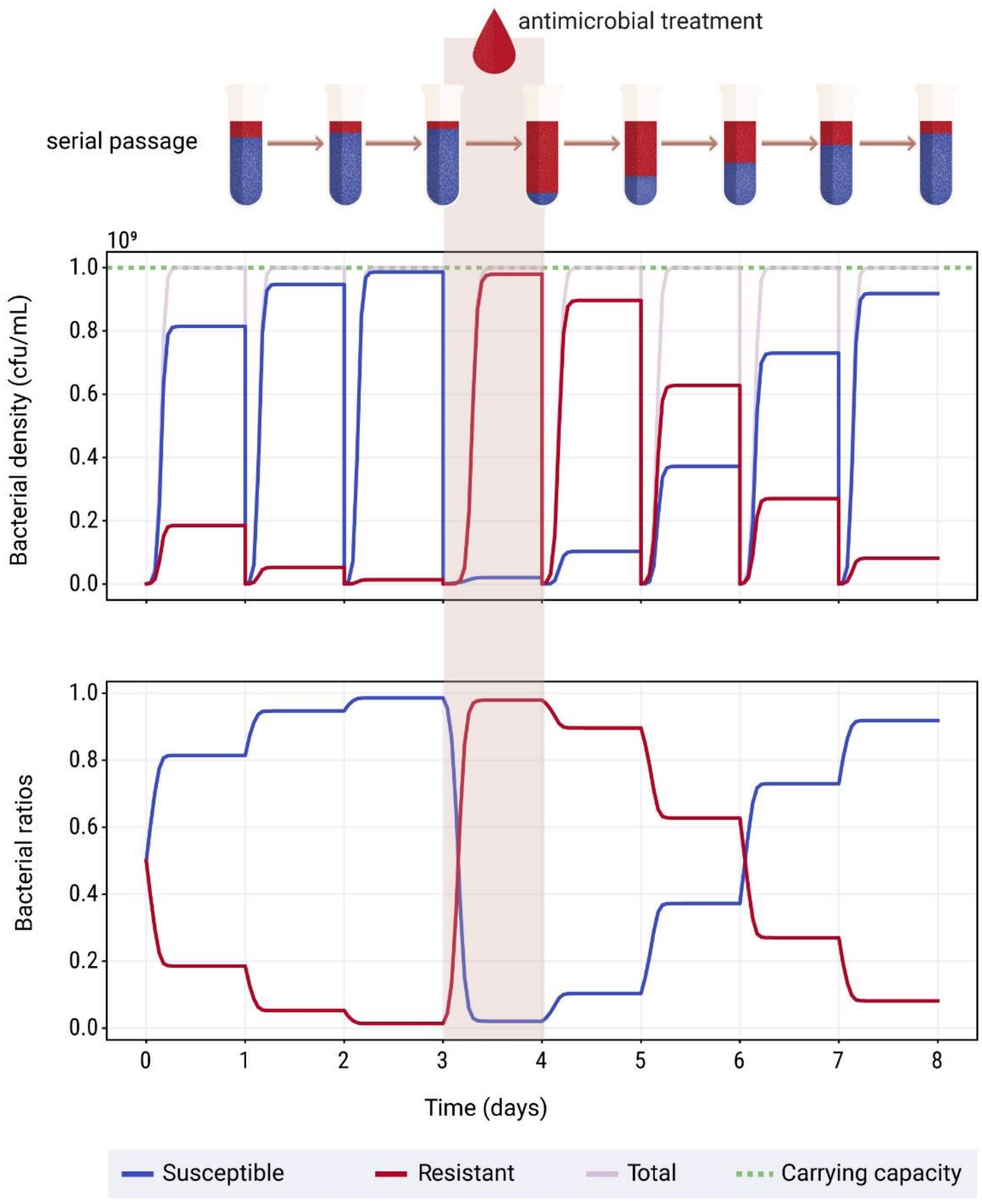
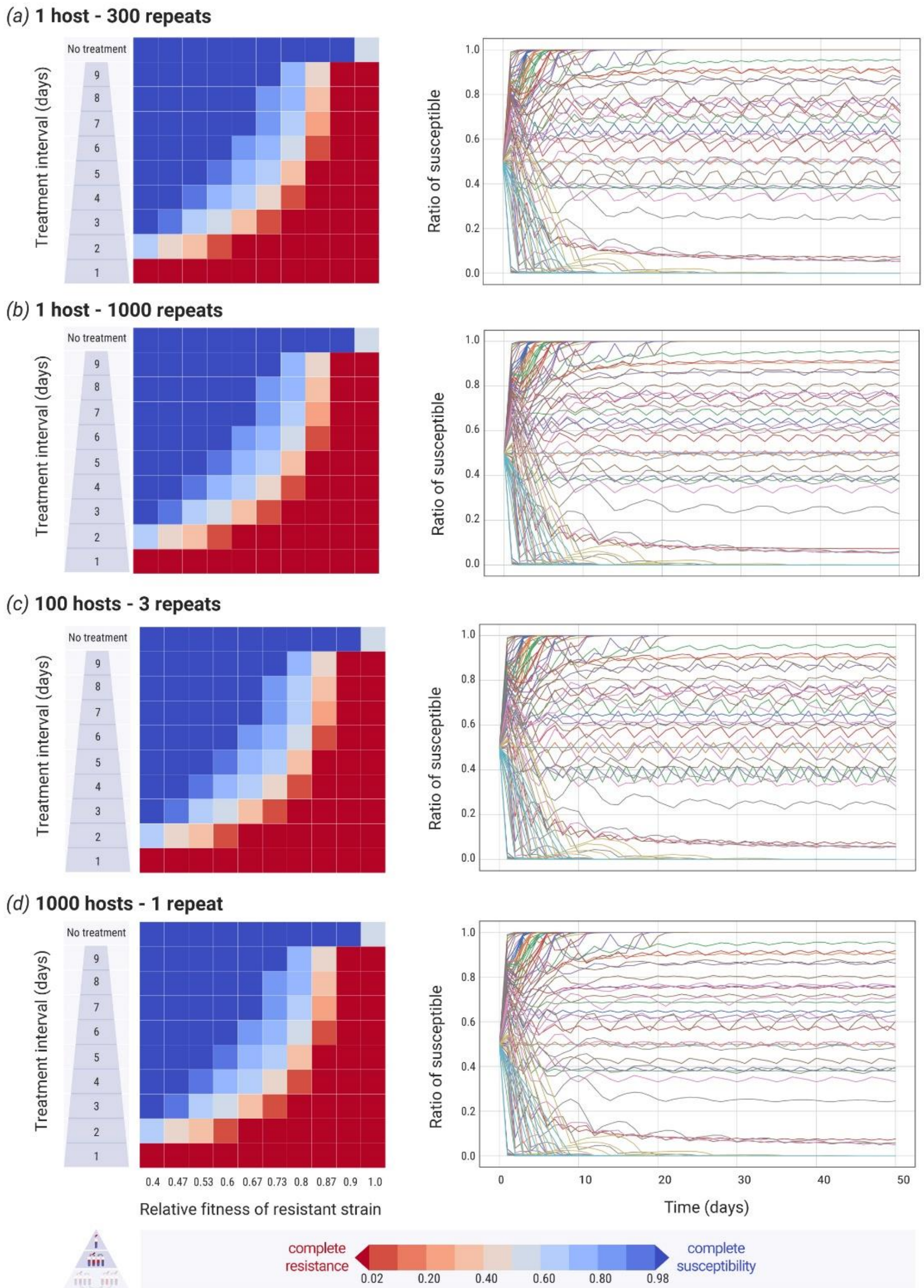
Supplementary Material

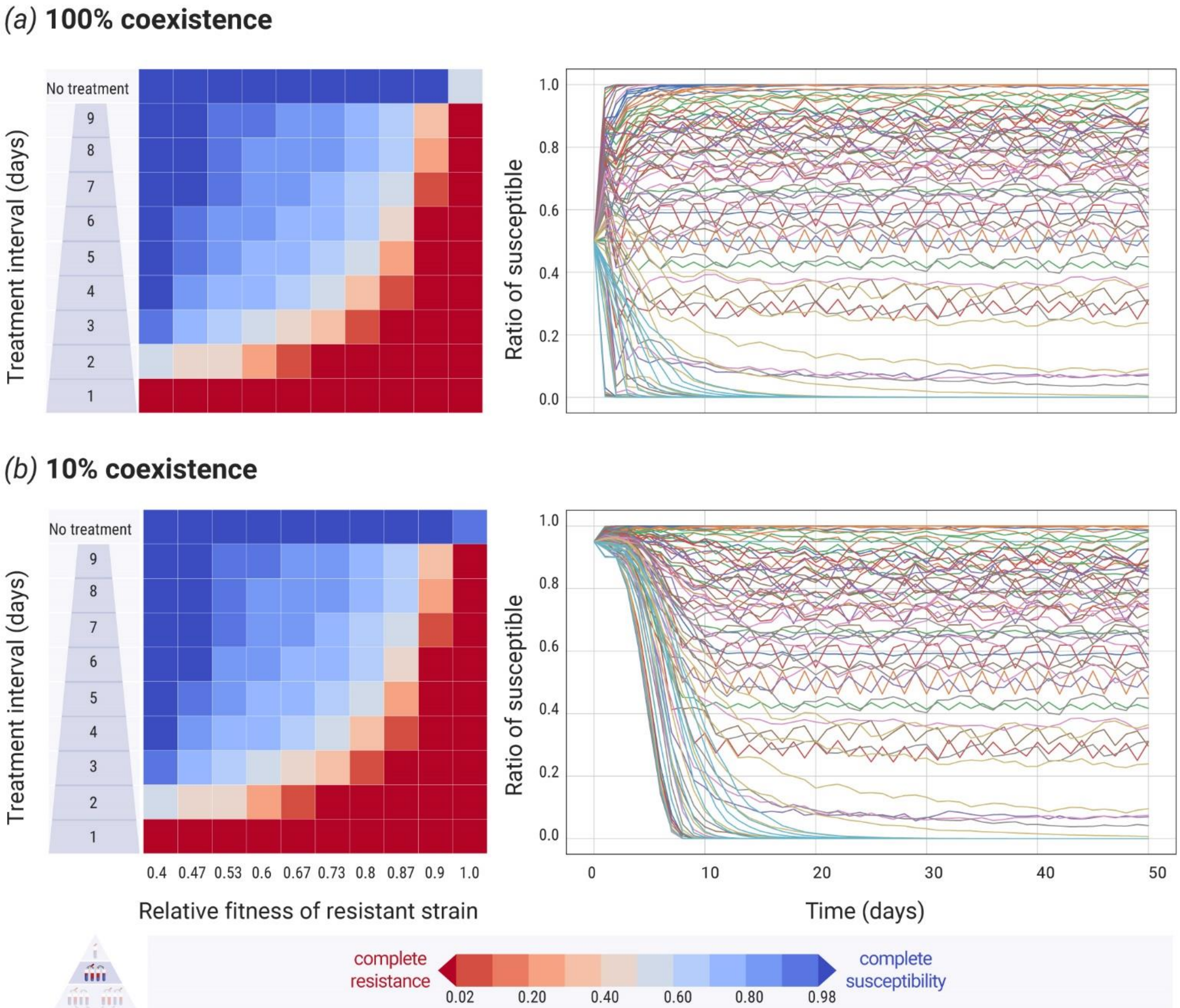
1 Supplementary Figures



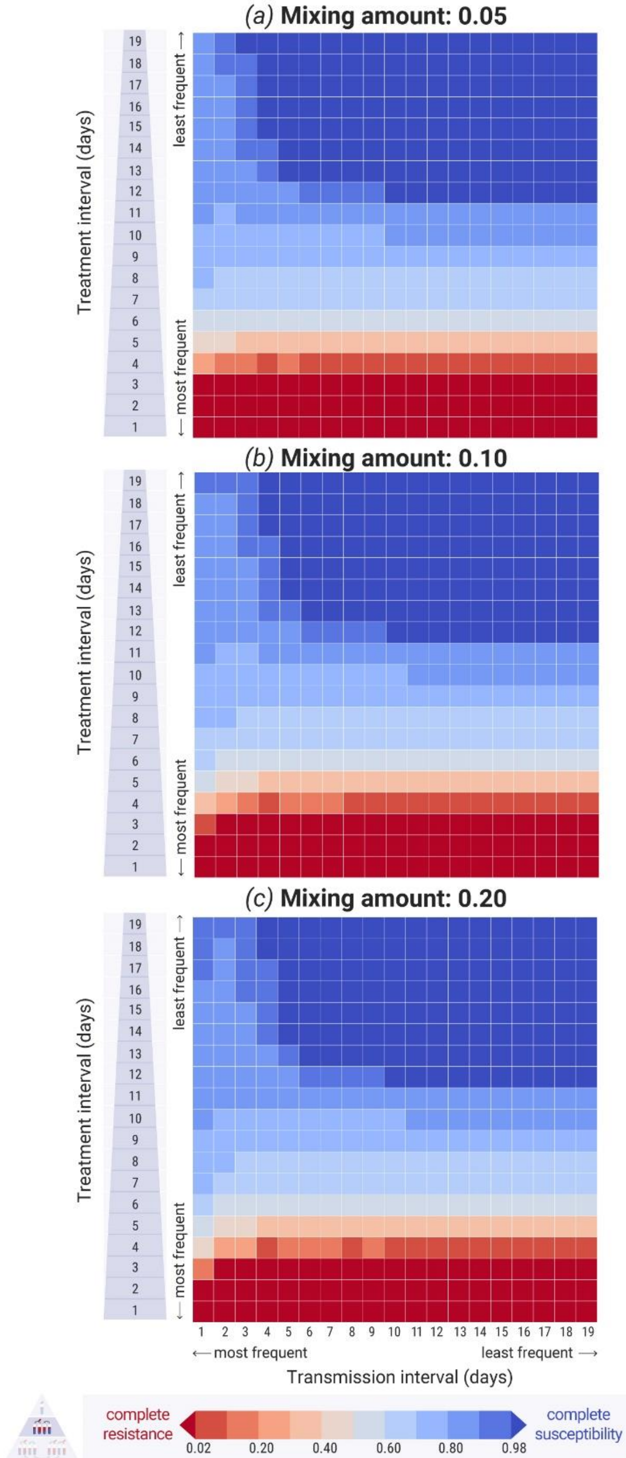
Supplementary Figure 1. Example of serial passage within one host for eight days. Top: Concentration of the susceptible and the resistant strain within the host across time (i.e. solutions of the differential equations). 'Total' is the sum of the susceptible and resistant bacteria. Every day the culture reaches the carrying capacity of the system. When the antimicrobial agent is delivered, the growth of the susceptible bacteria is stunted, and the resistant bacteria get the chance to grow. Bottom: Ratio of the susceptible and the resistant bacteria within the host across time (derived from the concentration).



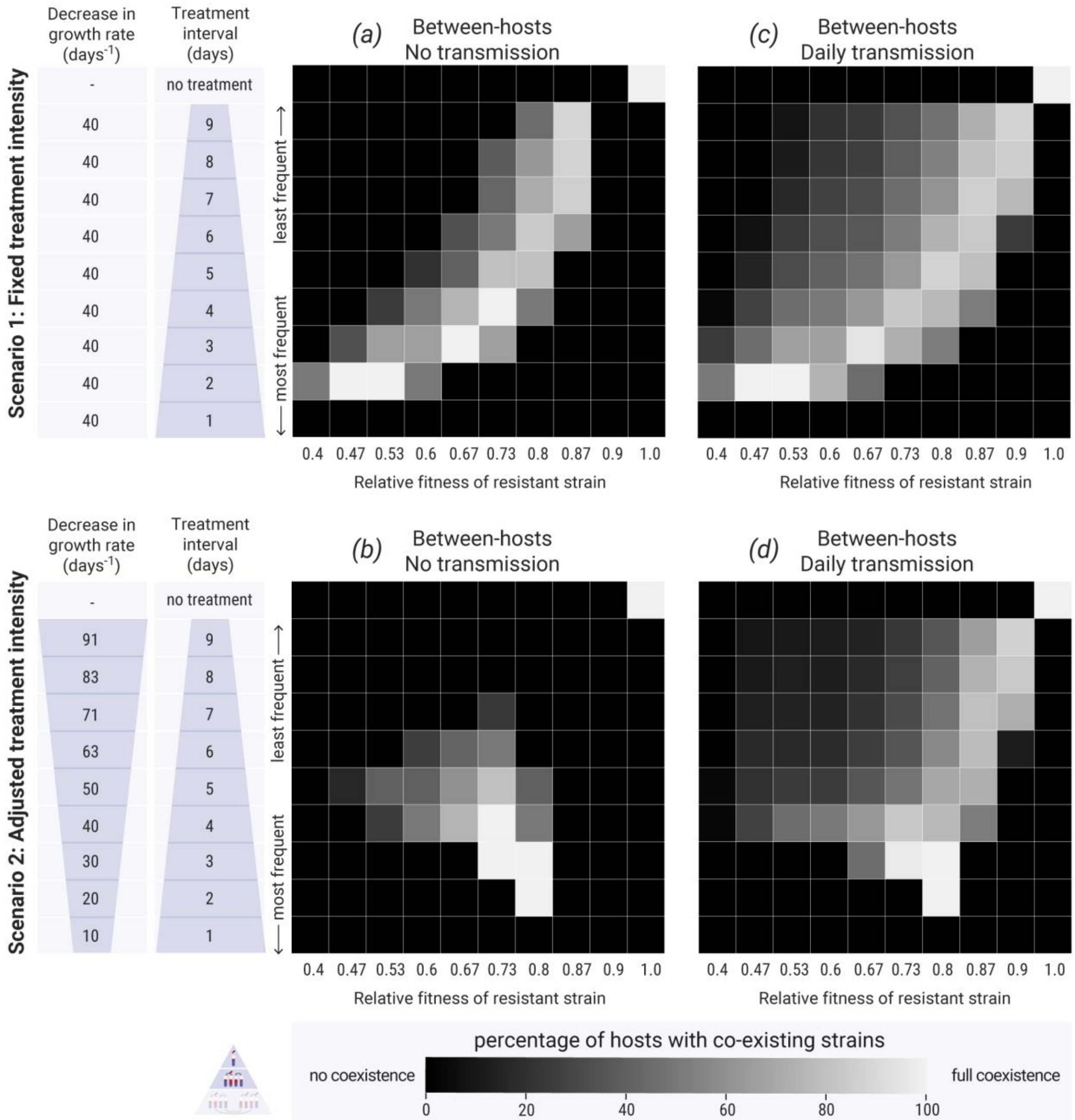
Supplementary Figure 2. Oscillations at equilibrium. Scenario 1, where the decrease in the intrinsic growth rate due to the antimicrobial treatment is fixed across experiments at $d_{Smax} = 40$ day^{-1}. Left panels: Average ratio of susceptibility at equilibrium for each experiment, across different treatment intervals (I_{antim}, y-axis) and relative fitness of the resistant strain (w, x-axis). The colour bar represents the average equilibrium ratio of susceptible bacteria in the host or in the population. Right panels: Line graphs of the average ratio of susceptible bacteria in the host or in the population (y-axis) in time (x-axis). Each line represents one experiment. **(A)** Within-host experiments with 300 repeats. **(B)** Within-host experiments with 1000 repeats. Oscillations at equilibrium are dampened thanks to the increased repeat number. **(C)** Between-host experiments with 100 hosts and 3 repeats. **(D)** Between-hosts experiments with 1000 hosts and 1 repeat. Oscillations at equilibrium are dampened due to the increased host number. Despite the differences, the pattern of the average values at equilibrium remains the same across the four cases.



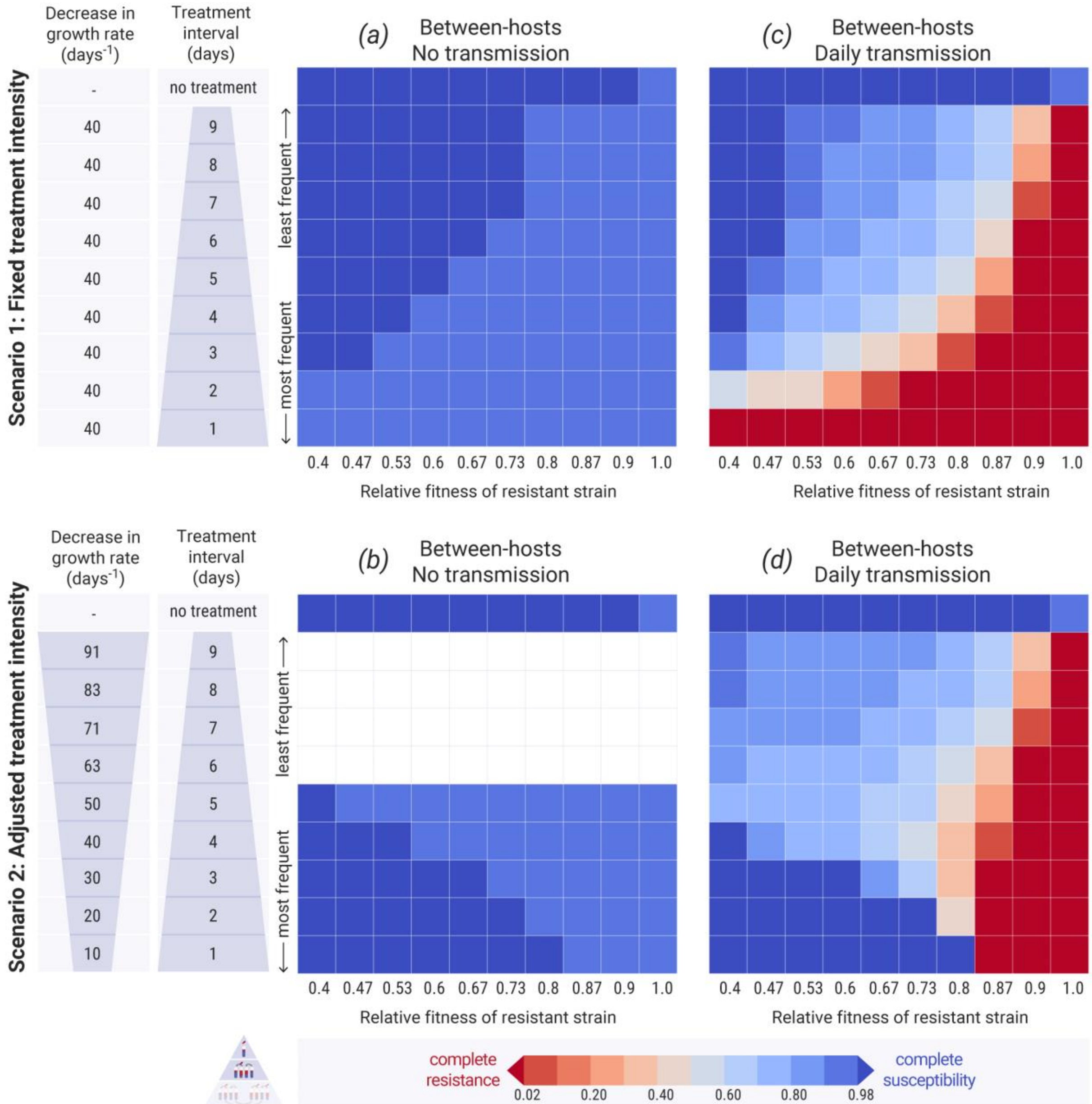
Supplementary Figure 3. Effect of initial ratio of the two strains. The initial prevalence of resistance in a population does not affect the outcome at the system's equilibrium if bacterial transmission takes place. Both cases are from Scenario 1, where the decrease in the intrinsic growth rate due to the antimicrobial treatment is fixed across experiments at $d_{Smax} = 40$ day^{-1}. Heatmaps: Results of the simulations across different treatment intervals (I_{antim}, y-axis) and relative fitness of the resistant strain (w, x-axis). Each cell of the heatmap represents the equilibrium values of one experiment. The colour bar represents the average equilibrium ratio of susceptible bacteria in the host or in the population. Line graphs: Ratio of susceptible bacteria across time. Each line represents one experiment. **(A)** All (100%) of the hosts carry equal amounts of the two strains at the beginning of the experiments, $S_0 = 5\ \times 10^5$ cfu/mL and $R_0 = 5\ \times 10^5$ cfu/mL. **(B)** The 90% of the hosts did not contain any resistant bacteria ($S_0 = 10^6$ cfu/mL and $R_0 = 0$ cfu/mL), and only 10% of the hosts carried resistant bacteria that comprised 50% of their content ($S_0 = 5\ \times 10^5$ cfu/mL and $R_0 = 5 \times 10^5$ cfu/mL).



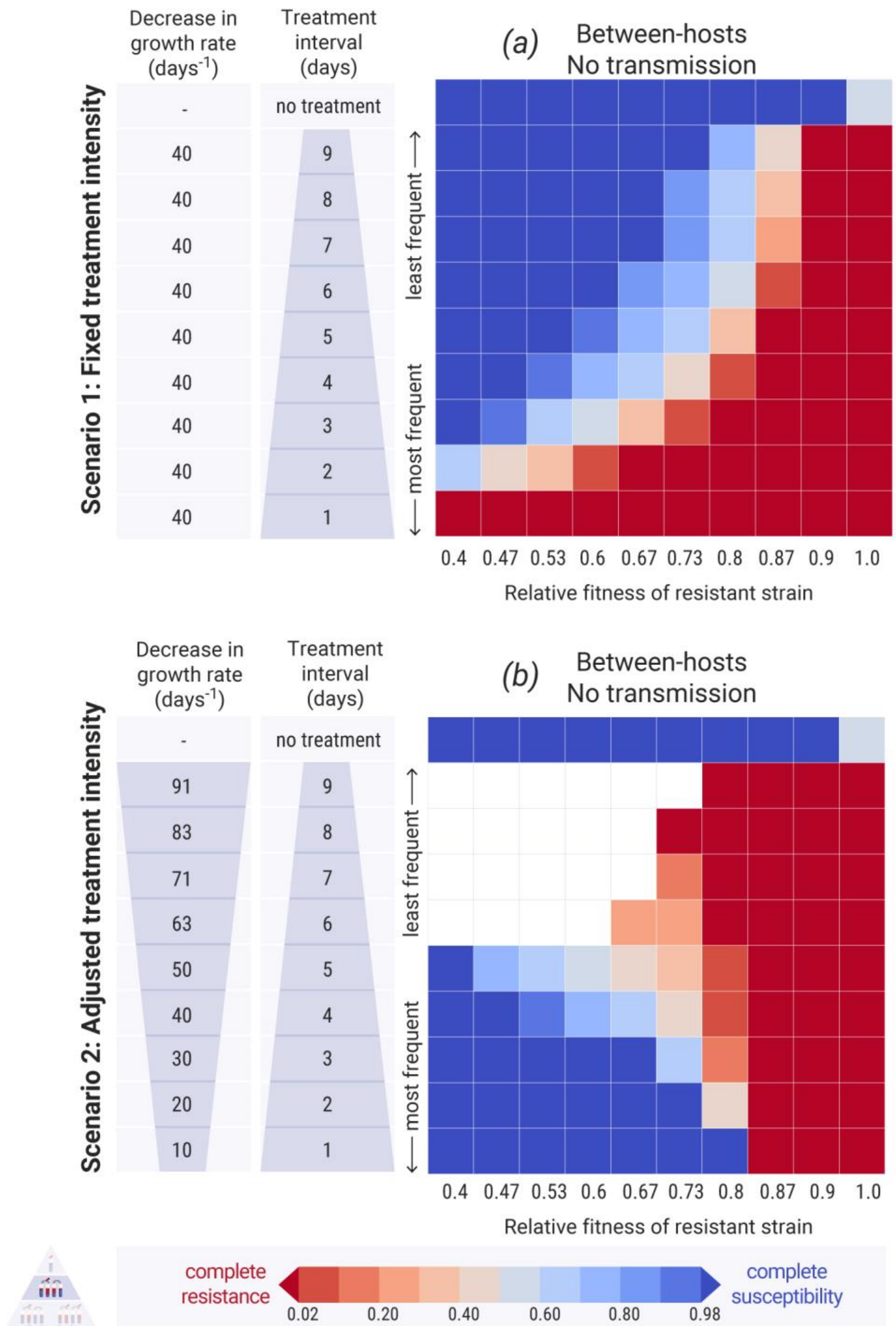
Supplementary Figure 4. Effect of transmission magnitude. Results of the between-hosts simulations across different treatment intervals (I_{antim}, y-axis) and transmission intervals (I_{trans}, x-axis). Each cell of the heatmap represents the equilibrium values of one experiment. The colour bar represents the average equilibrium ratio of susceptible bacteria in the host or in the population. All graphs come from Scenario 1, where the decrease in the intrinsic growth rate due to the antimicrobial treatment is fixed across experiments at $d_{Smax} = 40$ day^{-1}. The relative fitness of the resistant is set to strain a medium level, at $w = 0.80$. **(A)** Low mixing factor, $\mathrm{M} = 0.05$, during transmission, i.e. 5% of bacterial load. **(B)** Medium mixing factor, $\mathrm{M} = 0.1$, during transmission, at 10% of bacterial load. **(C)** Large mixing mixing factor, $\mathrm{M} = 0.2$, during transmission, at 20% of bacterial load.



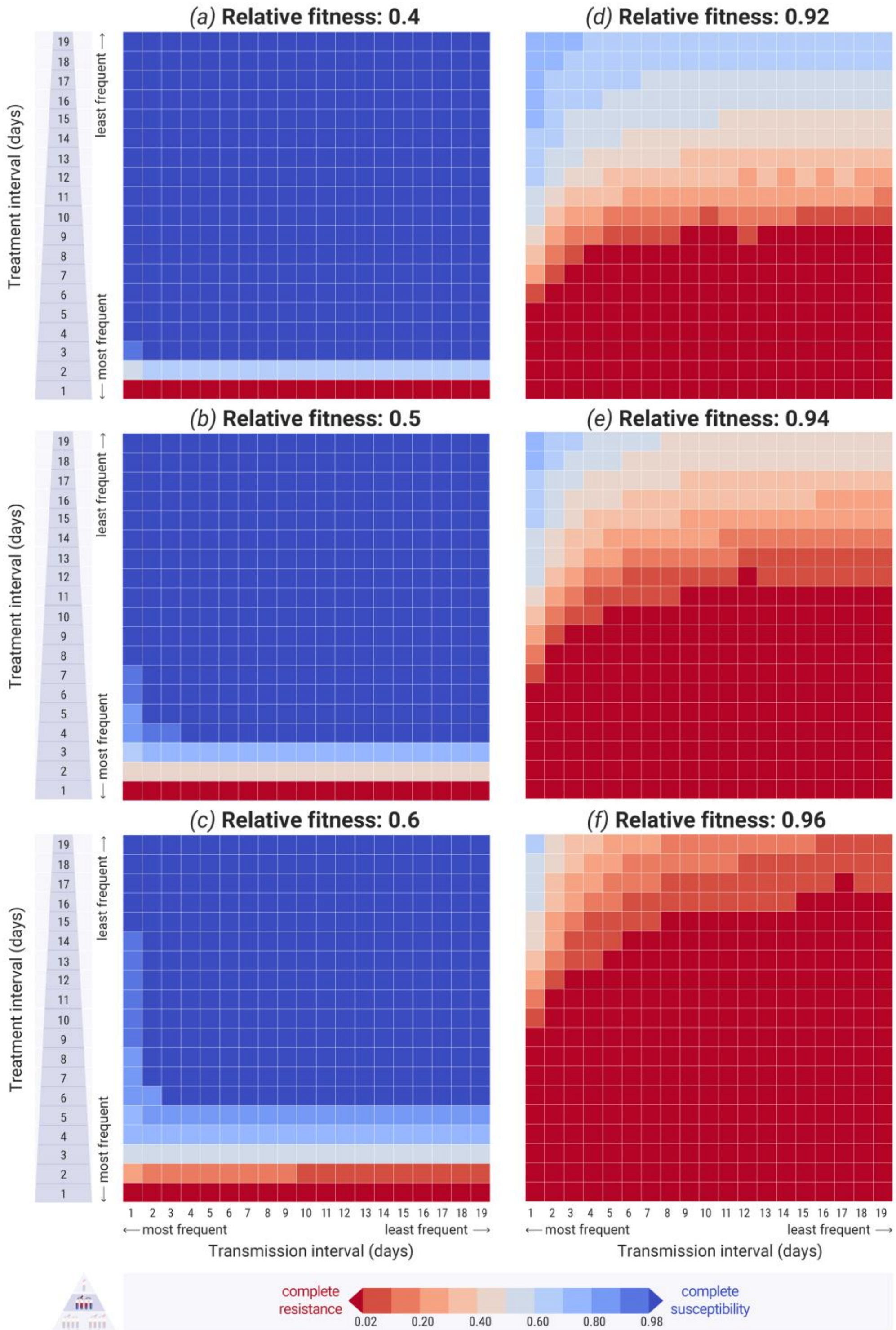
Supplementary Figure 5. Co-existence heatmaps. When multiple hosts are considered, there is potential for a disconnect between the level of resistance in the population and the amount of strain coexistence within the hosts. For example, intermediate levels of resistance can theoretically arise in two different cases. In the first case, the two strains could co-colonize all hosts, whereas, in the other case, half hosts could carry one strain and half the hosts the other strain. From the coexistence heatmaps, we confirmed that intermediate levels of resistance coincided with strain coexistence within the host, i.e. as the first case. This means that when the level of resistance in the population is medium, then almost all hosts carry both strains. Co-existence heatmaps were produced for all the simulations, and they always agreed with the levels of resistance in the population (data not shown). Each cell represents the percentage of hosts that carry both strains, at equilibrium, for each experiment. . **(A, C)** Scenario 1, where the decrease in the intrinsic growth rate due to the antimicrobial treatment is fixed across experiments at $d_{Smax} = 40$ day^{-1}. **(B, D)** Scenario 2, where the decrease in the growth rate due to the antimicrobial treatment, d_{Smax}, is adjusted by the treatment interval, and takes values between 10 and 91 day^{-1} (see Supplementary Table 1 for calculation). **(A, B)** Within-host simulations (no transmission). **(C, D)** Between-host simulations (with daily transmission).



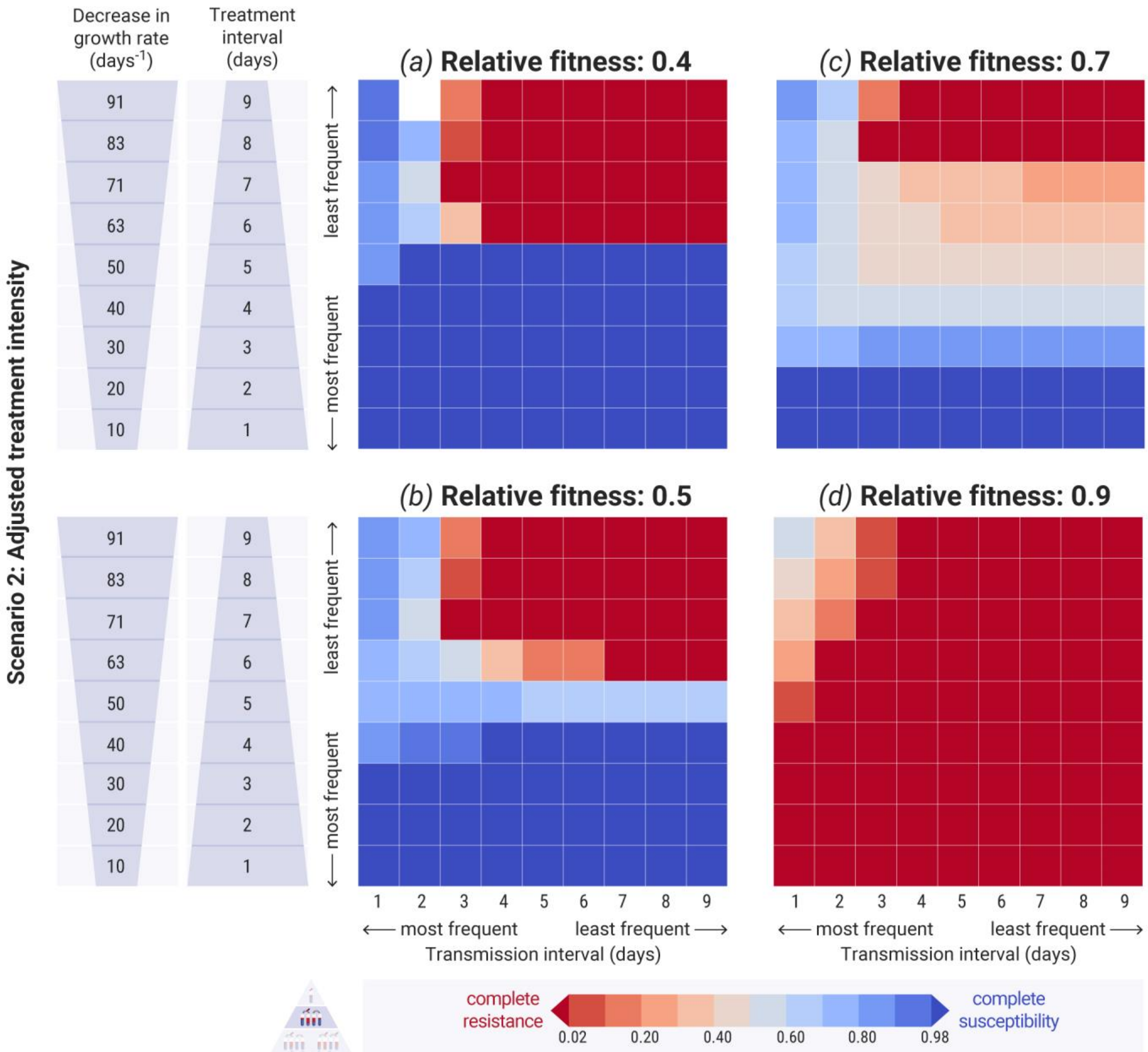
Supplementary Figure 6. Effect of low initial prevalence of resistance in a population. When the simulations were initiated with resistance contained in only a tenth of the host population, no amount of antimicrobial treatment would ever lead to the persistence of resistance in the population (assuming no mutation-driven resistance). Yet, with the introduction of daily transmission, the resulting pattern at equilibrium is exactly the same as in the main Figure 4. Starting from essentially extremely low resistance in a population, bacterial transmission facilitated the spread of the resistant strain that clearly benefited from the situation. Here, only 10% of the hosts carried the resistant strain at the beginning of the experiments. Results of the simulations across different treatment intervals (I_{antim}, y-axis) and relative fitness of the resistant strain (w, x-axis). Each cell of the heatmap represents the equilibrium values of one experiment. The colour bar represents the average equilibrium ratio of susceptible bacteria in the host population. **(A, C)** Scenario 1, where the decrease in the intrinsic growth rate due to the antimicrobial treatment is fixed across experiments at $d_{Smax} = 40$ day^{-1}. **(B, D)** Scenario 2, where the decrease in the growth rate due to the antimicrobial treatment, d_{Smax}, is adjusted by the treatment interval, and takes values between 10 and 91 day^{-1} (see Supplementary Table 1 for calculation). **(A, B)** Between-host simulations without transmission; **(C, D)** Between-host simulations with daily transmission.



Supplementary Figure 7. Within-population experiments without transmission. In essence, a single host experiment repeated 300 times (main Figure 4) produced the same average result as a 100-host experiment repeated three times herein. Results of the simulations across different treatment intervals (I_{antim}, y-axis) and relative fitness of the resistant strain (w, x-axis). Each cell of the heatmap represents the equilibrium values of one experiment. The colour bar represents the average equilibrium ratio of susceptible bacteria in the host population. **(A)** Scenario 1, where the decrease in the intrinsic growth rate due to the antimicrobial treatment is fixed across experiments at $d_{Smax} = 40$ day^{-1}. **(B)** Scenario 2, where the decrease in the growth rate due to the antimicrobial treatment, d_{Smax}, is adjusted by the treatment interval, and takes values between 10 and 91 day^{-1} (see Supplementary Table 1 for calculation).



Supplementary Figure 8. Effect of relative fitness of the resistant strain. Results of the between-hosts simulations across different treatment intervals (I_{antim}, y-axis) and transmission intervals (I_{trans}, x-axis). Each cell of the heatmap represents the equilibrium values of one experiment. The colour bar represents the average equilibrium ratio of susceptible bacteria in the host or in the population. All graphs come from Scenario 1, where the decrease in the intrinsic growth rate due to the antimicrobial treatment is fixed across experiments at $d_{Smax} =$ 40 day^{-1}. **(A-C)** The relative fitness of the resistant strain is set to a low level, at $w = 0.4$ to 0.6, indicating a high cost of resistance. **(E-G)** The relative fitness of the resistant is set to strain a higher level, at $w = 0.92$ to 0.96, indicating a low cost of resistance.



Supplementary Figure 9. Effect of relative fitness of the resistant strain. Results of the between-hosts simulations across different treatment intervals (I_{antim}, y-axis) and transmission intervals (I_{trans}, x-axis). Each cell of the heatmap represents the equilibrium values of one experiment. The colour bar represents the average equilibrium ratio of susceptible bacteria in the host or in the population. All graphs come from Scenario 2, where the decrease in the intrinsic growth rate due to the antimicrobial treatment is adjusted across experiments. **(A-B)** The relative fitness of the resistant strain is set to a low level, at $w = 0.4$ to 0.5, indicating a high cost of resistance. **(C-D)** The relative fitness of the resistant is set to strain a higher level, at $w = 0.7$ to 0.9, indicating a low cost of resistance.