Supplementary Information

Estimating the potential need and impact of SARS-CoV-2 test-and-treat programs with oral antivirals in low-and-middle-income countries

Alvin X. Han[1,*], Emma Hannay[2], Sergio Carmona[2], Bill Rodriguez[2], Brooke E. Nichols[1,2,3,†], Colin A. Russell[1,3,†,*]

[1]Department of Medical Microbiology & Infection Prevention, Amsterdam University Medical Center, University of Amsterdam, Amsterdam, The Netherlands

[2]Foundation for Innovative New Diagnostics (FIND), Geneva, Switzerland

[3]Department of Global Health, School of Public Health, Boston University, Boston, MA, USA

†Contributed equally

*Correspondence to Alvin X. Han (x.han@amsterdamumc.nl) and Colin A. Russell (c.a.russell@amsterdamumc.nl)

Supplementary Text

Technical details of the Propelling Action for Test And Treat (PATAT) model

PATAT is a stochastic agent-based model designed to investigate the use and impact of antigen-detecting rapid diagnostic tests (Ag-RDT) in controlling COVID-19 outbreaks in low-middle income countries.[1,2] The computational flow of a PATAT simulation is summarised 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 initialised 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. 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 neighbourhood proximity.

Schools

PATAT distinguishes between elementary and secondary schools. For each education level, schooling children are randomly sampled from the population based on given enrolment 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 schooling 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 to 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. As such, different number of formal and informal mean number of work contacts must be provided by the user and sizes of workplace contact network are randomly drawn from a Poisson distribution. An employed agent would only be associated with one workplace contact network.

Mass gatherings (Religious gathering)

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 user's 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 user's given shape and scale parameters. Churches are also ordered such that proximally ordered households in the same neighbourhood 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 mean defined by the user.

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 who will always recover from the disease or experience severe infection which could either lead to death or recovery. PATAT uses age-structured SARS-CoV-2 disease severity and mortality probabilities (Extended Data 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 can be found in Extended Data 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 (Extended Data Table 1). 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; $f_{load} = 1$).

Antiviral treatment

For individuals who were treated with antivirals that were deemed to result in severe disease, we performed a Bernoulli trial with the probability of averting severe disease (i.e. percentage risk reduction to severe disease outcomes), provided that they are currently in the presymptomatic phase or are experiencing mild disease. If the Bernoulli trial succeed, we would re-simulate their disease progression and within host viral dynamics using the procedures above but now under the assumption that they would develop only mild disease and conditioning that the maximum viral load is lower than before. Changes will only be made to the upcoming phases of disease progression from the current phase of infection.

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:

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

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), $f_{susceptiblity,j}$ is the age-dependent susceptibility of j, ρ_i and ρ_j are the contact rates of infector i and susceptible j respectively.

$\Phi_i$is randomly drawn from a negative binomial distribution with mean of 1.0 and shape parameter of 0.45.[4] As evidence have 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.[5] (Extended Data Table 1).

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.[6] 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.[7]

Testing by Ag-RDT

Unlike PCR which is highly sensitive due to prior amplification of viral genetic materials, the sensitivity of Ag-RDT 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 (0%); 35 – 30 (20.9%); 29 – 25 (50.7%); Ct ≤ 24 (95.8%).[8]

Testing by Ag-RDT may either occur via symptomatic testing at healthcare facilities or 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 HCF (Extended Data 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, 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.

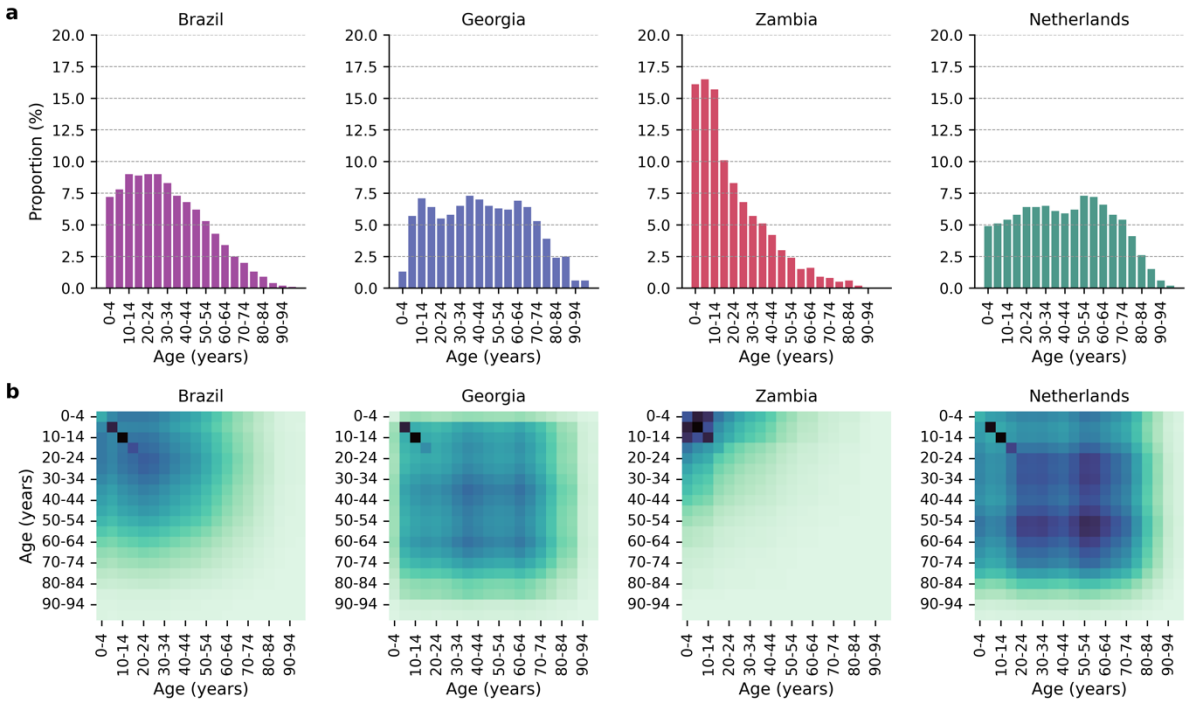
Isolation and quarantine

We assumed that agents would change their behaviour when (1) they start to present symptoms and go into self-isolation (10% compliance assumed, 71% endpoint adherence)[9]; (2) they test positive and are isolated for 10 days (50% compliance assumed, 86% endpoint adherence)[9]; or (3) they are household members (without symptoms) of positively-tested agents and are required to be in quarantine for 14 days (50% compliance assumed, 28% endpoint adherence)[9]. 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 low-middle income countries, we assumed that all isolated and quarantined individuals would do so at home. Although they have no contact with agents outside of their home, we assumed that they would maintain 90% contact rate with household members.

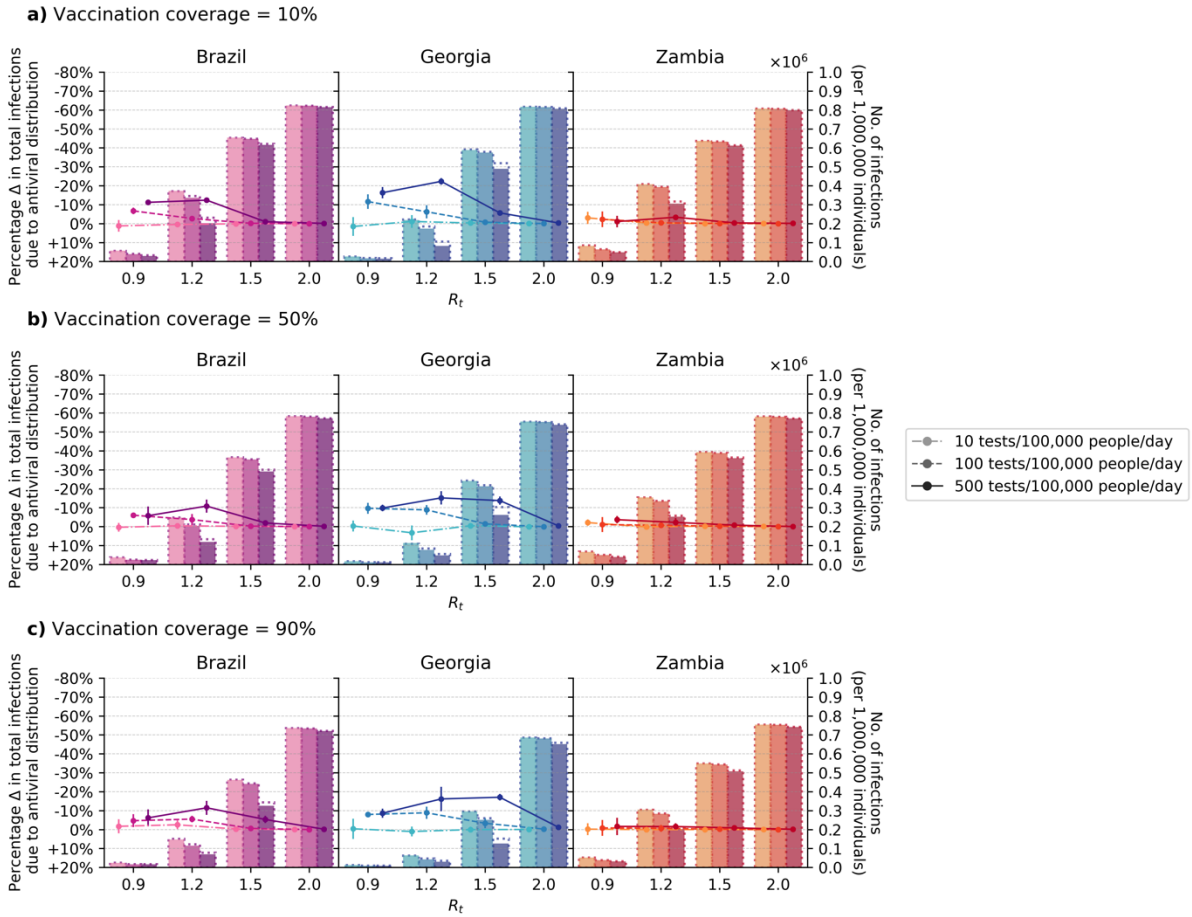
Model Validation

To validate our model, we compared our simulation results against actual reported cases and deaths in Lusaka, Zambia between 25 December 2020 and 24 March 2021. Zambia was experiencing a second wave of infections as a result of the Beta variant.[10] Actual confirmed case and death tallies were retrieved from the Zambia COVID-19 Dashboard (https://www.arcgis.com/apps/dashboards/3b3a01c1d8444932ba075fb44b119b63). During this time, Zambia was performing ~40 tests/100,000 people/day[11]. We assumed that initial R_e ~ 2.0 and simulated a 90-day epidemic wave under the aforementioned testing rate for 1,000,000 individuals using the demography parameters for Zambia (Extended Data Table 1) and performed 10 independent simulations using PATAT. We multiplied the estimated mean number of reported (i.e. diagnosed) cases and deaths from our simulations by three to proportionally scale up the results for three million people, the approximate population size in Lusaka, Zambia. Our simulation results fit well against both actual reported case and death counts (Mean absolute difference = ~290 (case counts), 8 (deaths); Extended Data Fig. 12).

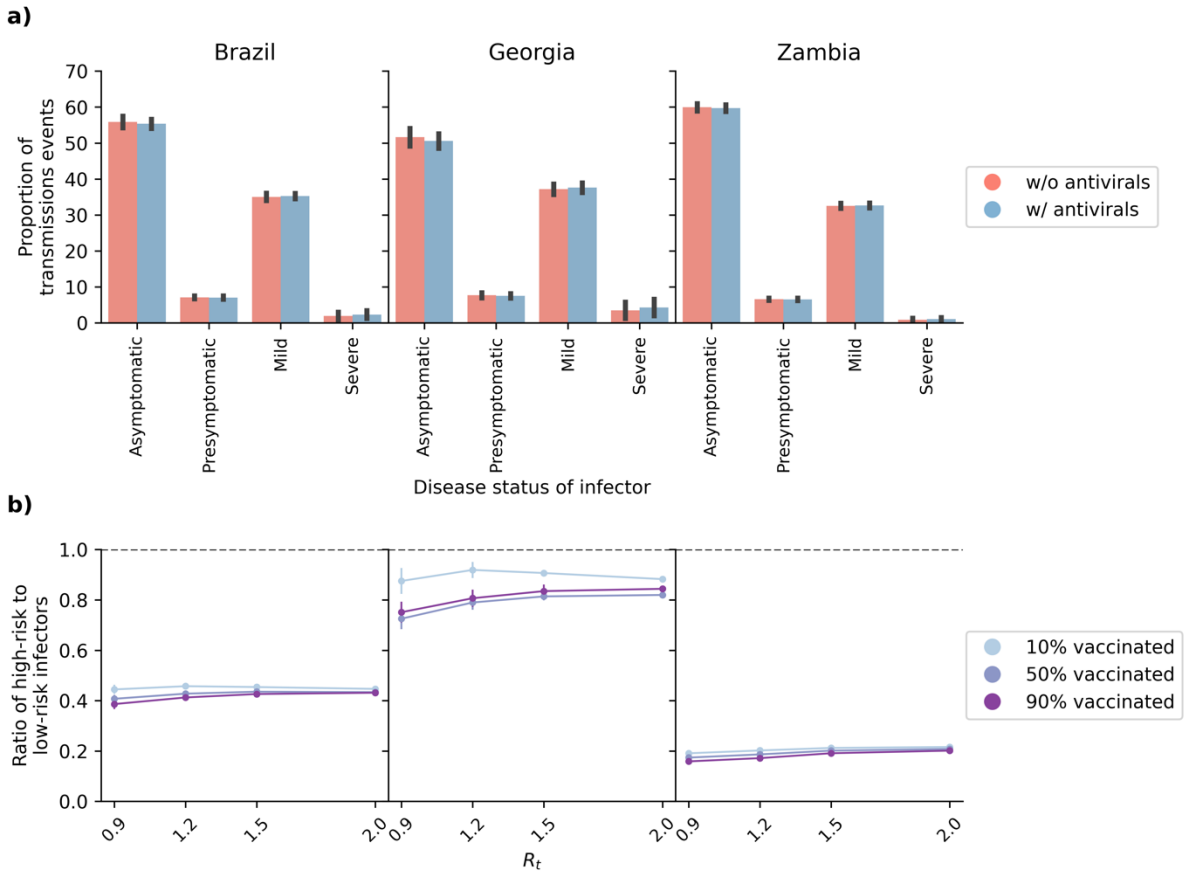
Extended Data Figures



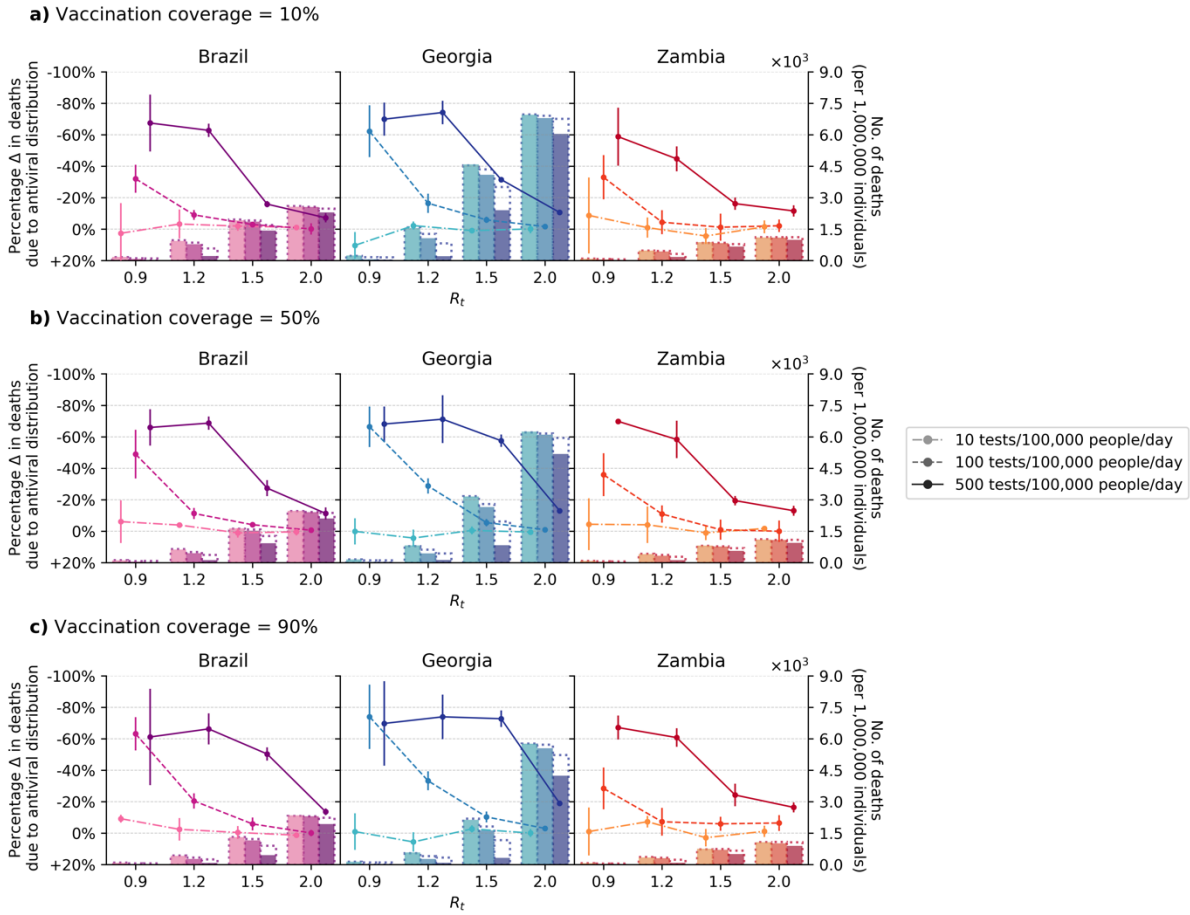
Extended Data Fig. 1: **Demography of simulated countries**. (**a**) Age distribution stratified in 5-year bins. (**b**) Heatmap showing frequency of contacts between individuals of different age groups in 5-year bins averaged across all contact networks generated by the PATAT simulation model.



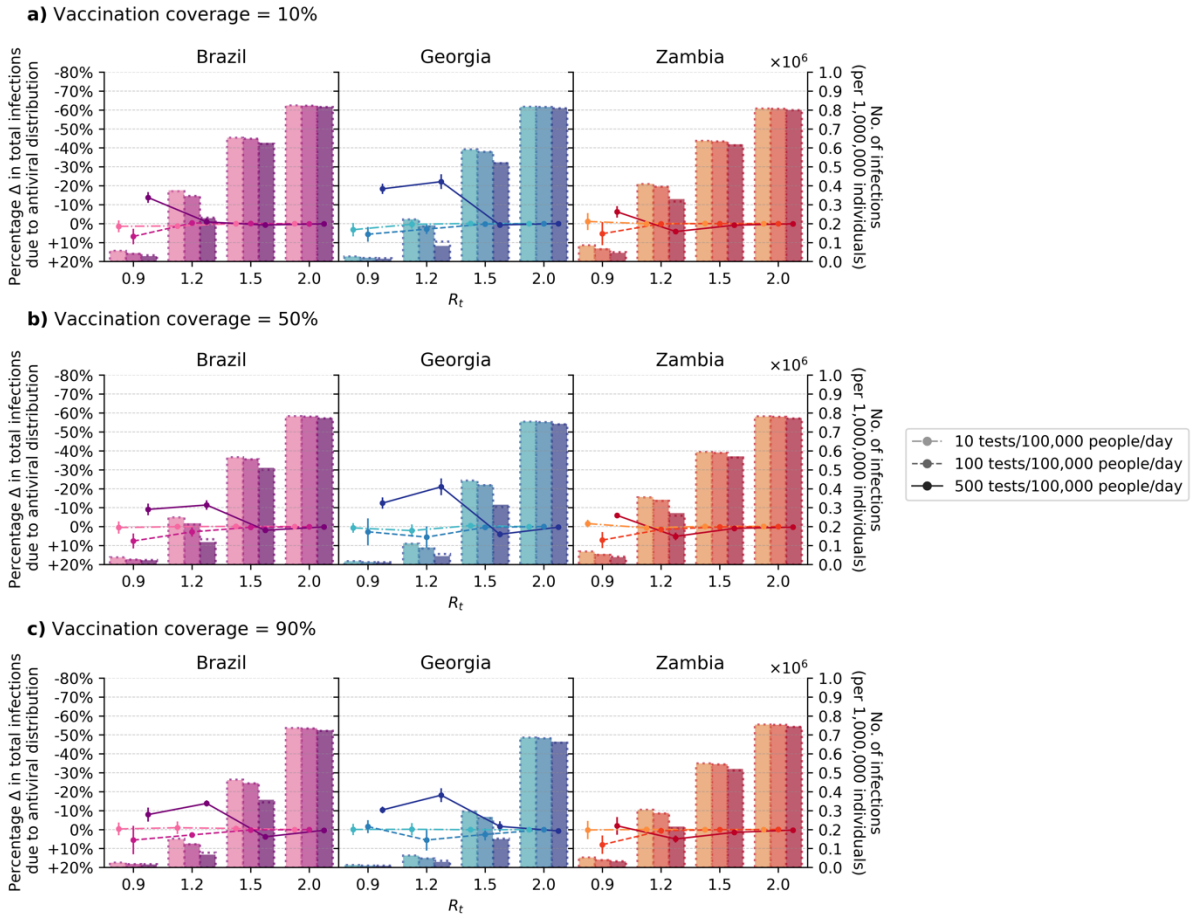
Extended Data Fig. 2: **Impact of oral antiviral therapy on infections in low- and middle-income countries**. No restrictions on access to symptomatic testing at clinics (i.e. all symptomatic individuals who sought testing at clinics would receive one if in stock) and high-risk household contacts of test-positive individuals were not tested. All eligible high-risk individuals (i.e. ≥60 years of age or an adult ≥18 years with a relevant comorbidity) who tested positive were given a course of oral antivirals. Line plots (left y-axis) show the percentage change in total infections relative to no distribution of antivirals under different levels of mean test availability (different shades of color) after a 90-day Omicron BA.1-like epidemic wave in a population of 1,000,000 individuals with (**a**) 10%, (**b**) 50%, and (**c**) 90% vaccination coverage for different epidemic intensities (measured by the initial instantaneous reproduction number (R_t); x-axis). Bar plots (right y-axis) show the number of infections in each corresponding scenario. The dotted outline of each bar shows the number of infections of each scenario if no antivirals were distributed.



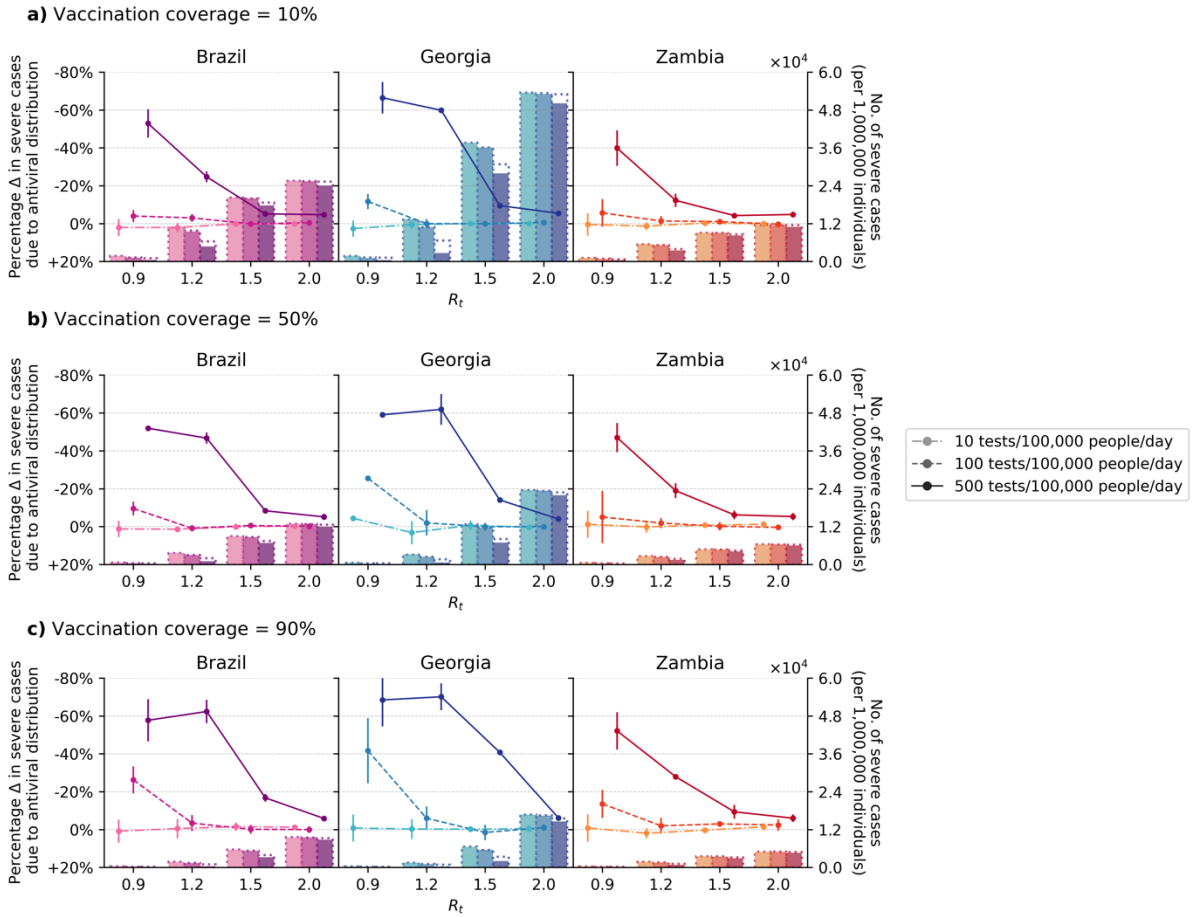
Extended Data Fig. 3: **Transmissions attributed to infectors of different disease and risk status**. (**a**) Bar plots show the mean proportion of transmissions events attributed to each type of infector (with standard deviation error bars), averaged across all simulated scenarios regardless if oral antivirals were distributed. (**b**) Line plots show the ratio of high-risk (i.e. ≥60 years of age or an adult ≥18 years with a relevant comorbidity) to low-risk infectors averaged across all testing rates for different epidemic intensity (measured by instantaneous reproduction number R_t).



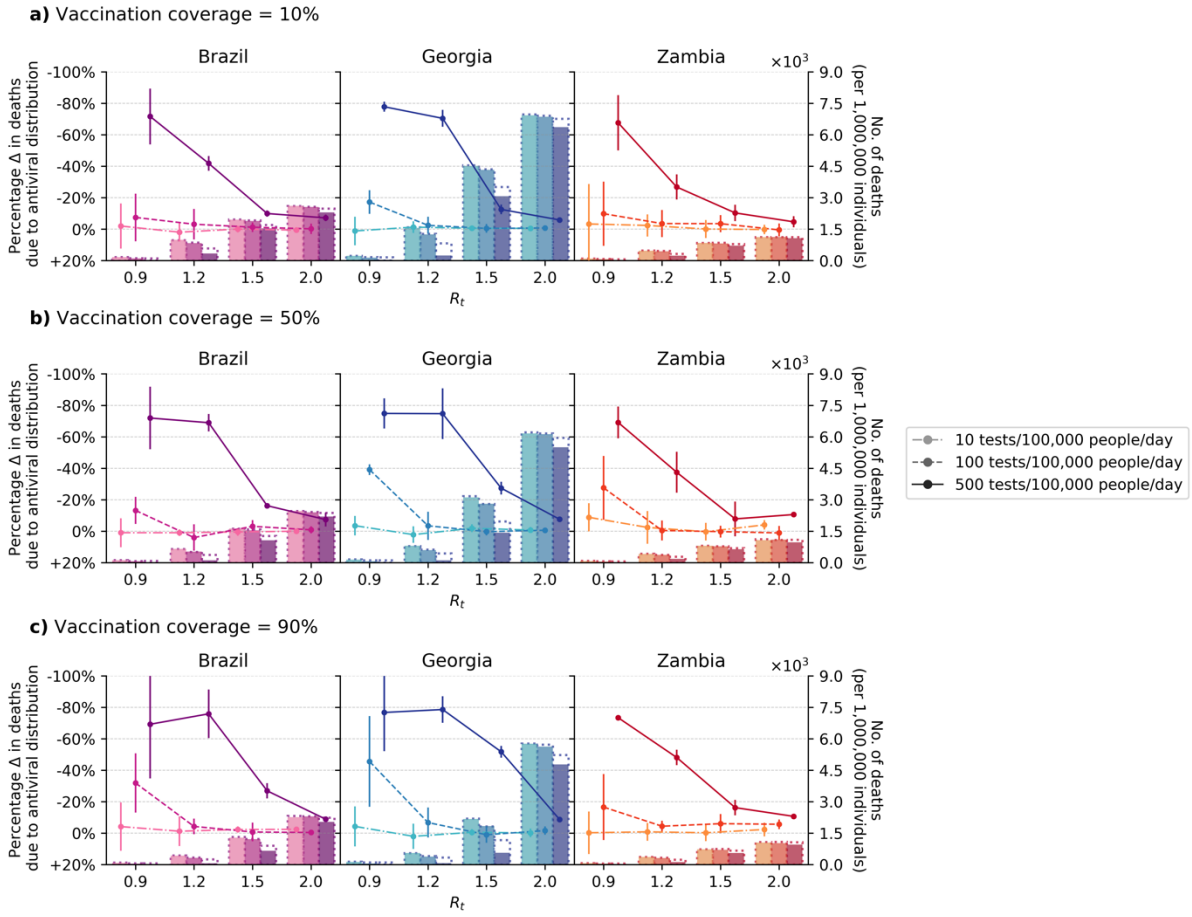
Extended Data Fig. 4: **Impact of oral antiviral therapy on deaths in low- and middle-income countries**. No restrictions on access to symptomatic testing at clinics (i.e. all symptomatic individuals who sought testing at clinics would receive one if in stock) and high-risk household contacts of test-positive individuals were not tested. All eligible high-risk individuals (i.e. ≥60 years of age or an adult ≥18 years with a relevant comorbidity) who tested positive were given a course of oral antivirals. Line plots (left y-axis) show the percentage change in deaths relative to no distribution of antivirals under different levels of mean test availability (different shades of color) after a 90-day Omicron BA.1-like epidemic wave in a population of 1,000,000 individuals with (**a**) 10%, (**b**) 50%, and (**c**) 90% vaccination coverage for different epidemic intensities (measured by the initial instantaneous reproduction number (R_t); x-axis). Bar plots (right y-axis) show the number of deaths in each corresponding scenario. The dotted outline of each bar shows the number of deaths of each scenario if no antivirals were distributed.



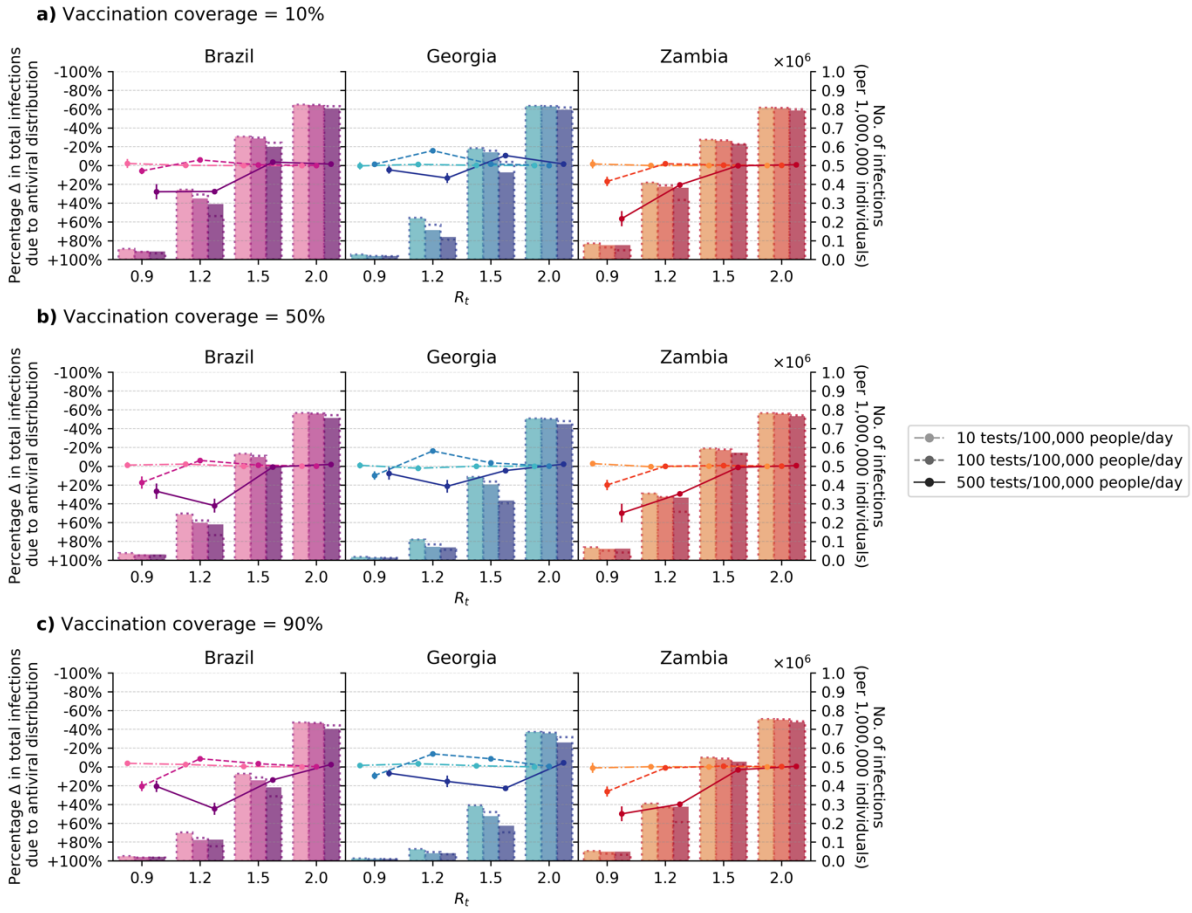
Extended Data Fig. 5: **Impact of oral antiviral therapy on infections in low- and middle-income countries**. No restrictions on access to symptomatic testing at clinics (i.e. all symptomatic individuals who sought testing at clinics would receive one if in stock). High-risk household contacts of test-positive individuals were given antigen rapid diagnostic tests to self-test for three consecutive days. All eligible high-risk individuals (i.e. ≥60 years of age or an adult ≥18 years with a relevant comorbidity) who tested positive, including high-risk household contacts who tested positive, were given a course of oral antivirals. Line plots (left y-axis) show the percentage change in total infections relative to no distribution of antivirals under different levels of mean test availability (different shades of color) after a 90-day Omicron BA.1-like epidemic wave in a population of 1,000,000 individuals with (**a**) 10%, (**b**) 50%, and (**c**) 90% vaccination coverage for different epidemic intensities (measured by the initial instantaneous reproduction number (R_t); x-axis). Bar plots (right y-axis) show the number of infections in each corresponding scenario. The dotted outline of each bar shows the number of infections of each scenario if no antivirals were distributed.



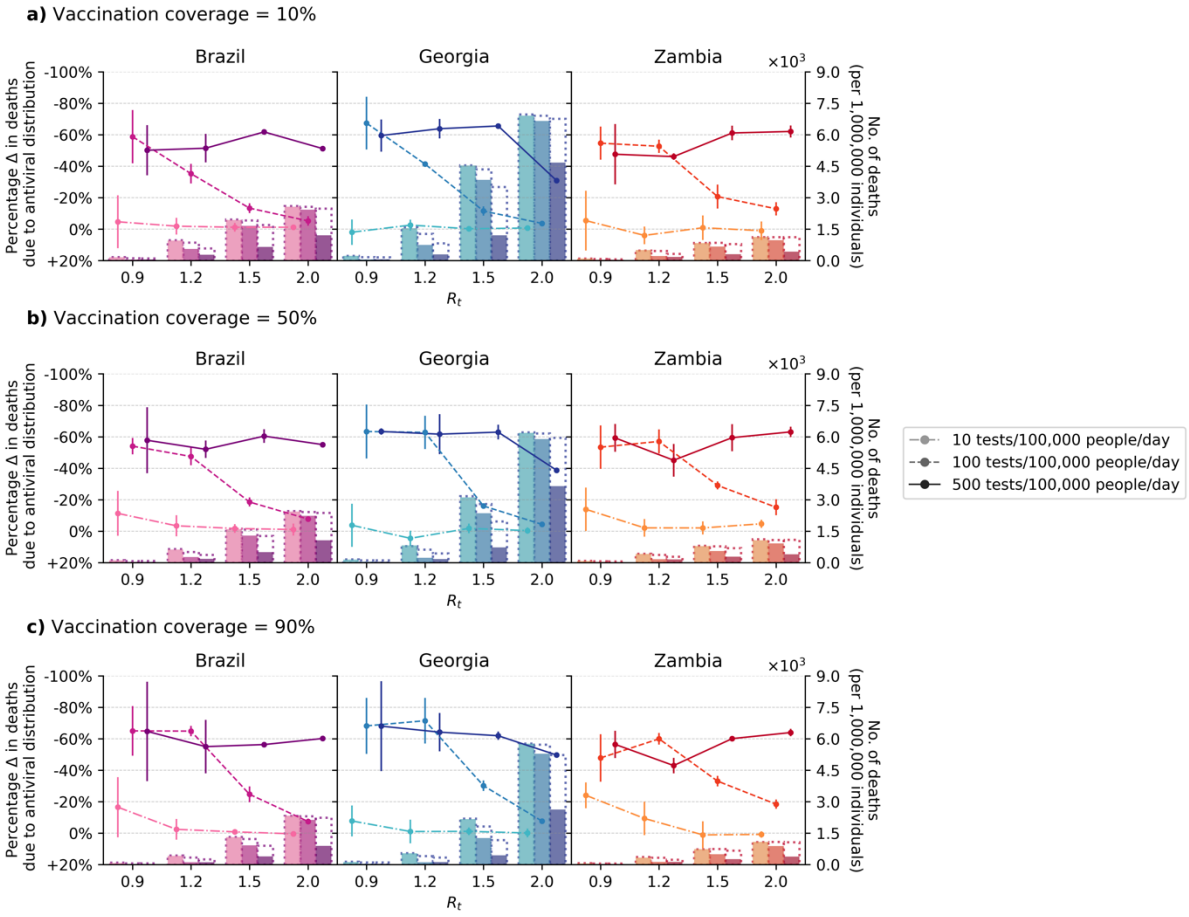
Extended Data Fig. 6: **Impact of oral antiviral therapy on severe cases in low- and middle-income countries**. No restrictions on access to symptomatic testing at clinics (i.e. all symptomatic individuals who sought testing at clinics would receive one if in stock). High-risk household contacts of test-positive individuals were given antigen rapid diagnostic tests to self-test for three consecutive days. All eligible high-risk individuals (i.e. ≥60 years of age or an adult ≥18 years with a relevant comorbidity) who tested positive, including high-risk household contacts who tested positive, were given a course of oral antivirals. Line plots (left y-axis) show the percentage in severe cases relative to no distribution of antivirals under different levels of mean test availability (different shades of color) after a 90-day Omicron BA.1-like epidemic wave in a population of 1,000,000 individuals with (**a**) 10%, (**b**) 50%, and (**c**) 90% vaccination coverage for different epidemic intensities (measured by the initial instantaneous reproduction number (R_t); x-axis). Bar plots (right y-axis) show the number of infections in each corresponding scenario. The dotted outline of each bar shows the number of severe cases of each scenario if no antivirals were distributed.



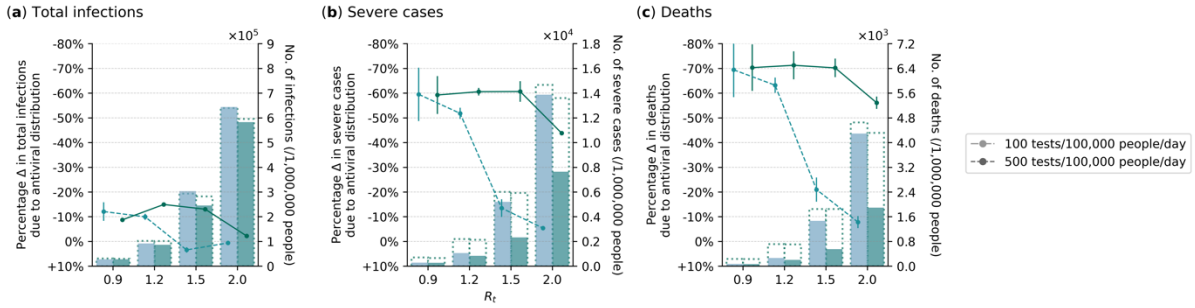
Extended Data Fig. 7: **Impact of oral antiviral therapy on deaths in low- and middle-income countries**. No restrictions on access to symptomatic testing at clinics (i.e. all symptomatic individuals who sought testing at clinics would receive one if in stock). High-risk household contacts of test-positive individuals were given antigen rapid diagnostic tests to self-test for three consecutive days. All eligible high-risk individuals (i.e. ≥60 years of age or an adult ≥18 years with a relevant comorbidity) who tested positive, including high-risk household contacts who tested positive, were given a course of oral antivirals. Line plots (left y-axis) show the percentage change in deaths relative to no distribution of antivirals under different levels of mean test availability (different shades of color) after a 90-day Omicron BA.1-like epidemic wave in a population of 1,000,000 individuals with (**a**) 10%, (**b**) 50%, and (**c**) 90% vaccination coverage for different epidemic intensities (measured by the initial instantaneous reproduction number (R_t); x-axis). Bar plots (right y-axis) show the number of infections in each corresponding scenario. The dotted outline of each bar shows the number of deaths of each scenario if no antivirals were distributed.



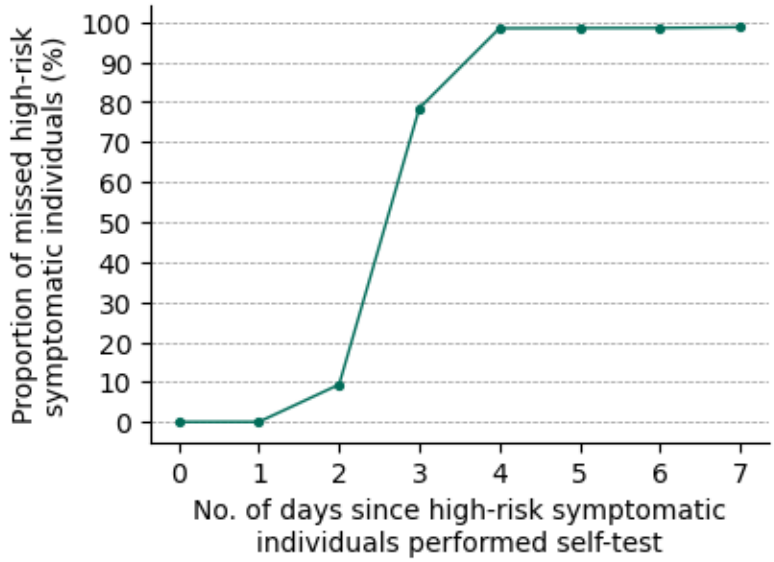
Extended Data Fig. 8: **Impact of oral antiviral therapy on <u>infections</u> when <u>restricting symptomatic testing at clinics to high-risk individuals only</u> in low- and middle-income countries**. High-risk household contacts of test-positive individuals were <u>not</u> tested. All eligible high-risk individuals (i.e. ≥60 years of age or an adult ≥18 years with a relevant comorbidity) who tested positive were given a course of oral antivirals. Line plots (left y-axis) show the percentage change in total <u>infections</u> relative to no distribution of antivirals under different levels of mean test availability (different shades of color) after a 90-day Omicron BA.1-like epidemic wave in a population of 1,000,000 individuals with (**a**) 10%, (**b**) 50%, and (**c**) 90% vaccination coverage for different epidemic intensities (measured by the initial instantaneous reproduction number (R_t); x-axis). Bar plots (right y-axis) show the number of <u>infections</u> in each corresponding scenario. The dotted outline of each bar shows the number of <u>infections</u> of each scenario if no antivirals were distributed.



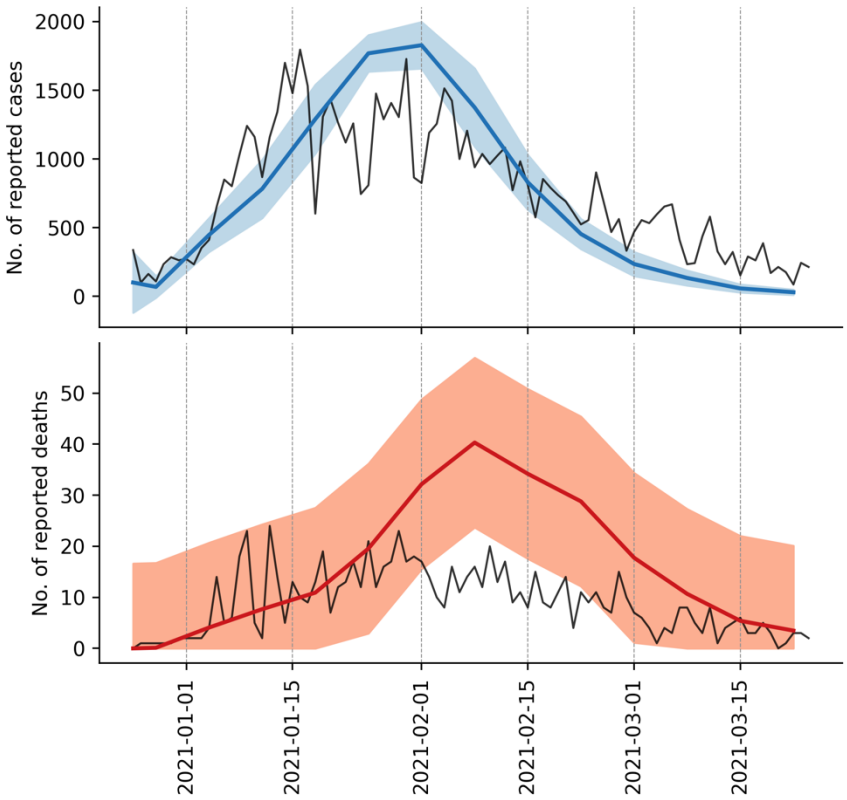
Extended Data Fig. 9: **Impact of oral antiviral therapy on deaths when restricting symptomatic testing at clinics to high-risk individuals only in low- and middle-income countries**. High-risk household contacts of test-positive individuals were not tested. All eligible high-risk individuals (i.e. ≥60 years of age or an adult ≥18 years with a relevant comorbidity) who tested positive were given a course of oral antivirals. Line plots (left y-axis) show the percentage change in deaths relative to no distribution of antivirals under different levels of mean test availability (different shades of color) after a 90-day Omicron BA.1-like epidemic wave in a population of 1,000,000 individuals with (**a**) 10%, (**b**) 50%, and (**c**) 90% vaccination coverage for different epidemic intensities (measured by the initial instantaneous reproduction number (R_t); x-axis). Bar plots (right y-axis) show the number of deaths in each corresponding scenario. The dotted outline of each bar shows the number of deaths of each scenario if no antivirals were distributed.



Extended Data Fig. 10: **Impact of oral antiviral therapy in a high-income country (Netherlands)**. No restrictions on access to symptomatic testing at clinics (i.e. all symptomatic individuals who sought testing at clinics would receive one if in stock). High-risk household contacts of clinic-provided test-positive individuals are given antigen rapid diagnostic tests to self-test for three consecutive days. Over-the-counter antigen rapid diagnostic tests (Ag-RDTs) are assumed to be widely available. As such, we assumed that only 10% of symptomatic individuals would seek clinical testing directly while 80% of those who opted not to seek clinic-provided testing would perform self-testing using over-the-counter Ag-RDTs. All high-risk individuals who tested positive through self-testing would seek reflexive testing at clinics on the same day. All eligible high-risk individuals (i.e. ≥60 years of age or an adult ≥18 years with a relevant comorbidity) who tested positive at clinics, either directly or through reflexive testing, were given a course of oral antivirals. Line plots (left y-axis) show the percentage change in (**a**) total infections, (**b**) severe cases and (**c**) deaths relative to no distribution of antivirals under different clinical testing rates (different shades of color) after a 90-day Omicron BA.1-like epidemic wave in a population of 1,000,000 individuals 80% vaccination coverage for different epidemic intensities (measured by the initial instantaneous reproduction number (R_t); x-axis). Bar plots (right y-axis) show the number of severe cases in each corresponding scenario. The dotted outline of each bar shows the number of severe cases of each scenario when no antivirals were distributed.



Extended Data Fig. 11: **Reflexive testing delay after self-testing with over-the-counter antigen rapid diagnostic tests (Ag-RDTs)**. Line plot shows the proportion of high-risk symptomatic individuals that would miss the treatment window of oral antivirals if they had sought reflexive testing at clinics *n* days late after performing a self-test using over-the-counter Ag-RDTs. These individuals would have averted severe disease outcomes if they were prescribed oral antivirals on the same day as their self-test. These results were obtained from simulating a 90-day Omicron BA.1-like epidemic wave in a population of 1,000,000 individuals in the Netherlands. We assumed that over-the-counter Ag-RDTs are widely available such that most (80%) symptomatic individuals who did not seek clinic-provided testing directly would instead perform a self-test using over-the-counter Ag-RDTs. Only high-risk individuals who tested positive using self-tests are assumed to seek reflexive testing at clinics to be prescribed the antivirals.



Extended Data Fig. 12: **Model validation**. We compared the mean number of reported cases (blue line, top panel) and deaths (red line, bottom panel) estimated by our simulations (10 simulations in total) against the actual case and death counts (black lines) in Lusaka, Zambia during the second wave of infections between 25 December 2020 and 24 March 2021. Actual case and death counts were retrieved from the Zambia COVID-19 Dashboard (https://www.arcgis.com/apps/dashboards/3b3a01c1d8444932ba075fb44b119b63). The blue and red shaded regions in each plot denotes the standard deviation of reported cases (top panel) and deaths (bottom panel) respectively.

Extended Data Tables

Extended Data Table 1: Variables and parameters used in PATAT.

Parameter	Values/Distribution	Source
Population demography		
Total population size	1,000,000	
Mean household size	Brazil, Georgia: 3.3 Zambia: 5.0 Netherlands: 2.1	[12–15]
Age structure (in bins of 5 years)	Brazil: [0.072, 0.078, 0.090, 0.089, 0.090, 0.090, 0.083, 0.073, 0.068, 0.062, 0.053, 0.043, 0.034, 0.025, 0.020, 0.013, 0.009, 0.004, 0.002, 0.001] Georgia: [0.013, 0.057, 0.071, 0.064, 0.055, 0.058, 0.065, 0.073, 0.070, 0.065, 0.063, 0.062, 0.069, 0.064, 0.053, 0.039, 0.024, 0.025, 0.006, 0.006] Zambia: [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] Netherlands: [0.049, 0.051, 0.054, 0.058, 0.064, 0.064, 0.065, 0.061, 0.059, 0.062, 0.073, 0.072, 0.066, 0.058, 0.054, 0.041, 0.026, 0.015, 0.006, 0.002]	[12,13,15,16]
Minimum prime adult age	20 years	Assumed
Proportion of women	51% (Brazil, Zambia), 52% (Georgia), 50% (Netherlands)	[15–18]
Minimum working age	15 years (Brazil, Georgia, Zambia), 16 years (Netherlands)	[15–18]
Employment rate	Brazil: 73% (male), 53% (female) Georgia: 77% (male), 82% (female) Zambia: 39% (male), 23% (female) Netherlands: 75% (male), 68% (female)	[15–18]
Formal employment rate	Brazil: 90% (male), 90% (female) Georgia: 64% (male), 74% (female) Zambia: 36% (male), 24% (female) Netherlands: 81% (male), 88% (female)	[15–18]
Schooling rate	Brazil: 97% (Primary), 83% (Secondary) Georgia: 98% (Primary), 95% (Secondary) Zambia: 79% (Primary), 40% (Secondary) Netherlands: 99% (Primary), 92% (Secondary)	[12,13,19,20]
School gender parity	Brazil: 0.97 (Primary), 0.98 (Secondary) Georgia: 1.00 (Primary and secondary) Zambia: 1.00 (Primary), 0.90 (Secondary) Netherlands: 1.00 (Primary and secondary)	[12,13,19,20]
Religious gathering participation rate	Brazil: 41% Georgia: 13% Zambia: 70% Netherlands: NA (Assumed)	[21]

Mean employment contacts (formal)	20	Assumed
Mean employment contacts (informal)	5	Assumed
Mean class size	Brazil: 20 (Primary), 26 (Secondary) Georgia: 20 (Primary and Secondary) Zambia: 37 (Primary and secondary) Netherlands: 25 (Primary and secondary, assumed)	[12,22,23]
Mean school size	Brazil: 500 (Primary), 400 (Secondary) (Assumed) Georgia: 135 (Primary and secondary) Zambia: 700 (Primary and secondary, assumed) Netherlands: 224 (Primary), 1442 (Secondary)	[15,16]
Student-teacher ratio	Brazil: 20 (Primary), 17 (Secondary) Georgia: 8 (Primary and secondary) Zambia: 42 (Primary and secondary) Netherlands: 12 (Primary), 15 (Secondary)	[12,24]
Mean religious gathering size (s.d.)	Brazil, Georgia: 200 (100) Zambia: 500 (100) Netherlands: NA	Assumed
Mean random contacts in religious gathering per person	10	Assumed
Mean random community contacts per day	10	Assumed
SARS-CoV-2 transmissions 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, 1.24, 1.24, 1.47, 1.47, 1.47, 1.47]	[5,7]
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]	[25,26]
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]	[25,26]
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]	[9,27]
Latent period (days)	Omicron BA.1: Lognormal (4.0, 1.3)	[7,28–30]
Pre-symptomatic period (days)	Omicron BA.1: Lognormal (1.8, 1.7)	[7,28,30]
Period between symptom onset and severe disease (days)	Lognormal (6.6, 4.9)	[28]
Period between severe disease and death (days)	Lognormal (8.6, 6.7)	[28]
Recovery period for symptomatic agents with mild disease (days)	Omicron BA.1: Lognormal (5.35, 0.37*)	[30,31]
Recovery period for asymptomatic agent (days)	Omicron BA.1: Lognormal (5.35, 0.37*)	[30,31]
Recovery period of agents with severe disease (days)	Lognormal (18.1, 6.3)	[25]

Peak Ct values	Omicron BA.1: Normal (23.3, 0.58*)	[30]
Cross-immunity to variant virus after infection by extant virus	Omicron BA.1: 20%	[32,33]
Severity (chance of hospitalization) of variant relative to extant virus	Omicron BA.1: 40%	[34]
Testing parameters		
Delay in visiting healthcare facility for symptomatic testing (days)	Lognormal (1.0, 0.5)	Assumed
Ag-RDT specificity	0.989	[8]
Isolation/quarantine parameters		
Isolation period	10 days	
Quarantine period	14 days	
Self-isolation period	10 days	
Reduction in contact rates under isolation/quarantine (in order of households, schools, workplaces, religious gathering and random community)	[10%, 100%, 100%, 100%, 100%]	

*Standard deviation values inferred from 95% confidence interval computed in reference.

References

1. Han, A. X. *et al.* Strategies for using antigen rapid diagnostic tests to reduce transmission of SARS-CoV-2 in low- and middle-income countries: a mathematical modelling study applied to Zambia. *medRxiv* 2022.06.16.22276516 (2022) doi:10.1101/2022.06.16.22276516.
2. Han, A. X. *et al.* SARS-CoV-2 diagnostic testing rates determine the sensitivity of genomic surveillance programs. *medRxiv* 2022.05.20.22275319 (2022) doi:10.1101/2022.05.20.22275319.
3. Quilty, B. J. *et al.* Quarantine and testing strategies in contact tracing for SARS-CoV-2: a modelling study. *Lancet Public Health* **6**, e175–e183 (2021).
4. Endo, A., Abbott, S., Kucharski, A. J. & Funk, S. Estimating the overdispersion in COVID-19 transmission using outbreak sizes outside China. *Wellcome Open Research 2020 5:67* **5**, 67 (2020).
5. Zhang, J. *et al.* Changes in contact patterns shape the dynamics of the COVID-19 outbreak in China. *Science (1979)* **368**, 1481–1486 (2020).
6. Wallinga, J. & Lipsitch, M. How generation intervals shape the relationship between growth rates and reproductive numbers. *Proceedings of the Royal Society B: Biological Sciences* **274**, 599–604 (2006).
7. Kerr, C. C. *et al.* Covasim: An agent-based model of COVID-19 dynamics and interventions. *PLoS Comput Biol* **17**, e1009149- (2021).
8. Brümmer, L. E. *et al.* Accuracy of novel antigen rapid diagnostics for SARS-CoV-2: A living systematic review and meta-analysis. *PLoS Med* **18**, e1003735- (2021).
9. Brazeau, N. F. *et al.* Report 34 - COVID-19 Infection Fatality Ratio Estimates from Seroprevalence | Faculty of Medicine | Imperial College London. (2020) doi:10.25561/83545.
10. Tembo, J. *et al.* Evaluation of SARS-CoV-2 diagnostics and risk factors associated with SARS-CoV-2 infection in Zambia. *International Journal of Infectious Diseases* **120**, 150–157 (2022).
11. FIND. Test tracker - FIND. https://www.finddx.org/covid-19/test-tracker/ (2022).
12. Zambia Statistics Agency. Zambia Demographic and Health Survey 2018. https://www.zamstats.gov.zm/index.php/publications/category/8-demorgraphy?download=364:zambia-demographic-and-health-survey-2018 (2018).

13. Brazilian Institute of Geography and Statistics. IBGE | 2010 census. https://censo2010.ibge.gov.br/ (2010).
14. National Statistics Office of Georgia. census - მთავარი. http://census.ge/# (2014).
15. Statistics Netherlands. StatLine. https://opendata.cbs.nl/statline/#/CBS/en/ (2022).
16. National Statistics Office of Georgia. საქართველოს სტატისტიკის ეროვნული სამსახური. https://www.geostat.ge/ka (2022).
17. Zambia Statistics Agency. 2019 Labour Force Survey Report. https://www.zamstats.gov.zm/index.php/publications/category/7-labour (2019).
18. Brazilian Institute of Geography and Statistics. Pesquisa Nacional por Amostra de Domicílios Contínua Trimestral - PNADC/T. https://sidra.ibge.gov.br/pesquisa/pnadct/tabelas (2022).
19. UNESCO Institute for Statistics. Georgia | UNESCO UIS. http://uis.unesco.org/country/GE (2022).
20. UNESCO Institute for Statistics. Netherlands | UNESCO UIS. http://uis.unesco.org/country/NL (2022).
21. Pew Research Center. The Age Gap in Religion Around the World. https://www.pewresearch.org/religion/2018/06/13/the-age-gap-in-religion-around-the-world/ (2018).
22. OECD. Education at a Glance 2021 : OECD Indicators | Education at a Glance | OECD iLibrary. https://www.oecd-ilibrary.org/education/education-at-a-glance-2021_b35a14e5-en (2021).
23. Ministry of Education and Science of Georgia. Teach & Learn With Georgia. http://www.tlg.gov.ge/content.php?id=643&lang=eng (2022).
24. The World Bank. World Bank Open Data | Data. https://data.worldbank.org/ (2022).
25. Verity, R. *et al.* Estimates of the severity of coronavirus disease 2019: a model-based analysis. *Lancet Infect Dis* **20**, 669–677 (2020).
26. Ferguson, N. M. *et al.* Report 9: Impact of non-pharmaceutical interventions (NPIs) to reduce COVID-19 mortality and healthcare demand. (2020) doi:10.25561/77482.
27. O'Driscoll, M. *et al.* Age-specific mortality and immunity patterns of SARS-CoV-2. *Nature 2020 590:7844* **590**, 140–145 (2020).
28. Linton, N. M. *et al.* Incubation Period and Other Epidemiological Characteristics of 2019 Novel Coronavirus Infections with Right Truncation: A Statistical Analysis of

Publicly Available Case Data. *Journal of Clinical Medicine 2020, Vol. 9, Page 538* **9**, 538 (2020).

29. Kang, M. *et al.* Transmission dynamics and epidemiological characteristics of Delta variant infections in China. *medRxiv* 2021.08.12.21261991 (2021) doi:10.1101/2021.08.12.21261991.
30. Hay, J. A. *et al.* Viral dynamics and duration of PCR positivity of the SARS-CoV-2 Omicron variant. *medRxiv* 2022.01.13.22269257 (2022) doi:10.1101/2022.01.13.22269257.
31. Wölfel, R. *et al.* Virological assessment of hospitalized patients with COVID-2019. *Nature 2020 581:7809* **581**, 465–469 (2020).
32. Pouwels, K. B. *et al.* Impact of Delta on viral burden and vaccine effectiveness against new SARS-CoV-2 infections in the UK. *medRxiv* 2021.08.18.21262237 (2021) doi:10.1101/2021.08.18.21262237.
33. Imperial College London. Report 49 - Growth, population distribution and immune escape of Omicron in England | Faculty of Medicine | Imperial College London. https://www.imperial.ac.uk/mrc-global-infectious-disease-analysis/covid-19/report-49-Omicron/ (2021).
34. Imperial College London. Report 50 - Hospitalisation risk for Omicron cases in England | Faculty of Medicine | Imperial College London. https://www.imperial.ac.uk/mrc-global-infectious-disease-analysis/covid-19/report-50-severity-omicron/ (2022).