the rest used for community testing; or (2) per-week demand of tests at healthcare clinics will be satisfied first for the current week before allocating the leftovers for community testing in the subsequent week.

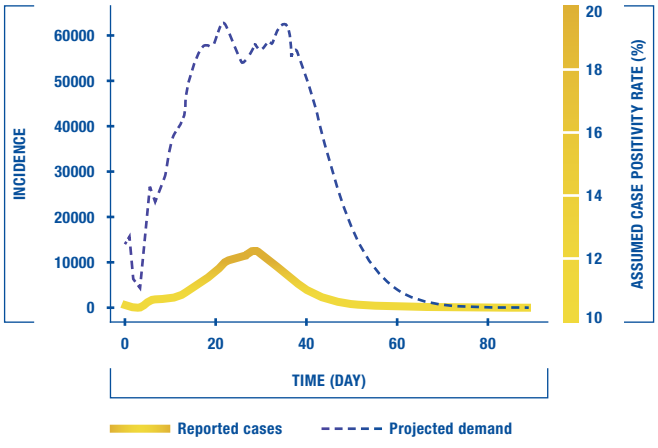
An example of the second scenario would be that on Monday of each week, we assume that one week's worth of Ag-RDT stock is available for testing that week. If the allocation of tests is 100 tests per 100,000 persons per day then 700 tests per 100,000 people are delivered to healthcare clinics for that week. If all 700 tests are used before the following Monday, no more testing can be performed until the new delivery of tests on Monday. If some portion of the 700 tests remain unused and there is no community testing programme, then those remaining tests are added to the tests delivered for the following week. If some portion of the 700 tests remain unused and there is a community testing programme, then those remaining tests are used for community testing in that week.

HEALTHCARE-PROVIDED SYMPTOMATIC TESTING DEMAND

One of the key challenges for establishing a testing programme is estimating demand. This is particularly challenging for SARS-CoV-2 because the range of symptoms substantially overlaps with other infections, like influenza, and therefore substantially increases testing demand. We assumed that symptomatic SARS-CoV-2-infected agents would seek testing at healthcare clinics based on a probability distribution that inversely correlate with the distance between the agent's household and the nearest healthcare clinic (**Supplemental Figure 5** and **Supplemental Table 1**)[4].

Furthermore, we also simulated a daily demand of clinic tests from agents that were not infected by SARS-CoV-2 but seek clinic-based professional use symptomatic testing for other reasons (i.e. individuals presenting COVID-19-like symptoms or close contacts of agents who tested positive previously). This non-COVID-19 related demand for testing was estimated by assuming a 10% test positivity rate at the start and end of an epidemic curve and 20% test positivity rate at the peak, linearly interpolating the demand for periods between these time points (**Figure 2**). These estimates are based on observed case positivity rates in multiple countries during the second half of 2021[5]. If there are limited healthcare clinic test stocks for the day, the available tests are randomly distributed among symptomatic SARS-CoV-2-infected patients and those seeking tests for other reasons. We assumed that all agents who failed to receive a test due to test shortage would not seek clinic-provided testing again for the rest of their infection. If these agents had previously decided to self-isolate upon presenting symptoms, they may continue to do so (see below). Otherwise, we assumed that they would continue to mix within the community.

Figure 2. Projected symptomatic testing demand based on assumed case positivity rate. This projected demand includes both SARS-CoV-2 infected persons who were tested and reported, as well as those who seek symptomatic testing for other reasons (e.g. individuals presenting COVID-19-like symptoms but are not infected by SARS-CoV-2).



ISOLATION AND QUARANTINE

We assumed that agents would change their behaviour when:

1. **they start to present symptoms and go into self-isolation without testing (10% compliance assumed, 71% endpoint adherence[6]);** Endpoint adherence is the probability that an isolated/quarantined individual will remain in isolation/quarantine up to the last day of the stipulated isolation/quarantine period;

2. **they tested positive and were isolated for 10 days** (50% compliance assumed, 86% endpoint adherence[6]); or

3. **they were household members of agents testing positive for SARS CoV-2 who did not present any symptoms** and were asked to go into quarantine for 14 days (50% compliance assumed, 28% endpoint adherence[6]).

Once an agent goes into isolation/quarantine, we linearly interpolate their probability of adherence to stay in isolation/quarantine over the respective period. Given the lack of infrastructure and resources to set up dedicated isolation/quarantine facilities in many LMICs, we assumed that all isolated and quarantined individuals would do so at home. Although they would have no contact with agents outside of their home, we assumed that they would maintain 90% contact rate with household members.

SIMULATION VARIABLES

We performed all simulations assuming a populations size of 1 million agents, creating contact networks and healthcare clinics based on data collected from Zambia[7–10] and Malawi[4] (**Supplemental Table 1**). We initialized each simulation with 1% of the population being infected by SARS-CoV-2 and ran the model over a 90-day period. We permutated a range of R_0 values (i.e. 0.9, 1.1, 1.2, 1.5, 2.0, 2.5 and 3.0) against varying Ag-RDT stock availability (100, 200, 400, 800, 1000, 2000, 3000, 4000, 5000 tests per 100,000 persons per day).

As a baseline, we simulated a set of runs under different R_0 values with no testing at all. We performed two sets of analyses for the aforementioned range of R_0 and test availability – one with same-day quarantine of household members of agents testing positive and another without. While we assumed that quarantined household members reduce their contact rates minimally with infected members who were isolated in the same home, this distinction is important because quarantine of household members still reduces their social contacts with individuals outside of their homes, and thus should have the net impact of changing the contact patterns of more individuals for each test used and should increase the utility of those tests.

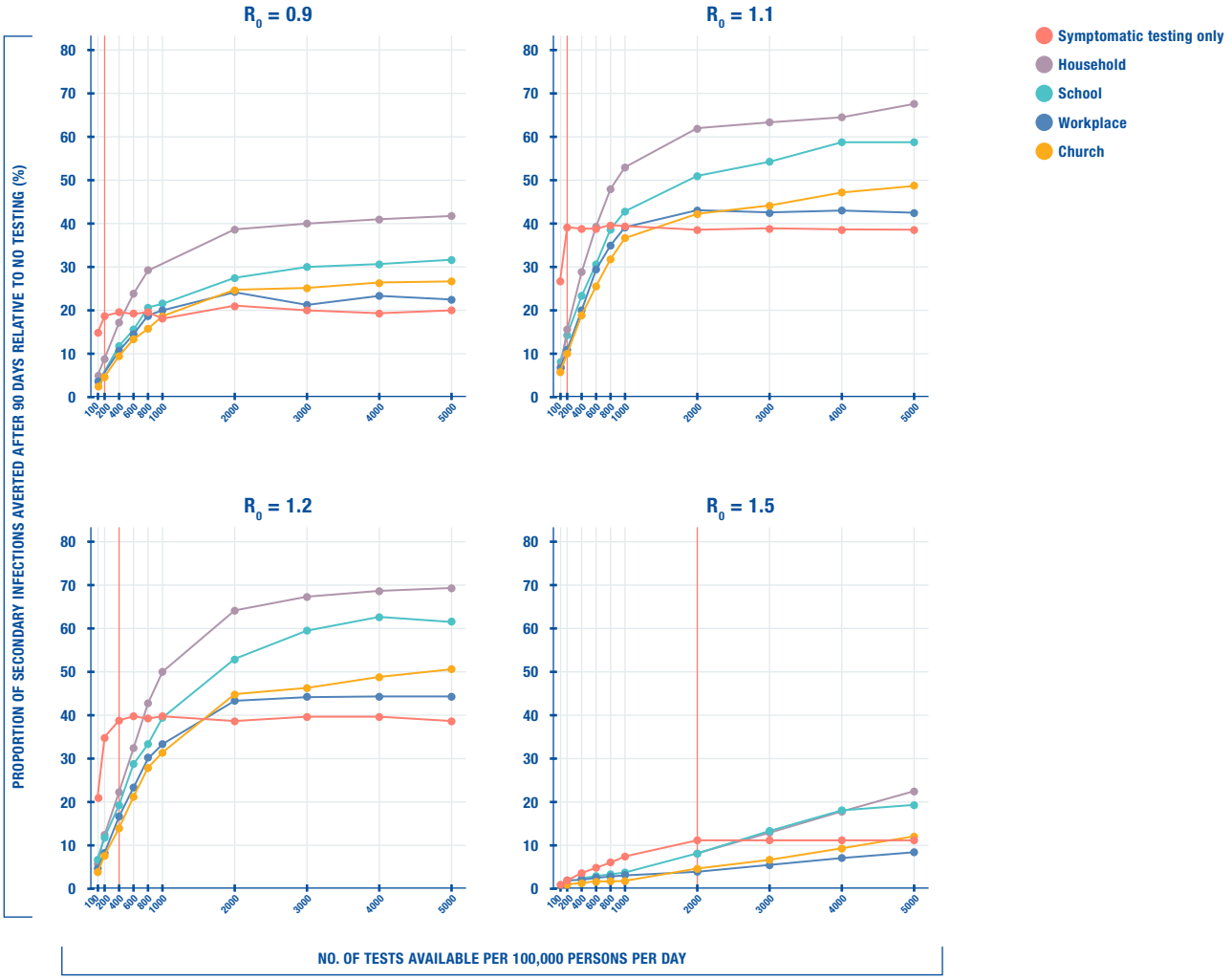
All other key parameters are tabulated in **Supplemental Table 1** and further technical details of the PATAT model are described in the **Appendix**.

RESULTS

HEALTHCARE-PROVIDED SYMPTOMATIC TESTING DEMAND SHOULD BE FULFILLED FIRST

We first simulated scenarios where either all Ag-RDT stocks were used for symptomatic testing or only 15% of weekly available stocks were allocated for symptomatic testing and the rest used for community testing. As a measure of impact for each testing strategy, we computed the proportion of infections averted compared with the baseline where no testing was done. Regardless of the social setting where community test distribution was implemented or the value of R_0, we found that setting aside large proportions of Ag-RDTs for community testing generally led to a lower proportion of infections averted (worse outcomes) than if all tests were used for symptomatic testing only (**Figure 3**). Community testing would usually only outperform symptomatic testing when the same number of available tests had saturated symptomatic testing demand (i.e. all symptomatic SARS-CoV-2-infected agents who sought symptomatic tests were tested). This conclusion remains the same when household members of all agents testing positive were quarantined (**Supplemental Figure 1**).

Figure 3. Impact of either using all available Ag-RDTs for symptomatic testing or a majority of them (85%) for community testing in various settings (even distribution only; without quarantine of household members). The proportion of secondary infections averted after 90 days relative to the no testing baseline for different number of tests available per 100,000 persons per day is plotted for each test distribution strategy. The vertical red line denotes the number of tests required to saturate symptomatic testing demand.



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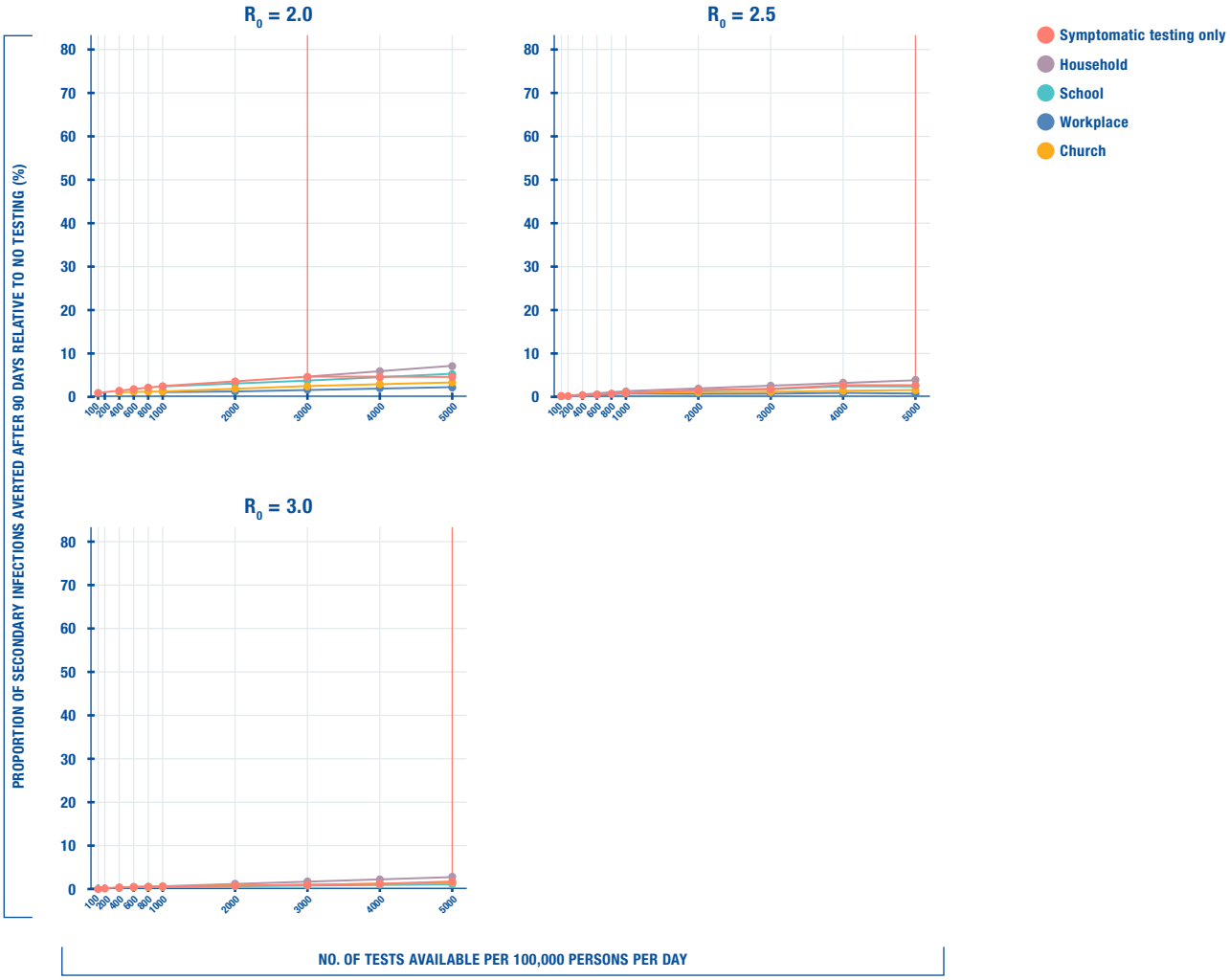
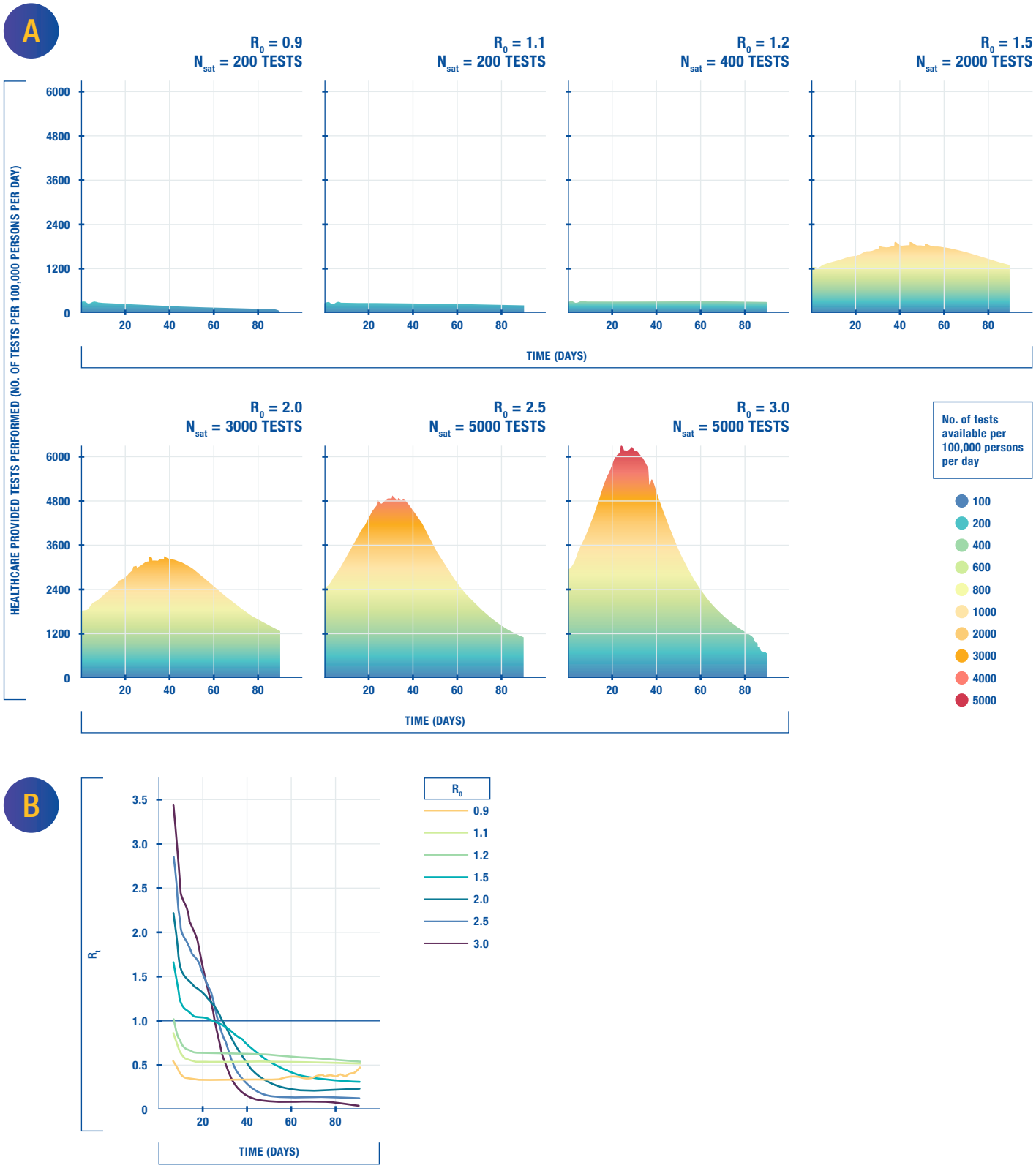


NUMBER OF TESTS REQUIRED TO SATURATE HEALTHCARE-PROVIDED SYMPTOMATIC TESTING DEMAND

The minimum number of tests required to saturate symptomatic testing demand increases rapidly with R_0 (**Figure 3-4A**). Importantly, the current recommended target of 100 tests per 100,000 persons per day (tests/100k/day) was insufficient in meeting symptomatic testing demand for the entire range of R_0 values simulated. We had factored in 80–90% of uninfected agents who sought symptomatic testing for other reasons (e.g. presented COVID-19-like symptoms, etc.) on top of symptomatic SARS-CoV-2 infected agents who sought to be tested (i.e. 10–20% test positivity rate over epidemic course). As clinics cannot know which agents were infected by SARS-CoV-2 a priori, there must be enough Ag-RDTs available for symptomatic testing, so that everyone who visited them for testing were tested.

Even when $R_0 \leq 1.2$ (where the average instantaneous reproduction number (R_t) was <1 during the first week of the epidemic; **Figure 4B**), at least 200–400 tests/100k/day was needed to ensure that all symptomatic SARS-CoV-2-infected agents who sought testing were tested. When $R_0 \geq 1.5$ (where we observed exponential growth in infections and average R_t during the first week of the epidemic was > 1.5), at least 10 times more tests, in the range of 2000–5000 tests/100k/day, was needed to test all test-seeking symptomatic patients with COVID-19. These conclusions were similar even when we quarantine household members of agents testing positive (**Supplemental Figure 2**).

Figure 4. Symptomatic testing demand during an epidemic (without quarantine of household members).
(A) Number of symptomatic tests performed per 100,000 persons per day over time for different R_0. Each differently coloured shaded curve denotes a different number of tests available per 100,000 persons per day. We assumed that all healthcare facilities in the community will have new stocks of one week's worth of Ag-RDTs every Monday. The symptomatic testing demand include both symptomatic SARS-CoV-2-infected agents who seek testing at healthcare facilities and those who seek symptomatic testing for other reasons based on assumed case positivity rates (see Methods). The area between the curve plotting number of tests needed to saturate symptomatic testing demand (N_{sat}) and any other curves plotting $N<N_{sat}$ is the amount of symptomatic testing shortage accumulated over time.
(B) 7-day moving average of instantaneous reproduction number (R_t) over simulated epidemic period (90 days) for different assumed basic reproduction number (R_0).



MARGINAL IMPACT OF SYMPTOMATIC TESTING PRIOR TO SATURATING DEMAND

We then quantified the marginal benefit of having more tests allocated for symptomatic testing prior to demand saturation, in terms of infection reduction over the simulated epidemic. To do so, we linearly regressed the number of infections averted against test availability to compute the number of additional infections averted per 100 more Ag-RDTs before saturating symptomatic testing demand (**Figures 5A-B**). If we only isolate agents testing positive without further quarantine, the largest marginal benefit of increasing Ag-RDT availability for symptomatic testing prior to demand saturation is achieved when R_0 = 1.1–1.2, with close to 20,000 additional infections averted for every 100 more Ag-RDTs available for symptomatic testing (**Figure 5B; Table 1**). When operating at levels of tests availability that meet all symptomatic testing demand, the greatest impact is also achieved when R_0 = 1.1–1.2 with ~40% of total infections averted (**Figure 5A**).

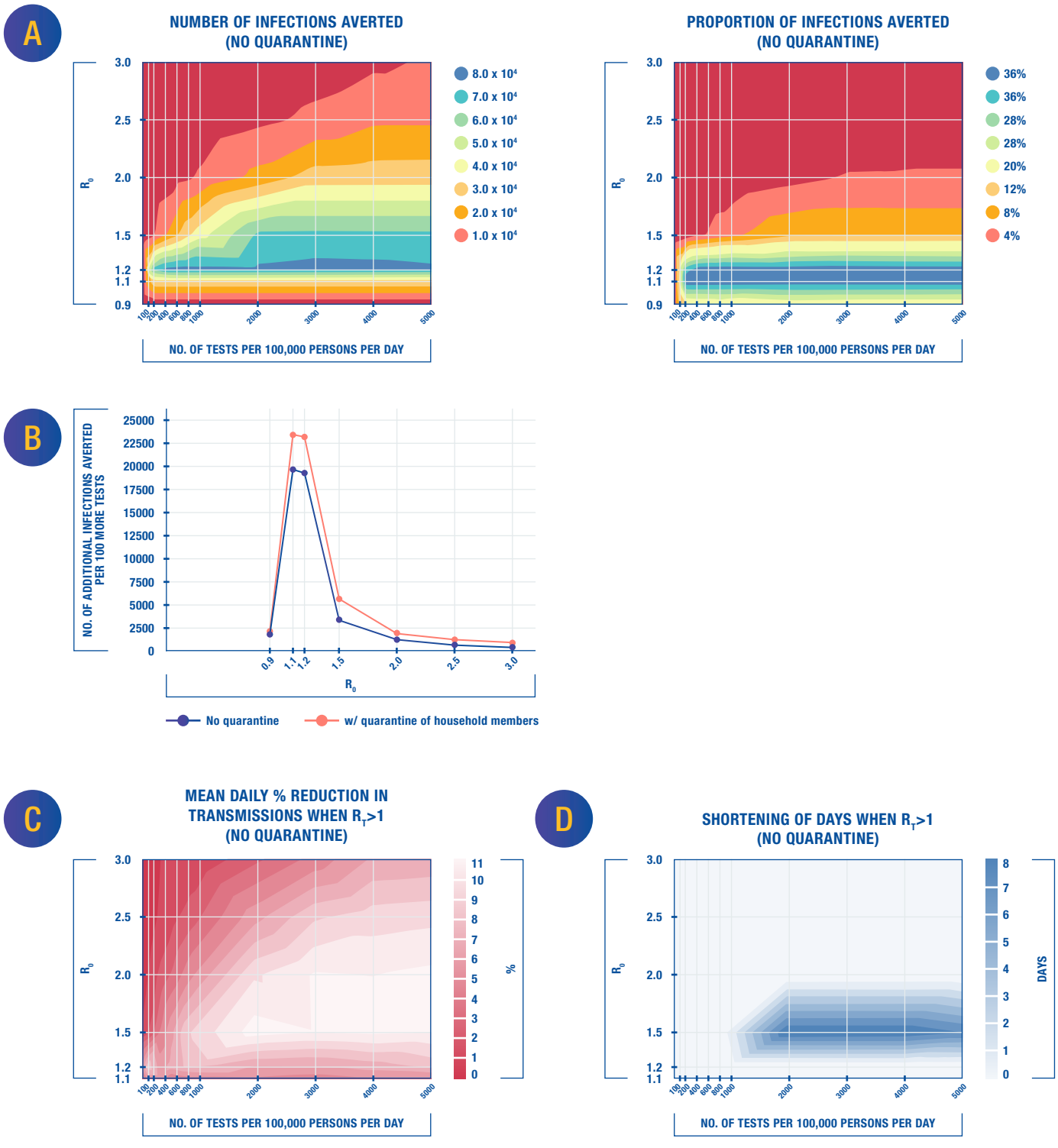
However, the benefits of having more tests allocated for symptomatic testing diminish exponentially with increasing values of R_0 – both in terms of the marginal benefit prior to demand saturation as well as the maximum impact achieved at demand saturation (**Figure 5A-B and Table 1**). Nonetheless, there are other impacts besides infection reduction that could be gained from performing more symptomatic testing at values of R_0>1.2. For instance, for R_0 values between 1.5 and 2.0 without quarantining household members, it is possible to reduce daily transmissions by up to 11% with increasing levels of test availability during the growth phase of the epidemic (R_t>1; **Figure 5C**). Additionally, when R_0~1.5 and test availability is in the range of 2000 tests or more, it is possible to shorten the duration of the epidemic's growth phase (and in turn, the epidemic itself) by about one week (**Figure 5D**).

The aforementioned marginal benefits of symptomatic testing can be further augmented if household members of agents testing positive were required to quarantine as well (**Supplemental Figure 3**). However, depending on R_0 and level of test availability, the percentage of infections averted only improved modestly by 2–10%. As we assumed that agents would isolate and quarantine in their own homes (see section on community testing in households below for justification and details), infectious agents in isolation will continue to be in contact, and as such, often infect healthy household members in quarantine with them.

Table 1. Number of additional infections averted for every 100 more Ag-RDTs available prior to saturating symptomatic testing demand for different R_0 values.

With quarantine of household members	R_0	No. of additional infections averted per 100 more tests
NO	0.9	1,772
	1.1	19,807
	1.2	19,372
	1.5	3,655
	2.0	1,149
	2.5	401
	3.0	216
YES	0.9	2,205
	1.1	23,444
	1.2	23,250
	1.5	5,702
	2.0	1,999
	2.5	853
	3.0	441

Figure 5. Marginal impact of symptomatic testing prior to saturating demand (without quarantine of household members).
(A) Contour plots depicting infections averted relative to the no testing baseline for simulations with different R_0 values and varying number of available Ag-RDTs. Number of infections averted relative to no testing baseline after 90 days (left panel); proportion of secondary infections averted relative to no testing baseline after 90 days (right panel).
(B) Number of additional infections averted for every 100 more Ag-RDTs available prior to saturating symptomatic testing demand for different R_0 values. Dashed red line shows marginal benefit with quarantine of household members while solid black line depicts that without quarantine.
(C) Mean daily percentage reduction in transmissions while instantaneous R_t of simulated epidemic is still > 1 for different R_0 values and varying number of Ag-RDTs available for symptomatic testing only.
(D) Shortening of the number of days when instantaneous R_t of simulated epidemic is still > 1 for different R_0 values and varying number of Ag-RDTs available for symptomatic testing only.

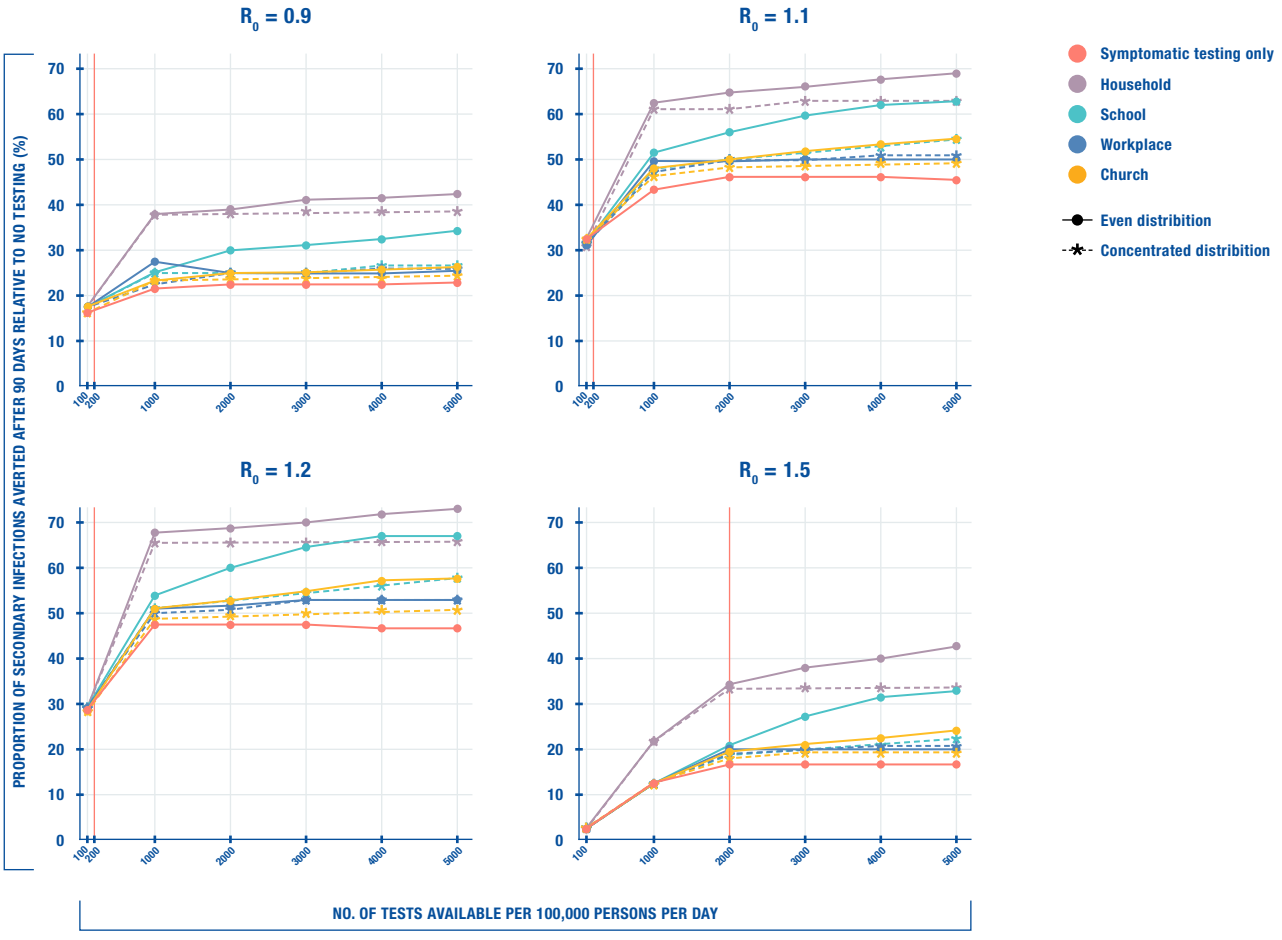


A SYMPTOMATIC-TESTING-FIRST STRATEGY TO COMMUNITY TESTING

Given the importance of symptomatic testing, we then simulated an alternate test stock allocation approach for community testing that prioritizes the fulfillment of symptomatic testing demand first. Rather than setting aside a fixed proportion of tests for community testing every week, all available Ag-RDTs for one week will be used for symptomatic testing demand first that week. If there are any tests leftover in the previous week, these Ag-RDTs will then be distributed for community testing in the current week. In other words, as opposed to saving unused test stocks during the pre-exponential growth phase for the greater symptomatic testing needs during the epidemic peak (as was the case when all tests were used for symptomatic testing only), these tests would be used to screen for asymptomatic and other infected agents who did not seek symptomatic testing. We also investigated two ways in which community tests were distributed among the intended social setting – either 1) evenly and randomly distribute the tests to as many agents associated with these settings as possible, or 2) concentrate the available tests to a fixed number of persons throughout the epidemic period.

Even under this symptomatic-testing-first approach, community testing in most social settings, with the exception of households, would only yield greater impact in infection reduction when test availability is higher than what is needed to meet symptomatic testing needs (**Figure 6**). Overall, household testing yielded the greatest improvement in infections averted for all simulated R_0 values, followed by schools if $R_0 \leq 1.5$. On the contrary, testing in churches and formal workplaces only result in modest improvements over symptomatic testing only. Comparing even and concentrated distribution of community tests, it is clear that a more equitable distribution to as many agents as possible tends to produce larger reductions in total infections. The difference between even and concentrated community test distributions also increases with larger test availability. These results were similarly observed when household members of agents testing positive were quarantined (**Supplemental Figure 4**).

Figure 6. Symptomatic-testing-first strategy to community testing (without quarantine of household members). When community testing is performed under this strategy, the leftover tests from the previous week's stock allocated for symptomatic testing are used for community testing in various setting in the current week. Two different types of community test distribution approaches (even or concentrated; see Methods) were simulated. The proportion of secondary infections averted after 90 days relative to the no testing baseline for different number of tests available per 100,000 persons per day is plotted for each test distribution strategy. The vertical red line denotes the number of tests required to saturate symptomatic testing demand.



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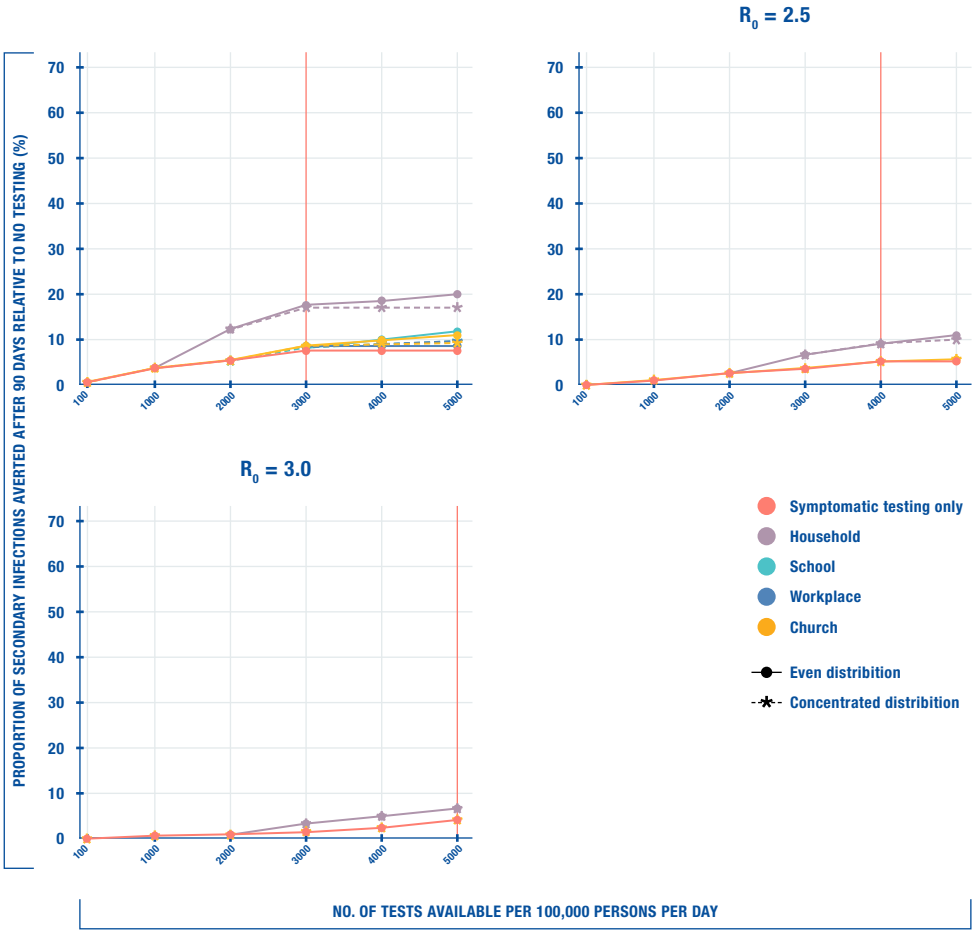


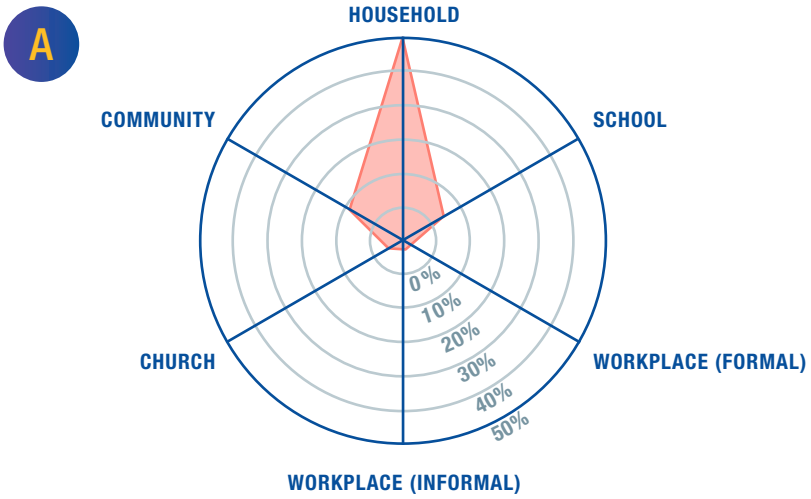
COMMUNITY TESTING IN HOUSEHOLDS

Strikingly, in a symptomatic-testing-first approach where any weekly leftover tests from symptomatic testing, particularly during the pre-exponential growth phase of the epidemic, were used for community testing, household community testing actually outperformed the symptomatic-testing-only strategy prior to satisfying symptomatic testing demand. This, however, is only possible when absolute levels of testing were very high (**Figure 6** and **Supplemental Figure 4**). There are several reasons as to why household testing performed the best in our simulations, while community testing in other settings such as churches and formal workplaces was less effective. First, we assumed a mean household size of 5 persons and generated large multigenerational homes, as commonly found in many LMICs. Second, population in LMICs also tend to skew young (i.e. 48.3% of the population are expected to be ≤15 years in age[7]). Furthermore, overall employment rates are low (i.e. assumed 39% and 23% among men and women respectively[8]) and a large majority of employed agents likely work in informal employment settings (i.e. assumed 64% and 76% among employed men and women respectively[8]), where workplace test distribution is assumed to be difficult or infeasible. Third, dedicated isolation and quarantine facilities are likely rare in low-resource settings. Thus, we assumed that agents testing positive and their close contacts could only isolate themselves in their own homes. As such, almost 60% of all infections observed in a typical simulation arose from transmissions in households (**Figure 7A**). Random community transmissions aside, schools are then the second most common setting where transmissions occurred (~14%) and workplaces, be it formal or informal, the least common (<3%).

Interestingly, even though we assumed that 70% of all households regularly attended large church congregations every Sunday, churches contributed to a limited proportion of total infections (~5%). Yet, if we compare the results between household and church testing at levels of test availability large enough to satisfy symptomatic testing demand (e.g. N=5000), the total number of diagnosed cases over time is actually largely similar for both community testing strategies (**Figure 7B**). In fact, testing in churches yielded a relatively larger number of cumulative diagnoses by the end of the simulated epidemic but household testing suppressed R_t more during the growth phase of the epidemic, resulting in a greater number of infections averted over time. An explanation for this is simply that there tend to be more transmissions happening in households, as discussed before. However, the reasons behind this observation are far more nuanced.

To elucidate this further, we quantified the impact of how community testing within a social setting could impact the level of transmissions in other settings. As PATAT tracks the setting where each transmission event took place, we are able to compute the proportion of "spillover" events where the setting in which the infector was infected differs from where they infect their infectee (e.g. if an infector infected an individual in the household setting but the infector was themselves infected in school). We found that relative to church testing, household testing not only reduced the number of infections taking place in households, it also decreased the number of "spillover" events between most non-identical settings (**Figure 7C-D**).

Figure 7. Community testing in households outperforms other settings.
(A) Typical breakdown of infections based on the social setting where transmissions occurred for the simulations presented in this work.
(B) As an example, results from simulations using different testing strategies where R_0=1.5, no quarantine of household members of agents testing positive assumed, and Ag-RDT availability of 5000 tests per 100,000 persons per day. Community testing (even distribution) was performed with a symptomatic-testing-first approach. The average total number of diagnosed cases (left), instantaneous reproduction number (R_t; middle) and number of infections averted (right) over the epidemic period are plotted.
(C, D) Transmission "spillover" between different settings. The top row of stacked plots shows the breakdown of infections exported into each transmission sink setting (i.e. where the infectee of a transmission was infected) from other source settings (i.e. where the corresponding infector of a transmission was infected). The stacked bars are coloured by the source settings. The bottom row of bar plots shows the contribution of transmission exports into other settings from different source settings (i.e. the infectee of a transmission event was infected in a setting that is not the same as where their infector was infected).
(C) No testing baseline results from the example case as in (B).
(D) Results from either implementing a symptomatic-testing-first community testing in households (left column) or church (right column). The dashed bar outlines are the no testing baseline results as in (C).



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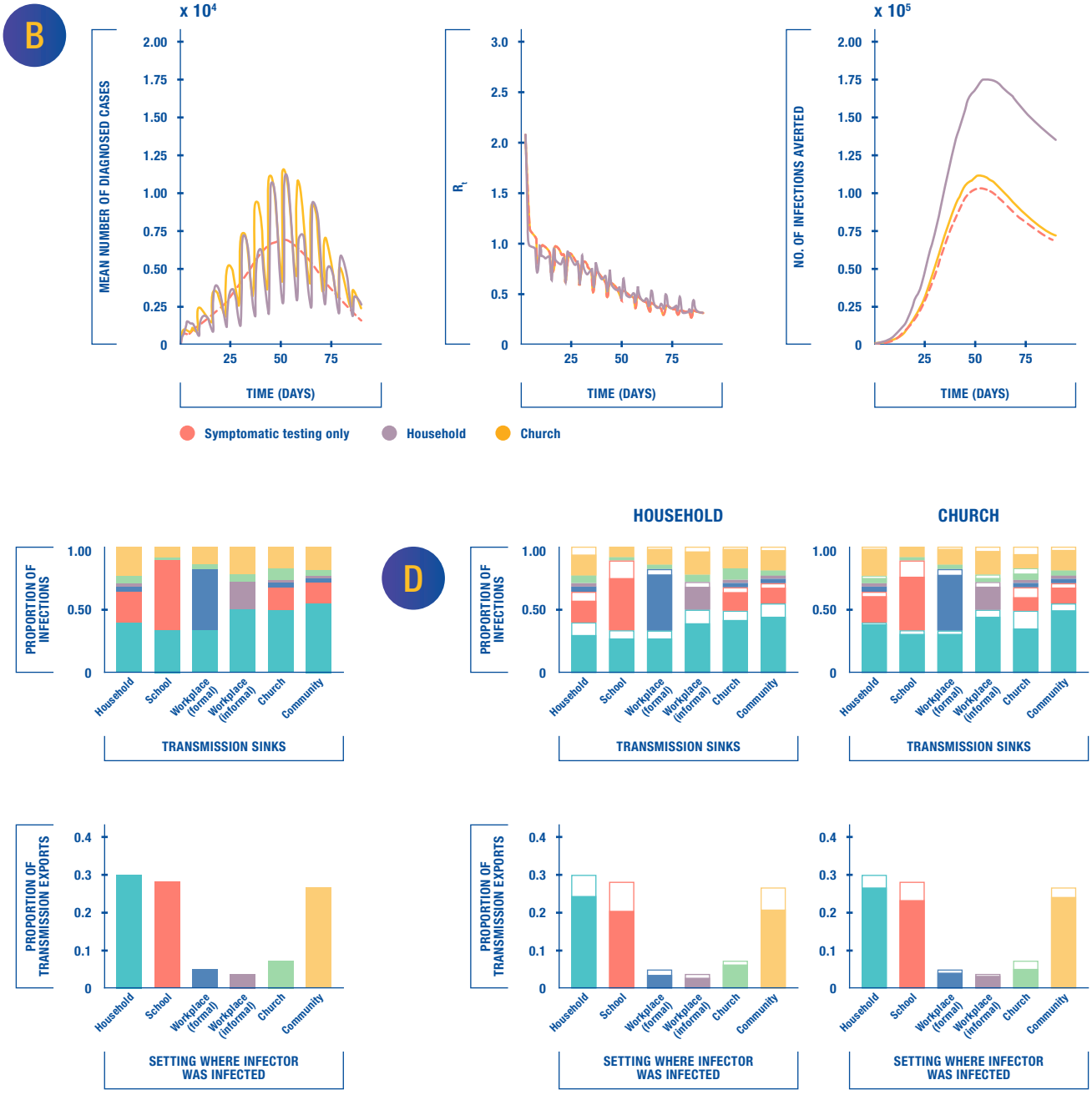


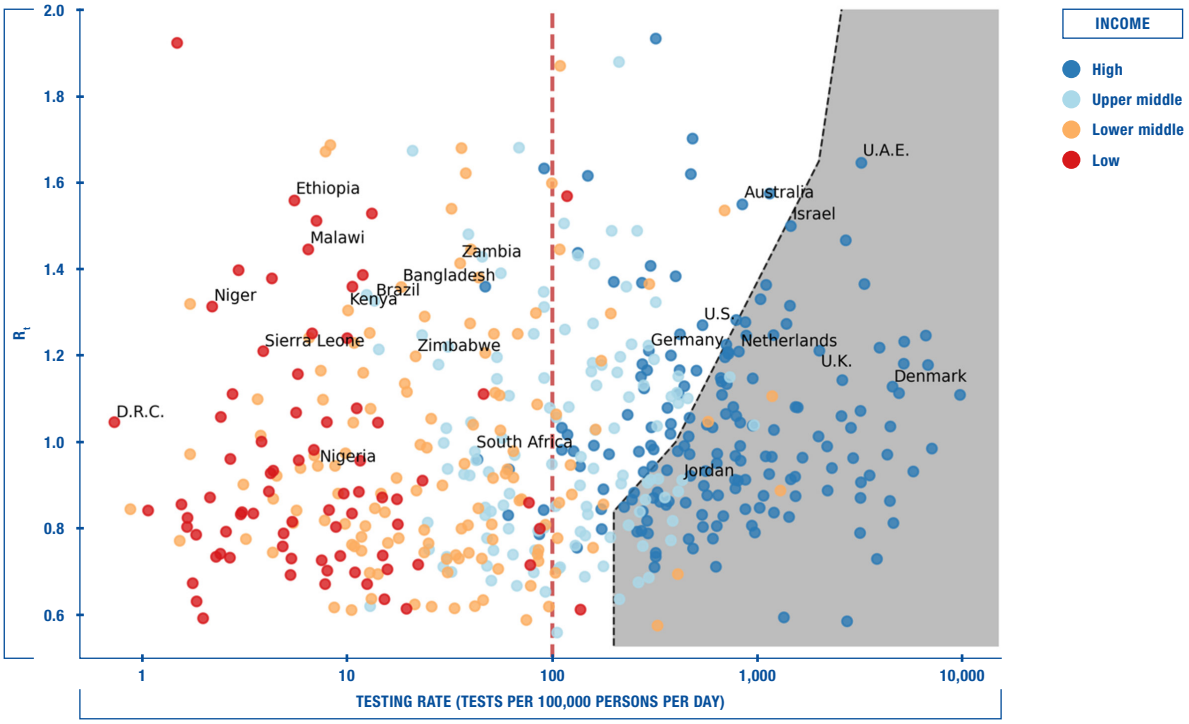
DISCUSSION

Using PATAT, an agent-based simulation model that combined various use-cases and design elements used in the Phase 1 modelling study, we interrogated the impact that testing with rapid antigen diagnostics has in reducing SARS-CoV-2 transmissions in LMICs. **We found that community testing will only achieve high levels of infection reduction after demand for testing from individuals with symptoms of COVID-19 is satisfied.** As expected, symptomatic testing demand primarily depends on and rapidly increases with R_0. Importantly, the current ACT-A Diagnostics Pillar's minimum target of providing 100 tests per 100,000 persons per day fell far short in meeting this demand, even with scenarios where $R_t<1$ (i.e. equivalent to simulated epidemics where $R_0 \leq 1.2$), and thus even much less so for R_t that would result in exponential growth of infections (i.e. equivalent to simulated epidemics where $R_0 \geq 1.5$).

In other words, even before facilitating any form of community testing, the current greatest priority should be to increase investments in testing availability in meeting symptomatic testing demand. As SARS-CoV-2 outbreaks can have R_0 appreciably above 1.5 (i.e. equivalent to initial $R_t>1.6$), it is important that we combine testing with other measures such as social distancing and other non-pharmaceutical interventions so as to maximize impact. **If R0<1.5, or can be reduced to that point through other public health interventions, increasing testing capacity from 100 tests/100k/day to 200-400 tests/100k/day provides the greatest proportional reduction in secondary transmissions.** In short, testing itself has the potential to be most effective at reducing transmission when $R_0<1.5$.

To corroborate our results to the real-world data, we matched the monthly average testing rate (https://www.finddx.org/covid-19/test-tracker/) to the monthly average R_t values estimated from COVID-19 case counts[11] of each country between December 2021 and March 2022 when the Omicron variant-of-concern (VOC) spread rapidly across multiple countries (**Figure 8**). Although the demographic profiles differ between high-income countries (HICs) and LMICs, we found that HICs were expectedly testing at rates that were sufficient or even larger than what was likely needed to saturate the symptomatic testing demand we had estimated for LMICs at similar epidemic intensity. Additionally, as Omicron cases surged, even HICs such as the United States (U.S.), Germany and Australia were reportedly facing test shortages[12–14]. Based on our results, we also found that these countries likely fell short of meeting symptomatic testing demand under equivalent secondary transmission potential. Finally, if we assume that most HICs are testing at rates that sufficiently meet symptomatic testing demand, we found that most of them were testing at least 200 tests/100k/day, which is in line with our recommendation of minimum testing capacity for LMICs.

Figure 8. Global reported COVID-19 testing rate between December 2021 and March 2022 during which Omicron spread rapidly across multiple countries. Each data point denotes the average monthly reported COVID-19 testing rate of a country against the average instantaneous reproduction number (R_t) computed in the same month and is coloured by the income level of the country. Selected data points that are annotated with country names denotes the testing rate on the month at which R_t is the highest during the four-month time period. The shaded area denotes the level of test availability we had estimated to saturate symptomatic testing demand given different equivalent initial R_t values (**Figure 4**). The red vertical line at 100 tests per 100,000 persons per day is the minimum testing rate target set by the ACT-A Diagnostics Pillar. Testing rate data were sourced from the SARS-CoV-2 Test Tracker by FIND (https://www.finddx.org/covid-19/test-tracker/) while R_t was computed from reported COVID-19 case counts[11].



If there is enough test availability for community testing after symptomatic testing demand has been saturated, it is also important to also consider where to prioritize community testing. Given that a larger proportion of infections is expected to occur within households which can be further amplified by larger household sizes observed in many LMICs, **even distribution of tests across households every week after attempts to meet symptomatic testing demand in the previous week would result in the greatest infections averted.** While testing at mass gatherings such as churches every Sunday, for instance, would lead to comparable levels of diagnosis, doing so only effectively totals the amount of infections that had happened previously in the week to decrease infections at these gatherings. In **Figure 7B**, the number of diagnosed cases from community testing at church and households were similar. However, in **Figure 7D**, testing at church mostly decreased the amount of infections occurring at churches while testing at households decreases "spillover" transmissions across different social settings. This is because most transmissions occurred in households. As such, testing at churches on Sundays primarily impacts tallying infections that happened before Sunday. Disseminating tests evenly across households, on the other hand, is more effective in not just lowering transmissions happening in households but lessening the amount of "spillover" transmissions between different social settings. Self-testing could play a key role in helping to satisfy symptomatic testing demand and be a focal point for household community testing.

THERE ARE LIMITATIONS WITH THE CURRENT VERSION OF THE MODEL AND ANALYSES.

First, we assumed all healthcare facilities have access to any available Ag-RDT stocks. In other words, we did not consider disparities in stocks across different healthcare clinics (e.g. larger number of tests may be allocated for community clinics serving larger and denser neighborhoods or more tests may be used in tertiary facilities) and how this might impact meeting symptomatic testing demand and consequently infection reduction. This will be investigated in future work.

Second, we only modelled scenarios where test-and-isolation was the only public health intervention. Symptomatic testing demand would expectedly be lower if other non-pharmaceutical interventions (NPIs) were introduced, and thus potentially improve the utility of community testing at lower test availability. However, the impact of NPIs is confounded by temporal effects[15,16] and thus may be difficult to parameterize their mean effects on infection control and in turn, testing demand. Since NPIs effectively decreases the number of secondary transmissions and in turn, R_t, we expect that the testing demand for a population subjected to NPIs and testing would mirror that estimated for a population subject to testing only but at lower R_t values. Analogously, we also did not model how levels of vaccination- and infection-acquired immunity affect testing demand explicitly. However, by the same reasoning that increased population immunity lowers R_t, the testing demand for a partially immune population should be similar to that of a naïve population at lower R_t values as well.

We will, nevertheless, update future simulations to better reflect the underlying immune landscape of the population in order to obtain more precise estimates of its impact on testing utility and demand. Additionally, as antiviral therapies such as Paxlovid and molnupiravir are introduced into LMICs[17], we will also investigate how different distribution strategies of antiviral treatment would impact testing in the future.

Third, while low volumes of tests may only yield negligible impacts on infection reduction, they may still provide useful information on the prevalence and trajectory of the ongoing epidemic. As such, we will also be exploring the value of information that can be drawn from varying levels of testing in the next report.

Fourth, we have currently investigated the utility of routine, untargeted asymptomatic community testing. However, current WHO guidance prioritizes testing of asymptomatic individuals with known exposures to SARS-CoV-2 such as close contacts of positively-tested people or healthcare workers caring for COVID-19 patients[18]. Furthermore, we had also limited testing option of symptomatic individuals to those provided by healthcare clinics. As mentioned earlier, self-testing in different community settings, including at healthcare facilties[19], could be useful in satisifying symptomatic testing demand. We will continue to explore these alternative test distribution strategies in future work.

Finally, we had parameterized incubation and virus shedding periods using those empirically measured from wild-type SARS-CoV-2 for this work. However, generation intervals have shortened considerably for recent VOCs such as Delta[20] and Omicron and could impact the utility of testing in identifying an infection before it becomes infectious. We will update our simulations using recent VOCs as the circulating virus in the future. Nonetheless, as demonstrated by the corrobation of our results on symptomatic testing demand against empirical testing data collected during the spread of Omicron globally, the minimum required test availability of 200 tests/100k/day estimated from our results still stand regardless of the circulating variant.

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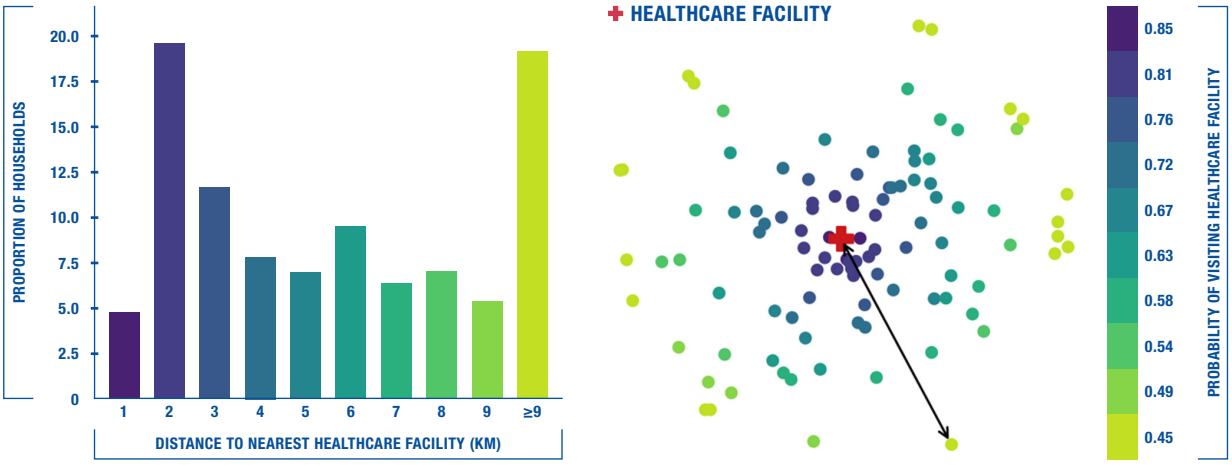
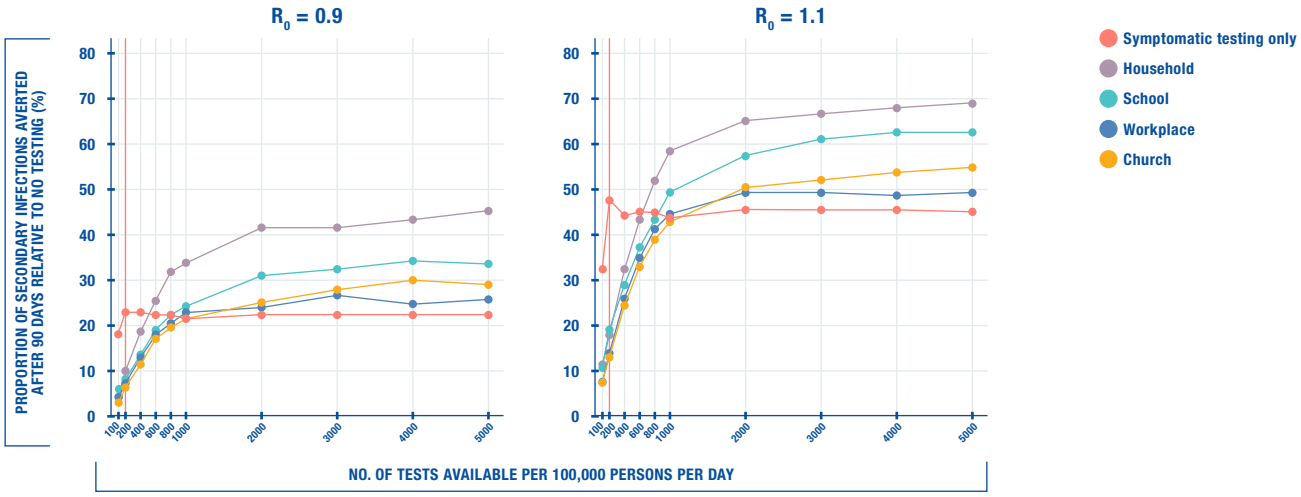
APPENDIX

SUPPLEMENTAL FIGURES

Supplemental Figure 1. **Distribution of households to nearest healthcare facility by distance and corresponding probability (matched by colours of histogram bar of the left and colour bar on the right) of visiting facility for symptomatic testing.** Distribution and probabilities are based on Dovel et al4 (Supplemental Table 1).



Supplemental Figure 2. **Impact of either using all available Ag-RDTs for symptomatic testing or a majority of them (85%) for community testing in various settings (even distribution only; with quarantine of household members).** The proportion of secondary infections averted after 90 days relative to the no testing baseline for different number of tests available per 100,000 persons per day is plotted for each test distribution strategy. The vertical red line denotes the number of tests required to saturate symptomatic testing demand.



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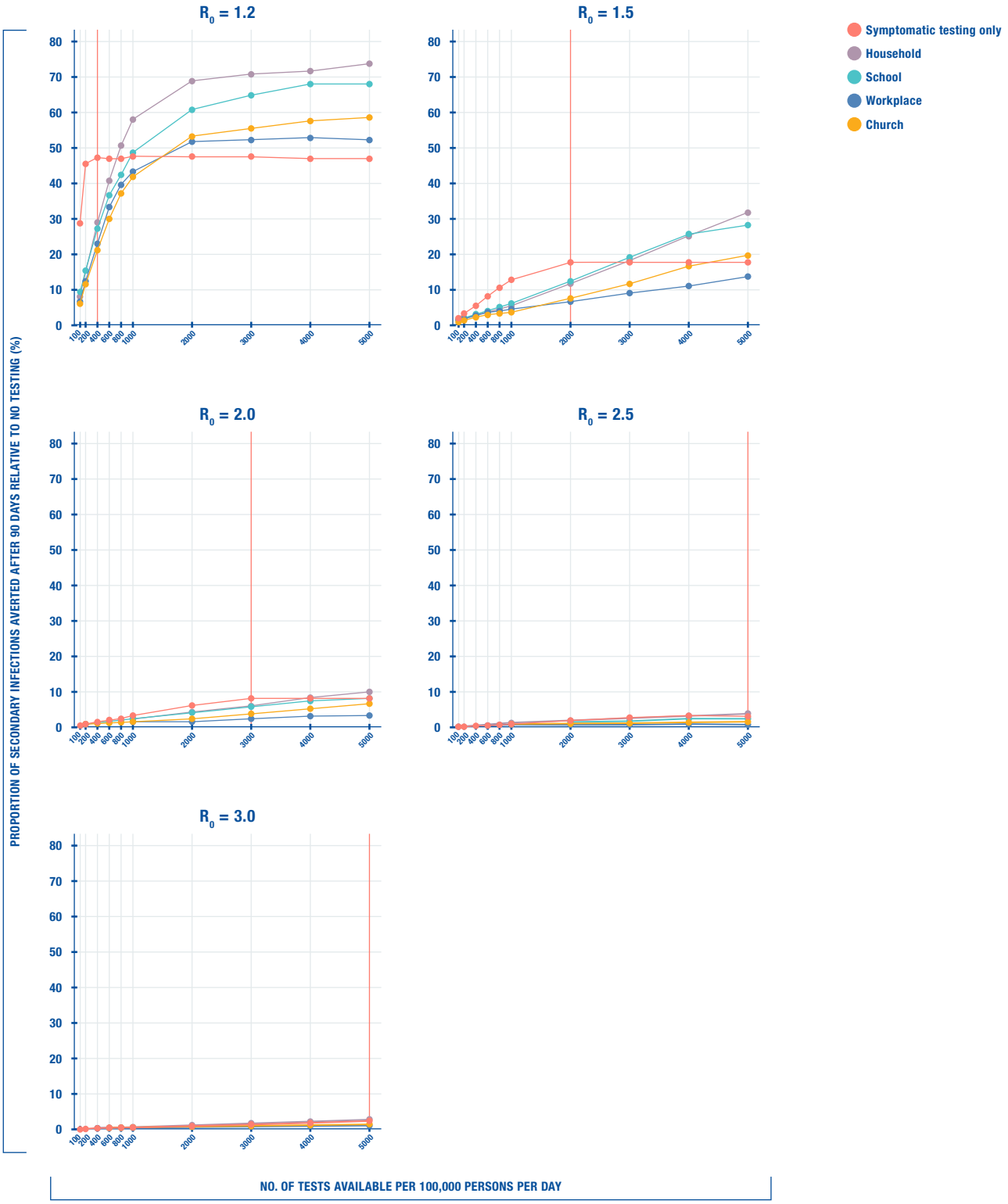
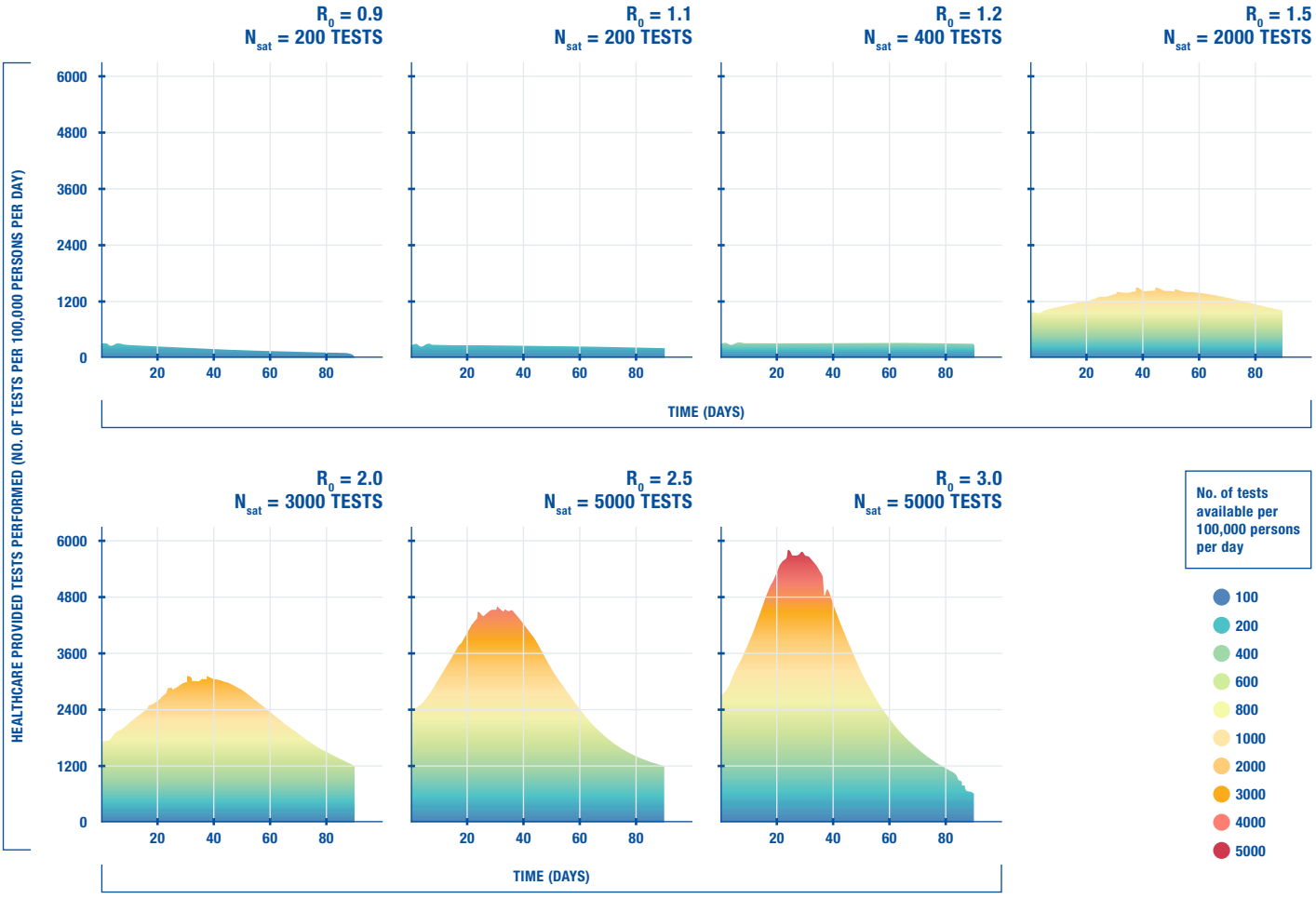
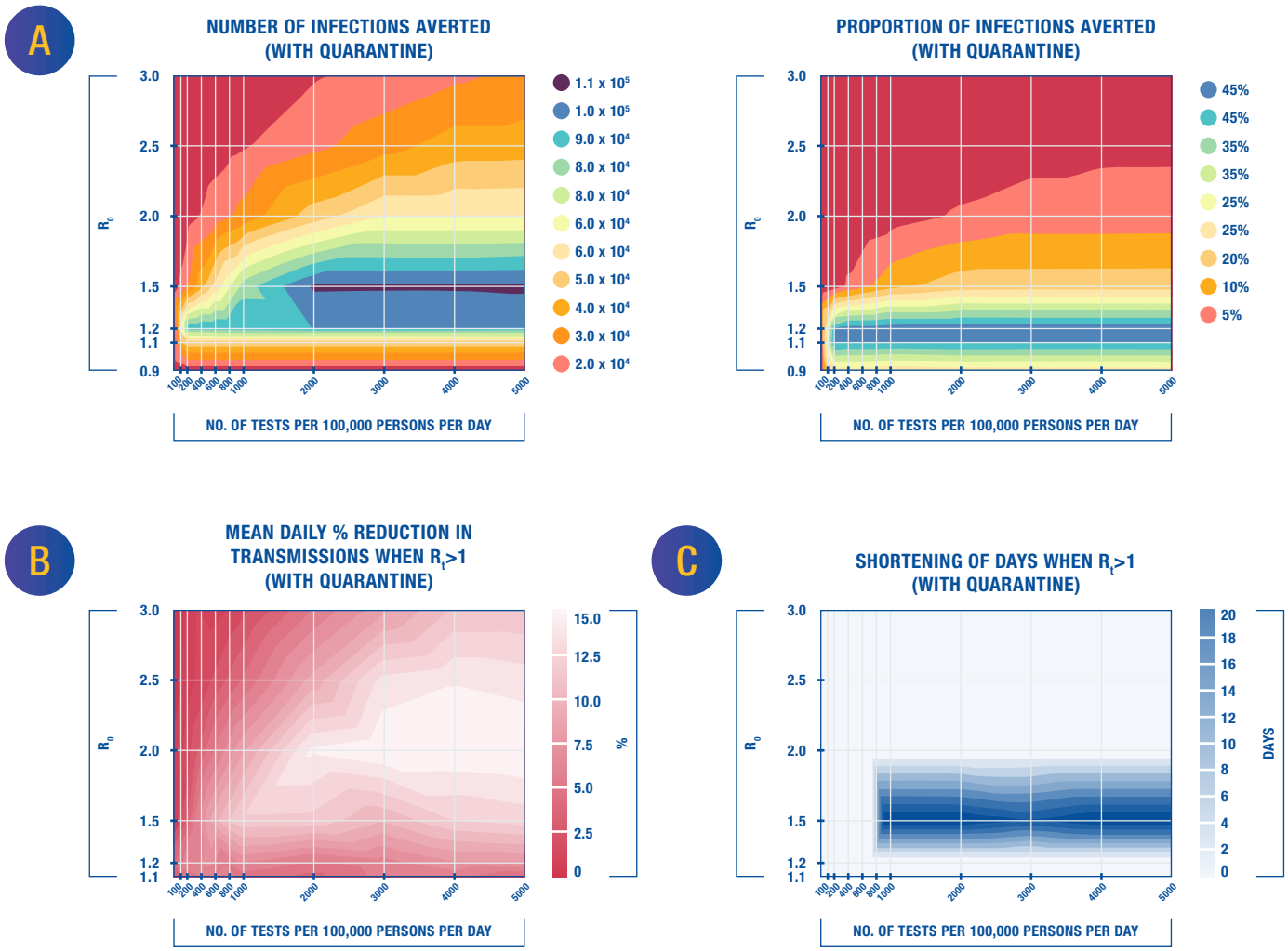


Supplemental Figure 3. **Symptomatic testing demand during an epidemic (with quarantine of household members).** Number of symptomatic tests performed per 100,000 persons per day over time for different R_0. Each differently coloured shaded curve denotes a different number of tests available per 100,000 persons per day. We assumed that all healthcare facilities in the community will have new stocks of one week's worth of Ag-RDTs every Monday. The symptomatic testing demand include both symptomatic SARS-CoV-2 infected agents who seek testing at healthcare facilities and those who seek symptomatic testing for other reasons based on assumed case positivity rates (see Methods). The area between the curve plotting number of tests needed to saturate symptomatic testing demand (N_{sat}) and any other curves plotting $N<N_{sat}$ is the amount of symptomatic testing shortage accumulated over time.



Supplemental Figure 4. **Marginal impact of symptomatic testing prior to saturating demand (with quarantine of household members). (A)** Contour plots depicting infections averted relative to the no testing baseline for simulations with different R_0 values and varying numbers of available Ag-RDTs. Number of infections averted relative to no testing baseline after 90 days (left panel); proportion of secondary infections averted relative to no testing baseline after 90 days (right panel). **(B)** Mean daily percentage reduction in transmissions while instantaneous R_t of simulated epidemic is still > 1 for different R_0 values and varying number of Ag-RDTs available for symptomatic testing only. **(C)** Shortening of the number of days when instantaneous R_t of simulated epidemic is still > 1 for different R_0 values and varying number of Ag-RDTs available for symptomatic testing only.



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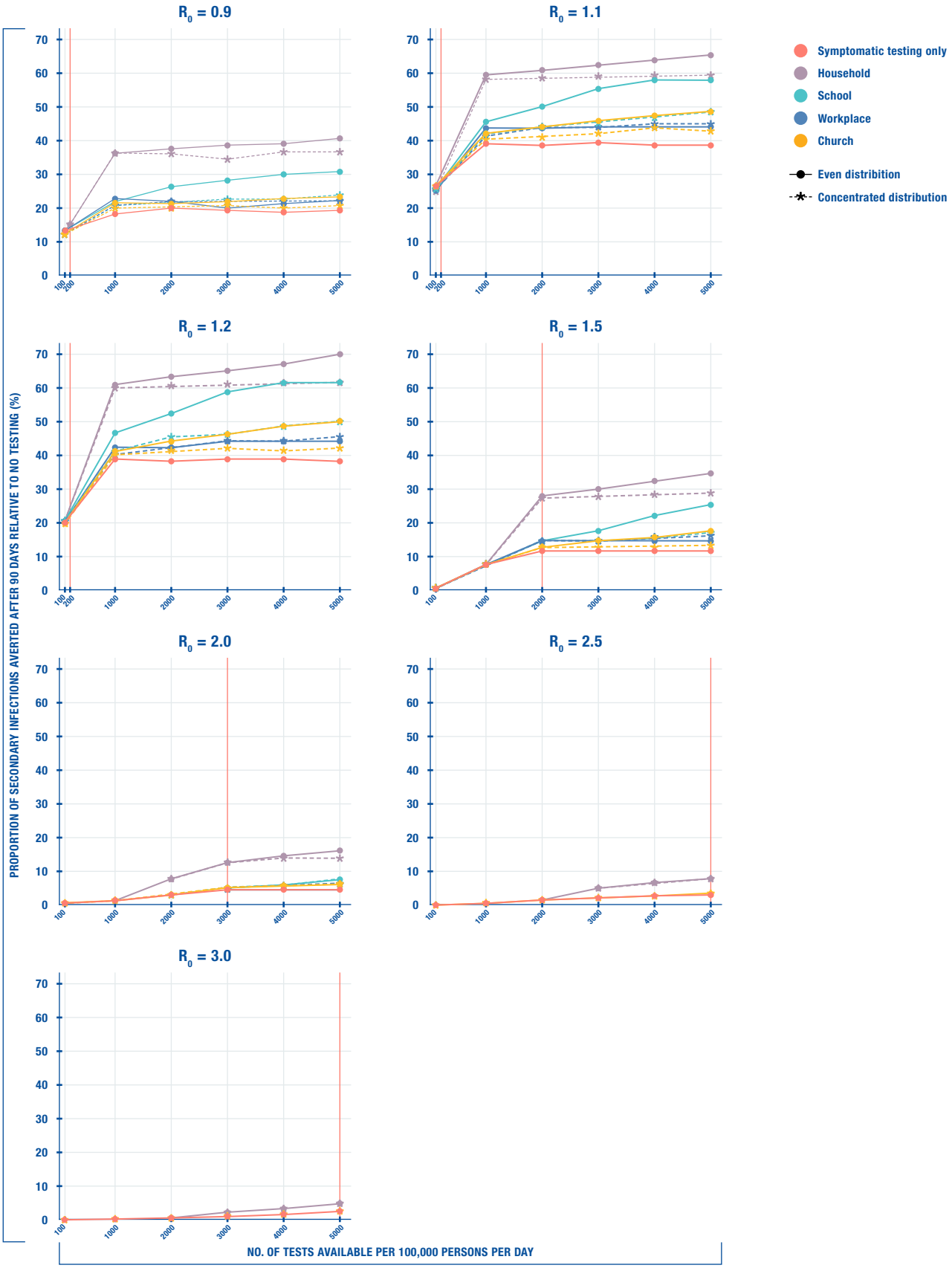

SUPPLEMENTAL TABLES

Supplemental Table 1. PATAT simulation parameters

Parameter	Values/Distribution	Source
POPULATION DEMOGRAPHY		
Total population size	1 million	
Mean household size	5.0	7
Age structure (in bins of 5 years)	[0.161, 0.165, 0.157, 0.101, 0.083, 0.068, 0.057, 0.051, 0.042, 0.030, 0.024, 0.015, 0.016, 0.009, 0.008, 0.005, 0.006, 0.002, 0.000, 0.000]	7
Minimum prime adult age	20 years	Assumed
Proportion of women	51%	8
Minimum working age	15 years	8
Employment rate	39% (male), 23% (female)	8
Formal employment rate	36% (employed male), 24% (employed female)	8
Schooling rate	79% (male), 40% (female)	7
School gender parity	1.0 (Primary), 0.9 (Secondary)	7
Church participation rate	70% of all households	Assumed
Mean employment contacts (formal)	20	Assumed
Mean employment contacts (informal)	5	Assumed
Mean class size	37 (Primary and secondary)	7
Mean school size	700 (Primary and secondary)	Assumed
Student-teacher ratio	42 (Primary and secondary)	7
Mean church size (s.d.)	500 (100)	Assumed
Mean random contacts in church per person	10	Assumed
Mean random community contacts per day	10	Assumed
SARS-COV-2 TRANSMISSION-RELATED PARAMETERS		
Age-structured relative susceptibility (in bins of 5 years)	[0.34, 0.34, 0.67, 0.67, 1.00, 1.00, 1.00, 1.00, 1.00, 1.00, 1.00, 1.00, 1.00, 1.00, 1.24, 1.24, 1.47, 1.47, 1.47, 1.47]	1,21
Age-structured probability of becoming symptomatic (in bins of 5 years)	[0.50, 0.50, 0.55, 0.55, 0.60, 0.60, 0.65, 0.65, 0.70, 0.70, 0.75, 0.75, 0.80, 0.80, 0.85, 0.85, 0.90, 0.90, 0.90, 0.90]	22,23
Age-structured probability of developing severe disease (in bins of 5 years)	[0.00050, 0.00050, 0.00165, 0.00165, 0.00720, 0.00720, 0.02080, 0.02080, 0.03430, 0.03430, 0.07650, 0.07650, 0.13280, 0.13280, 0.20655, 0.20655, 0.24570, 0.24570, 0.24570, 0.24570]	22,23

Parameter	Values/Distribution	Source
SARS-COV-2 TRANSMISSION-RELATED PARAMETERS		
Age-structured probability of death (in bins of 5 years)	[0.00002, 0.00002, 0.00002, 0.00002, 0.00010, 0.00010, 0.00032, 0.00032, 0.00098, 0.00098, 0.00265, 0.00265, 0.00766, 0.00766, 0.02439, 0.02439, 0.08292, 0.08292, 0.16190, 0.16190]	24,25
Latent period (days)	Lognormal (4.5, 1.5)	1,26
Pre-symptomatic period (days)	Lognormal (1.1, 0.9)	1,26
Period between symptom onset and severe disease (days)	Lognormal (6.6, 4.9)	26
Period between severe disease and death (days)	Lognormal (8.6, 6.7)	26
Recovery period for symptomatic agents with mild disease (days)	Lognormal (8.0, 2.0)	27
Recovery period for asymptomatic agent (days)	Lognormal (8.0, 2.0)	27
Recovery period of agents with severe disease (days)	Lognormal (18.1, 6.3)	23
TESTING PARAMETERS		
Delay in visiting healthcare facility for symptomatic testing (days)	Lognormal (1.0, 0.5)	Assumed
Ag-RDT specificity	0.989	2
Agents to healthcare facilities ratio	7,000:1	9,10
Distance-structured distribution of households to nearest healthcare facility (in bins of 1 km)	[0.048, 0.193, 0.119, 0.08, 0.074, 0.098, 0.068, 0.072, 0.056, 0.191]	4
Distance-structured probabilities of agent visiting nearest healthcare facility for symptomatic testing (in bins of 1 km)	[0.853, 0.808, 0.762, 0.717, 0.672, 0.626, 0.581, 0.536, 0.49, 0.445]	4
ISOLATION/QUARANTINE PARAMETERS		
Isolation period after testing positive for SARS-CoV-2	10 days	
Quarantine period of close contacts	14 days	
Self-isolation period upon onset of COVID-19 symptoms without testing	10 days	
Reduction in contact rates under isolation/quarantine (in order of households, schools, workplaces, church and random community)	[10%, 100%, 100%, 100%, 100%]	

TECHNICAL DETAILS OF THE PROPELLING ACTION FOR TESTING AND TREATMENT (PATAT)

PATAT is a stochastic agent-based model designed to investigate the use and impact of Ag-RDTs in controlling COVID-19 outbreaks in LMICs. The computational flow of a PATAT simulation is summarized as follows: First, an age-structured population of agents is created. Close contact networks are subsequently created based on the given demographic data. The simulation is then initialized and iterates over a given period of time where each time step corresponds to a day. The operations during each timestep encompass updating the disease progression of infected individuals, the status of isolated/quarantined agents, application of community testing strategies and computation of transmission events within contact networks.

POPULATION DEMOGRAPHY

Using input demographic data which includes information such as population age and sex distribution, household composition, employment and schooling rates, PATAT generates a population of individuals who are linked by a series of underlying contact network settings where transmission may occur. These contact network settings include households, schools, workplaces, regular mass gatherings (i.e. church) as well as random community contacts.

HOUSEHOLD

PATAT randomly generates a Poisson distribution of household sizes based on the given mean household size. A reference individual (e.g. head of the household) above an assumed prime adult age (e.g. 20 years) is first randomly assigned to each household. To account for multigenerational households, the remaining household members are then randomly sampled multinomially by the input age distribution of households. Although PATAT does not explicitly model the geolocation of agents, households are ordered to implicitly approximate neighborhood proximity.

SCHOOLS

PATAT distinguishes between primary and secondary schools. For each education level, school-aged children are randomly sampled from the population based on given enrollment rates and gender parity. Class sizes are then randomly drawn from a Poisson distribution based on the input mean class size while constrained by the number of school-aged children attending the same grade (i.e. age; a class include only students studying the same grade). Schools are created by random allotment of classes such that (1) all schools will have equitable distributions of classes of all grades for the given education level and (2) the total number of students approximately equals the expected school size. Classes are then populated by schooling agents such that (1) agents of proximally ordered households will tend to attend the same school and (2) children of the same grade (age) from identical households will not be assigned to the same class even though they may attend the same school. School teachers are then randomly drawn from the employed prime adult population based on the input teacher-to-student ratio and are assumed to have contact with each other during school days. Each class is randomly assigned to one teacher.

WORKPLACES

PATAT generates both formal and informal workplace contact networks based on separate employment rates. Youth (15–19 years) employment is also considered in the potential workforce. The distinction between formal and informal settings is made as mean employee contact rates likely differ between them. Furthermore, workplace distribution of Ag-RDTs for community testing is assumed to be feasible for formal employment entities only. Unlike schools, PATAT does not explicitly model for workplaces but sets up contact matrices between employed individuals who would be in regular contact at work. Different sizes of workplace contact networks are randomly drawn from a Poisson distribution based on the given mean employee contact size. An employed agent would only be associated with one workplace contact network.

MASS GATHERINGS (CHURCH)

High-density mass gatherings are considered in the model in the form of contacts among church congregations. The size of a church is assumed to follow a normal distribution with the given mean and variance. PATAT assumes that all members of a household will visit a church together every Sunday. Other than close contacts with each other, each household member would also have a random number of close contacts from other households that attend the same church. This random contact number is drawn from a Gamma distribution with the given shape and scale parameters. Churches are also ordered such that proximally ordered households in the same neighborhood would visit the same church.

RANDOM COMMUNITY

PATAT assumes that every agent within a given age range would have a random number of contacts with the community daily, drawn from a Poisson distribution with a given mean.

DISEASE PROGRESSION

PATAT implements a SEIRD epidemic model where the simulated population is distinguished between five compartments: susceptible, exposed (i.e. infected but is not infectious yet; latent phase), infected (which include the presymptomatic infectious period for symptomatic agents), recovered and dead. The infected compartments are further stratified by their presented symptoms, including asymptomatic, presymptomatic, symptomatic mild or severe. All symptomatic agents will also first undergo an infectious presymptomatic period after the exposed latent period. They will either develop mild symptoms (and always recover from the disease) or experience severe infection which could either lead to death or recovery. PATAT uses the same age-structured wild-type SARS-CoV-2 disease severity ($p_{sev,age}$) and mortality ($p_{dea,age}$) probabilities that were also used in Covasim1 (**Supplemental Table 1**). As a simplification, PATAT currently assumes that all agents presenting severe symptoms will be hospitalized and removed from the population.

The total duration of infection since exposure depends on the symptoms presented by the patient and is comprised of different phases (i.e. latent, asymptomatic, presymptomatic, onset-to-recovery/death). The time period of each phase is drawn from the same distributions used by Covasim as well (**Supplemental Table 1**).

WITHIN-HOST VIRAL DYNAMICS

For each infected agent, PATAT explicitly simulates their viral load trajectory of cycle threshold (Ct) values over the course of their infection using a stochastic model modified from the one previously developed by Quilty et al.[3] A baseline Ct value ($Ct_{baseline}$) of 40 is established upon exposure. The infected agent becomes infectious upon the end of the latent period and their Ct value is assumed to be ≤30. A peak Ct value is then randomly drawn from a normal distribution of mean 22.3 and SD of 4.2.[29] Peak Ct is assumed to occur upon symptom onset for symptomatic agents and one day after the latent period for asymptomatic individuals. Cessation of viral shedding (i.e. return to $Ct_{baseline}$) occurs upon recovery or death.

PATAT assumes that the transition rate towards peak Ct value should not be drastically different to that when returning to baseline upon cessation (i.e. there should be no sharp increase to baseline Ct value after gradual decrease to peak Ct value or vice versa). As such, the time periods of the different phases of infection are randomly drawn from the same quintile of their respective sample distribution. The viral load trajectory is then simulated by fitting a cubic Hermite spline to the generated exposed ($t_{exposed}$, $Ct_{baseline}$), latent (t_{latent}, Ct_{latent}=30), peak (t_{peak}, Ct_{peak}) and cessation values ($t_{recovered/death}$), $Ct_{baseline}$).

The slope of the fitted curve is assumed to be zero for all of them except during t_{latent} where its slope is assumed to be

$$\frac{Ct_{peak} - Ct_{baseline}}{t_{peak} - t_{exposed}}$$

PATAT then uses the fitted trajectory to linearly interpolate the viral load transmissibility factor ($f_{load,i}$) of an infectious agent i assuming that they are twice as transmissible at peak Ct value (i.e. f_{load}=2) relative to when they first become infectious (i.e. Ct value = 30; f_{load}=1).

TRANSMISSIONS

When an infectious agent *i* comes into contact with a susceptible individual *j*, the probability of transmission ($p_{transmission,(i,j)}$) is given by:

$$p_{transmission,(i,j)} = \beta \times \Phi_i \times f_c \times f_{asymp,i} \times f_{load,i} \times f_{immunity,j} \times f_{susceptiblity,j}$$

where β is the base transmission probability per contact, Φ_i is the overdispersion factor modelling individual-level variation in secondary transmissions (i.e. superspreading events), f_c is a relative weight adjusting β for the network setting *c* where the contact has occurred, $f_{asymp,i}$ is the assumed relative transmissibility factor if infector *i* is asymptomatic, $f_{immunity,j}$ measures the immunity level of susceptible *j* against the transmitted virus (i.e. $f_{immunity,j}$=1 if completely naïve; $f_{immunity,j}$=0 if fully protected), and $f_{susceptiblity,j}$ is the age-dependent susceptibility of *j*.

Φ_i is randomly drawn from a negative binomial distribution with mean of 1.0 and shape parameter of 0.45.[30] As evidence has been mixed as to whether asymptomatic agents are less transmissible, we conservatively assume there is no difference relative to symptomatic patients (i.e. $f_{asymp,i}$=1). The age-structured relative susceptibility values $f_{susceptiblity,j}$ are derived from odds ratios reported by Zhang et al.[22]

β is determined by running initial test simulations with a range of values on a naïve population with no interventions that would satisfy the target basic reproduction number R_0 as computed from the resulting exponential growth rate and distribution of generation intervals.[31] f_c is similarly calibrated during these test runs such that the transmission probabilities in households, workplaces, schools, and all other community contacts are constrained by a relative weighting of 10:2:2:1.[1]

TESTING BY AG-RDT

Unlike PCR which is highly sensitive due to prior amplification of viral genetic materials, the sensitivity of Ag-RDTs depends on the viral load of the tested patient. While the specificity of Ag-RDT is assumed to be 98.9%, its sensitivity depends on the Ct values of the tested infected agent: Ct >35 (sensitivity: 0%); Ct 35 – 30 (sensitivity: 20.9%); Ct 29 – 25 (sensitivity: 50.7%); Ct ≤24 (sensitivity: 95.8%).[2]

Testing by Ag-RDT may either occur via symptomatic testing at healthcare facilities or through healthcare-provided community testing. First, a symptomatic agent may opt to go into self-isolation upon symptom onset prior to being tested, as decided by a Bernoulli trial with probability $p_{self-isolation}$. Regardless if they were self-isolated, after $\tau_{delay,symp-test}$ days from symptom onset, the symptomatic agent may then decide to get tested with a Bernoulli probability of $p_{symp-test}$ that inversely correlates with the distance between the agent's household and the nearest healthcare clinic (**Supplemental Figure 5** and **Supplemental Table 1**). PATAT assumes that agents who have decided against symptomatic testing (i.e. failed Bernoulli trial) or received negative test results will not seek symptomatic testing again.

For community testing in schools, we followed the convention used in the Phase 1 modelling study. Given that teachers may act as inter-connecting agents linking between various classes, any available Ag-RDTs will always first be distributed to teachers in a school before they are distributed to students.

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