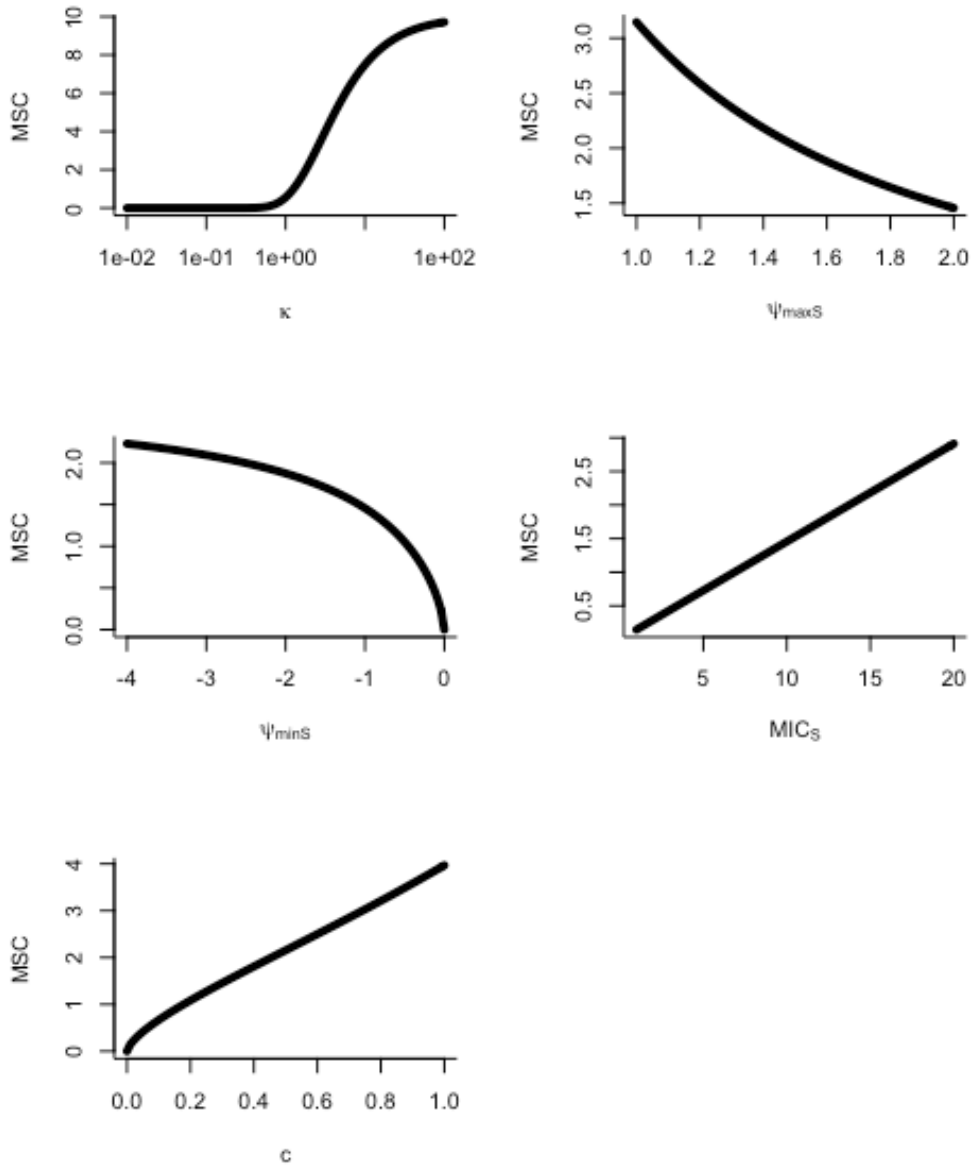

Figure S1: The MSC **is dependent on the pharmacodynamic variables of the susceptible strain *S* and the cost of resistance *c***. For parameter values, see fig 1a in main text and following Table S1.

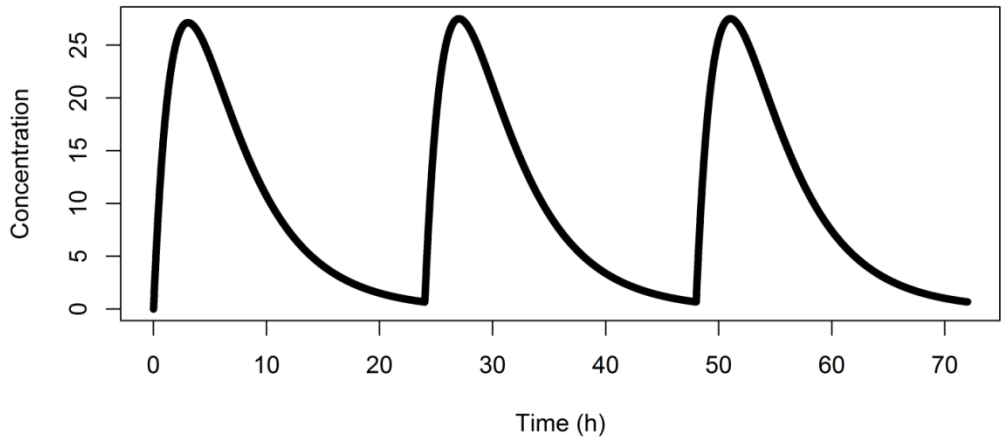

Fig. S2. **Pharmacokinetics of a given antimicrobial.** The curve can be captured by equation (6). This pharmacokinetics depicts that drug concentration reaches maximum shortly after dosing, then declines gradually before next dosing.

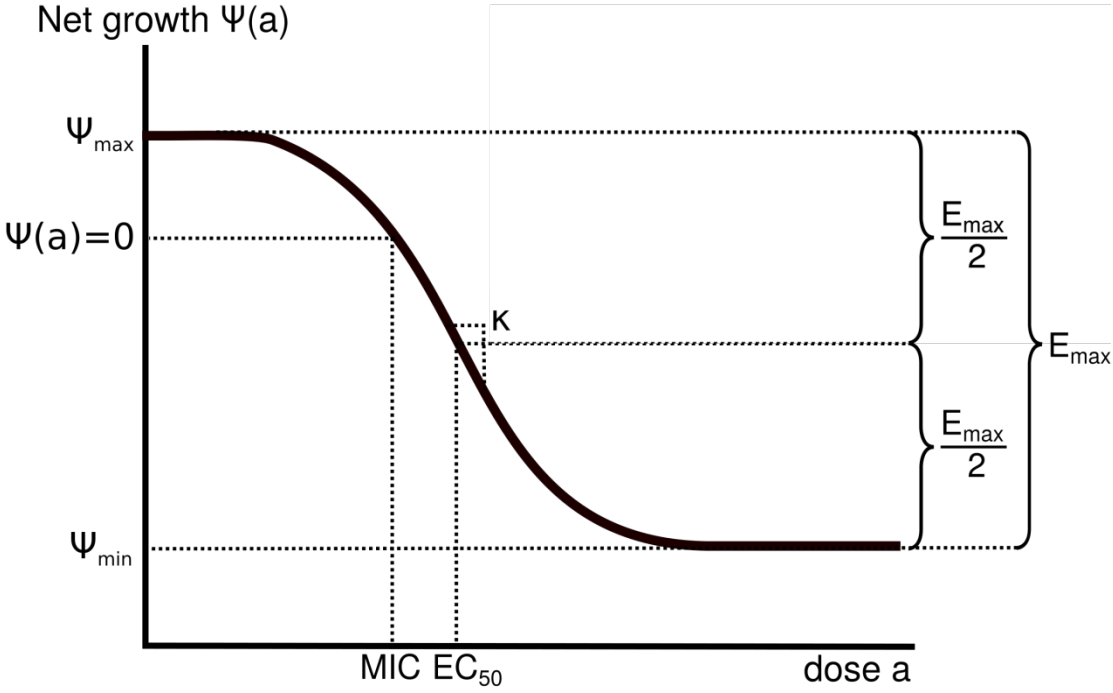

Fig S3. **Concept figure of the pharmacodynamic function and the pharmacological parameters.** The pharmacodynamic function $\psi(a)$ describes the net growth rate of a pathogen population in the presence of an antimicrobial with the dose a:

$$\psi(a) = \psi_{max} - d(a)$$

Here, ψ_{max} is the maximal net growth rate, i.e. $\psi_{max} = \psi(a = 0)$, and $d(a)$ represents the impact of the antimicrobial on the growth of the pathogen. In Regoes et al. (2004), two options are given to mathematically describe the term $d(a)$ with pharmacodynamic parameters:

$$d(a) = \frac{(\psi_{max} - \psi_{min})\left(\frac{a}{MIC}\right)^{\kappa}}{\left(\frac{a}{MIC}\right)^{\kappa} - \frac{\psi_{min}}{\psi_{max}}} = \frac{E_{max}\left(\frac{a}{EC_{50}}\right)^{\kappa}}{1 + \left(\frac{a}{EC_{50}}\right)^{\kappa}}$$

ψ_{min} is the minimal net growth rate with $\psi_{min} = \psi(a \to \infty)$, E_{max} is the maximum effect of the antimicrobial, with $E_{max} = \psi_{max} - \psi_{min}$, MIC is the dose at which the net growth equals 0 ($\psi(a = MIC) = 0$), κ is the slope parameter that describes the steepness of the curve, and EC_{50} is the dose of the antimicrobial at which half of the maximum effect is achieved ($\psi(a = EC_{50}) = \psi_{max} - \frac{E_{max}}{2}$). Note that $EC_{50} = MIC\left(-\frac{\psi_{min}}{\psi_{max}}\right)^{\frac{1}{\kappa}}$. All pharmacodynamic parameters are indicated in the figure.

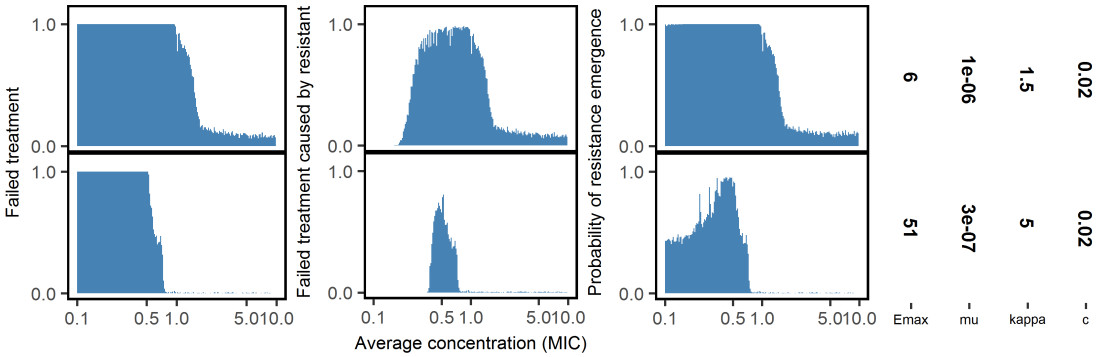

Fig S4. **Lower fitness costs donot affect the width of mutant selection window.** These simulations are equivalent to the results in figure 3B, with parameters representing antibiotics (top row) and AMPs (bottom row) with extremely low fitness cost, c = 0.02, as calculated by $\psi_{max,S} - \psi_{max,R}$. It shows fitness cost is of little importance on the width of MSW which is largely controlled by κ.

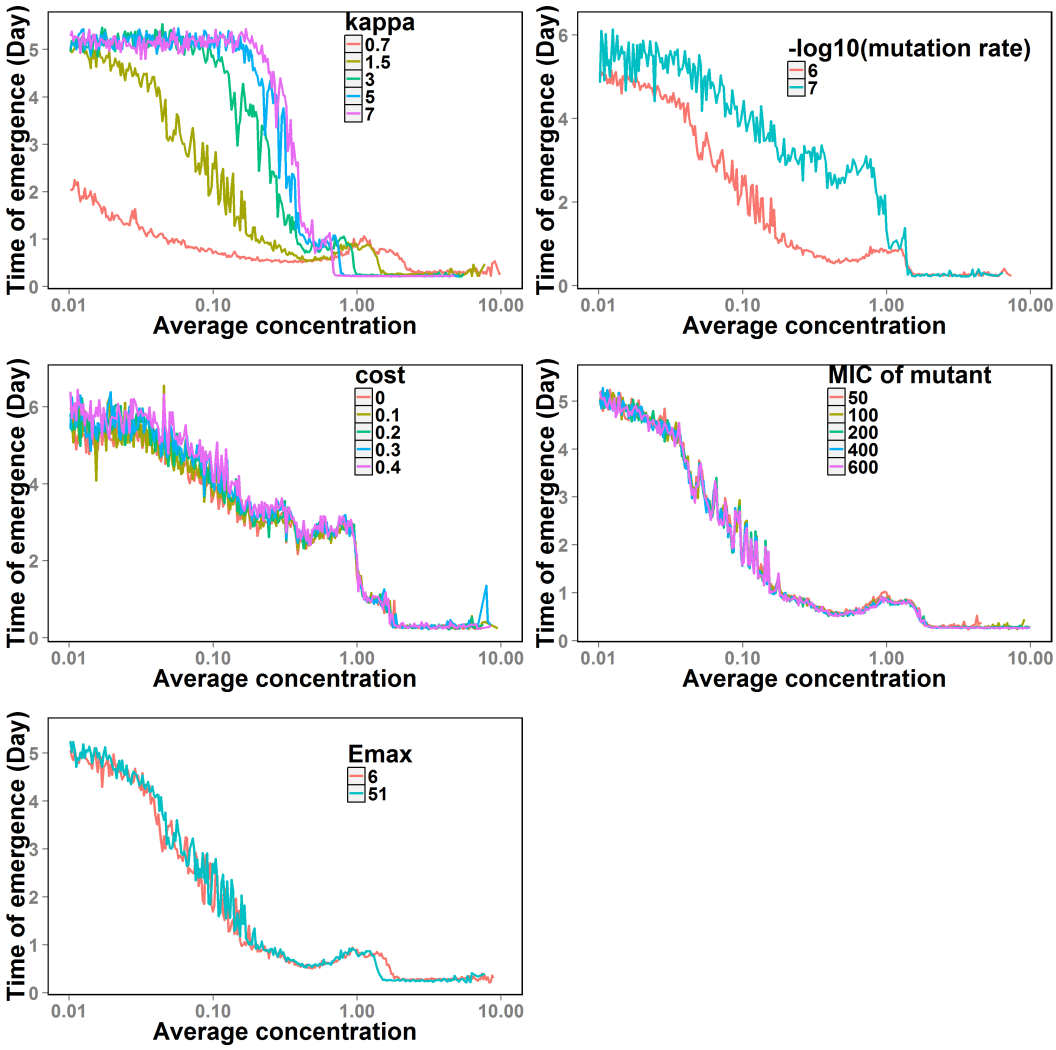

Fig. S5. **Average time of emergence of mutants.** Kappa and mutation rate determine the time of emergence of mutants. Higher kappa and lower mutation rate will result latter emergence of mutants. However, MIC of mutants, cost of mutants and maximal effect of antimicrobials do not significantly effect the time of emergence of mutants.

Table S1. Parameters and their values used in this study.

Parameters	Value	Unit	Description
a	0~1000	×MIC	The concentration of drugs
ψ	-50~1	h^{-1}	The growth rate of bacterial population
MIC	1~10	-	Minimal inhibitory concentration
κ	1.5, 5	-	Shape parameter of pharmacodynamic curve
d	-	h^{-1}	Death rate of bacterial population
c	0~1	-	Cost of resistance
S	0~10^6	CFU	Population size of sensitive strain
R	0~10^6	CFU	Population size of resistant strain
K	10^6	CFU	Capacity of system
μ	10^{-6}, 10^{-7}	-	Mutation rate
k_a	0.5	h^{-1}	Rate of drug absorption
k_e	0.2	h^{-1}	Rate of drug decay
D	-	×MIC	Dosage of a given drug
τ	1/24	h^{-1}	The dose frequency
$p_{S\to R}$	0~1	-	Probability of a treatment developing resistance

Psimax	Psimin	Kappa	MIC	Antibiotics
0.368	-5.959	0.740	0.426	Ampicilin
0.052	-5.927	1.242	0.848	Ciprofloxacin
0.045	-5.866	1.853	0.067	Gentamicin
0.205	-5.918	1.621	0.527	Kanamycin
0.159	-5.876	1.808	0.480	Neomycin
0.218	-4.171	0.445	1.371	Rifabutin
0.280	-0.783	0.904	1.627	Spectinomycin
0.008	-6.407	1.866	2.993	Tetracycline

Table S2. The measured pharmacodynamic parameters of different antibiotics for reference in this study.