Supplementary Materials:

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Supplementary table 1. Strains and plasmids

Strain name	Strain number	Relevant genotype	Resistance*	Reference
SL1344	SB300	Wild-type	Sm	[42]
SL1344 P2^{cat} (Wild-type invasive donor)	M995	*cat* on P2	Sm, Cm	[20]
SL1344^{noninv} P2^{cat} (Noninvasive donor)	M3182	*cat* on P2; *ΔinvG; ΔssaV*	Sm, Cm	[21]
14028S *aphT* (*S.*Tm recipient)	M3168	*lpfED::aphT*	Kan	[21]
14028S^{noninv} *aphT*	M3171	*lpfED::aphT*; *ΔinvG; ΔssaV*	Kan	[21]
14028S *cat*	M3155	*marT::cat*	Cm	[21]
SL1344 P2$^{cat\ \Delta oriT}$	M1407	*oriT::cat* on P2	Sm, Cm	[20]
SL1344 P2^{cat} TAG1	Z2141	*Tag2-cat* on P2	Sm, Cm	This work
SL1344 P2^{cat} TAG2	Z2142	*Tag11-cat* on P2	Sm, Cm	This work
SL1344 P2^{cat} TAG3	Z2143	*Tag13-cat* on P2	Sm, Cm	This work
SL1344 P2^{cat} TAG4	Z2144	*Tag19-cat* on P2	Sm, Cm	This work
SL1344 P2^{cat} TAG5	Z2145	*Tag21-cat* on P2	Sm, Cm	This work
SL1344^{SPI-2} P2^{cat} TAG1	Z2160	*Tag2-cat* on P2*; ΔssaV*	Sm, Cm	This work
SL1344^{SPI-2} P2^{cat} TAG2	Z2161	*Tag11-cat* on P2*; ΔssaV*	Sm, Cm	This work
SL1344^{SPI-2} P2^{cat} TAG3	Z2162	*Tag13-cat* on P2*; ΔssaV*	Sm, Cm	This work
SL1344^{SPI-2} P2^{cat} TAG4	Z2163	*Tag19-cat* on P2*; ΔssaV*	Sm, Cm	This work
SL1344^{SPI-2} P2^{cat} TAG5	Z2164	*Tag21-cat* on P2*; ΔssaV*	Sm, Cm	This work
14028S *TAG1*	Z2146	*Tag2-aphT*	Kan	This work
14028S *TAG2*	Z2147	*Tag11-aphT*	Kan	This work
14028S *TAG3*	Z2148	*Tag13-aphT*	Kan	This work
14028S *TAG4*	Z2149	*Tag19-aphT*	Kan	This work
14028S *TAG5*	Z2150	*Tag21-aphT*	Kan	This work
14028S P2$^{aphT\ \Delta oriT}$	Z2152	*oriT::aphT* on P2	Kan	This work
14028S P2^{cat}	Z2151	*cat*	Cm	This work
E. coli 8178 P2^{cured} (*E. coli* recipient)	M1403	P2 cured	None	[20]
SL1344 P2^{cured}	M1404	P2 cured	Sm	[20]
SL1344 P2^{cured} *aphT*	Z2159	P2 cured; *lpfED::aphT*	Sm, Kan	This work
E. coli 8178 P2^{cat}	Z1874	P2^{cat} from M995 conjugated into M1304	Cm	This work
E. coli ESBL15	Z2115	*CTX-M1* on pESBL15	Amp	[43]
SL1344 pESBL15	Z2139	*CTX-M1* on pESBL15; P2 cured	Amp	This work
Plasmid name	**Relevant genotype**		**Resistance**	**Reference**
P2	Wild-type		None	[20]
P2^{cat}	*cat*		Cm	[20]
P2^{cat} TAG	*Tag(2, 11, 13, 19, or 21)-cat*		Cm	This work
pESBL15	*CTX-M-1*		ESBL$^{\#}$	[43]
pM975	*bla*; used to confer ampicillin resistance		Amp	[44]

pCP20	FLP recombinase	Amp, Cm	[35]
pKD46	Arabinose-inducible λ *red* system	Amp	[35]

* Relevant resistances only: Sm = ≥50 µg/ml streptomycin; Cm = ≥6 µg/ml chloramphenicol; Kan = ≥50 µg/ml kanamycin; Amp = ≥100 µg/ml ampicillin. **Extended data Fig. 2** provides additional resistance information for key strains in this work.

ESBL phenotype based on resistance to ≥64 µg/ml ceftriaxone (3rd generation beta-lactam; also resistant to ≥100 µg/ml ampicillin).

Supplementary table 2. Primers

Primer name	Sequence	Purpose	Reference
WITS2-R	GAG TTG TTG GTA TTG CGG GT	qPCR	This work
WITS11-R	TGA GAT CGA GTG TGT GGG AT	qPCR	This work
WITS13-R	TGA GTG AGG GGT GTC TTT AGC	qPCR	This work
WITS19-R	GTT ATG GGG CTG GAT AGT GC	qPCR	This work
WITS21-R	GGA GAG TGA TCG GTG GTT GT	qPCR	This work
Cat_internal	CAA GAT GTG GCG TGT TAC GG	qPCR	This work
Kan_internal	ACC GGC GCA GGA ACA CTG	qPCR	This work
WITS2	ACC CGC AAT ACC AAC AAC TC	qPCR	[34]
WITS11	ATC CCA CAC ACT CGA TCT CA	qPCR	[34]
WITS13	GCT AAA GAC ACC CCT CAC TCA	qPCR	[34]
WITS19	GCA CTA TCC AGC CCC ATA AC	qPCR	[34]
WITS21	ACA ACC ACC GAT CAC TCT CC	qPCR	[34]
ydgA	GGC TGT CCG CAA TGG GTC	qPCR	[34]
oriT_nikA_KO	CCT TCT CTT TTT CGG AAT GAC TGC ATT CAC CGG AGA ATC CAT ATG AAT ATC CTC CTT AGT T	Deletion of *oriT* in P2	[20]
oriT_nikA_rev_KO	GCA TAA GAC TAT GAT GCA CAA AAA TAA CAG GCT ATA ATG GTG TGT AGG CTG GAG CTG CTT C	Deletion of *oriT* in P2	[20]
oriT_nikA_val	AGT TCC TCA TCG GTC ATG TC	Verification of *oriT* deletion	[20]
oriT_nikA_rev_val	GAA GCC ATT GGC ACT TTC TC	Verification of *oriT* deletion	[20]
WITS_P2_Phus_up	GCA TGA TAA TAA TAA TCA ATA ACA ATA AGC TGT GTC ACG TTT ACA TCA TGG CTG TCC GCA ATG GGT	Insertion of *WITS* in P2	This work
WITS_P2_Phus_dw	AAG GGT AAT GGC GGA AGC CGG ATA CCC AGC CGC CAG AGA AAT CGA ACA TAT CCC TTC CTT A	Insertion of *WITS* in P2	This work
insert_ p2_up	GTA CCG GTG CGT GAT AAC	Verification of *WITS* insert in P2	This work
insert_ p2_dw	CAA CAG CGT GAC CTG CC	Verification of *WITS* insert in P2	This work

Supplementary table 3. Input parameters and priors used in the stochastic simulations

Parameter	Function	Value	Units
r	Birth-rate	44 ln(2)	Per day
c	Clearance-rate	4 ln(2)	Per day
r_K	Residual birth-rate at carrying capacity	$4\ln(2)$	Per day
K	Carrying capacity	10^9	CFU/g feces
R(t=0)	Size of the recipient inoculum	10^7	CFU/g feces
N	Number of distinguishable plasmid populations	5	Dimensionless
η	Per recipient rate of conjugation from one donor type (i.e. donor re-seeding followed by conjugation)	**Uniform on the discrete grid** $10^{-12} - 10^{-1}$ in 0.5 log increments	Per day
γ	Per transconjugant-recipient pair rate of conjugation from transconjugants	**Uniform on the discrete grid** 10^{-12}	Per CFU/g feces per day

		– 10^{-1} in 0.5 log increments	

Supplementary table 4. Parameter estimates

Simulation	Maximum likelihood (η,γ) pair	η value from the marginal posterior distribution	γ value from the marginal posterior distribution
Main text (large grid; **Fig. 2C**)	η=3.16×10^{-10} (per day) γ=3.16×10^{-8} (per CFU/g feces per day)	3.16×10^{-10} (per day) HPD: [3.16×10^{-12}, 3.16×10^{-9}]	3.16×10^{-8} (per CFU/g feces per day) HPD: [1×10^{-8}, 0.1]
Inflammation (large grid; **Fig. 23A**)	η=1×10^{-9} (per day) γ=3.16×10^{-8} (per CFU/g feces per day)	3.16×10^{-10} (per day) HPD: [3.16×10^{-12}, 3.16×10^{-9}]	3.16×10^{-8} (per CFU/g feces per day) HPD: [1×10^{-8}, 0.1]
Main text (finer grid; **Fig. 24A**)	η=5.62×10^{-10} (per day) γ=3.16×10^{-8} (per CFU/g feces per day)	1.78×10^{-10} (per day) HPD: [1.78×10^{-12}, 3.16×10^{-9}]	5.62×10^{-8} (per CFU/g feces per day) HPD: [5.62×10^{-9}, 5.62×10^{-2}]
Inflammation (finer grid; **Fig. 24C**)	η=1×10^{-9} (per day) γ=3.16×10^{-8} (per CFU/g feces per day)	1.78×10^{-10} (per day) HPD: [3.16×10^{-12}, 3.16×10^{-9}]	5.62×10^{-8} (per CFU/g feces per day) HPD: [5.62×10^{-9}, 5.62×10^{-2}]

*HPD: Highest posterior density interval

Supplementary discussion:

A) Persistence of the mucosa-associated *S*.Tm population in the oral model.

Previous work has established that ciprofloxacin therapy efficiently depletes the gut luminal *S*.Tm population and penetrates tissues to concentrations well above the minimum inhibitory concentration (MIC; albeit slightly lower concentrations than in the gut lumen) [7]. These data suggest, that the mucosa-associated *S*.Tm cells are indeed exposed to >MIC levels during the course of the ciprofloxacin treatment [7]. Within three hours after the onset of the ciprofloxacin treatment, gut luminal *S*.Tm populations drop below the limit of detection (<100 per gram feces [7]). *S*.Tm loads in the gut tissue are reduced by 80%. However, 10^2-10^5 mucosa-associated bacteria survive the ciprofloxacin treatment for up to 10 days [7]. Once the ciprofloxacin treatment is terminated, these mucosa-associated persisters can re-seed the gut lumen and cause relapses, which are characterized by enteropathy and high gut luminal pathogen densities. Importantly, the *S*.Tm cells can be re-isolated from such relapses and are fully sensitive to ciprofloxacin [7,24]. Therefore, we use the term persistence in the present work, to describe the tissue-associated *S*.Tm population which survives the ciprofloxacin treatment.

B) Why do we supplement the drinking-water with antibiotics (i.e. ampicillin) after ending the ciprofloxacin treatment in the oral model?

After the end of the ciprofloxacin treatment, the ciprofloxacin is washed out of the gut. Once the gut luminal ciprofloxacin levels have dropped below the MIC, the re-seeding events (i.e. *S*.Tm persisters re-entering the gut lumen and switching back to their normal, ciprofloxacin-sensitive vegetative growth physiology) will re-establish the gut luminal *S*.Tm infection. While re-seeding events

are quite rare, they do initiate rapid pathogen growth in the gut lumen. Thus, stool pathogen loads reach 10^8-10^9 cfu/g after the ciprofloxacin is washed out of the gut, i.e. between 1-4 days after the end of the ciprofloxacin treatment. Whether this re-seeding occurs at day 1, 2, 3 or 4 varies from mouse to mouse. The variability is likely attributable to the rare and random process of re-seeding. This rapid re-growth of the luminal *S*.Tm population from few founders is explained by the fact that the microbiota is still disrupted by the previous ciprofloxacin treatment [45,46].

After the end of the ciprofloxacin treatment, we added ampicillin to the drinking, to ask whether rare events of donor re-seeding and limited donor re-growth would suffice to transfer conjugative plasmids into a recipient population. This would mimic situations with partially (or completely) intact gut microbiota which would normally prevent luminal *S*.Tm growth (colonization resistance [47]). Thus, by adding ampicillin to the drinking water, we could keep donor populations in the gut lumen small.

Indeed, small donor populations are observed in the stool of some mice, i.e. after recipients have colonized the gut lumen (after day 8). This is expected, as ampicillin is depleted in the gut luminal environment by the beta-lactamase enzymes that are expressed by the recipient bacteria (ATCC14028S, Amp^R). Conjugation of the P2^{cat} plasmid occurs quickly and depends primarily on donor-recipient contact (**Extended data Fig. 1d**) [48]. Our data show that rapid amplification by recipients that have obtained a plasmid (i.e., transconjugants) would result in dissemination of the plasmid in the population of bacteria colonizing the gut lumen (**Fig. 1a**), regardless of the success of the establishment of donor bacteria in the gut lumen niche. Together with our barcoding approaches and our mathematical model, this indicates that very few events of donor re-seeding (followed by initial plasmid transfer) suffice to transfer P2^{cat} into the vast majority of the recipient cells. Considering that the murine cecum lodges 10^2-10^5 persistent *S*.Tm P2^{cat} donors, that these *S*.Tm P2^{cat} persisters have extremely long life times (>>10 days), and that reversion to the vegetative phenotype followed by its release into the gut lumen is quite rare, these data suggest that a tissue-associated reservoir of persistent donors can dramatically prolong the periods of co-occurrence between the donor and a recipient strain. Thus, while the original donor population may well be eliminated from the gut lumen (e.g. by the host's antibody responses, by competing microbiota, or by competing pathogen strains [22,46]), the persistent tissue-associated population may continue to promote resistance plasmid transfer to other enteric bacteria for much longer.

C) Typhoid fever like model

In humans, *Salmonella enterica* serovar Typhi can persist in the gall bladder, causing chronic infections associated with long-term shedding [49-52]. Therefore, it is well possible that in humans the gall bladder also serves as a reservoir for persisters. These bacteria could re-seed the gut via the bile duct and thereby promote strain co-occurrence, favouring conjugative plasmid transfer. In the Typhoid fever-like model (i.e., the I.V. model), intravenous infection of donor *S.*Tm yielded bacteria in the liver, spleen, and in the gall bladder of some mice (**Fig. 2d, 4e, Extended data Fig. 5a**) followed by eventual plasmid transfer (**Fig. 2**). In the gall bladder of human patients that shed *Salmonella* spp., densities of >10^3 CFU are found [49]. It is tempting to speculate that such re-seeding-driven plasmid transfer could also occur in humans shedding *Salmonella* spp. from the gall bladder.

D) Description of the mathematical model

We model the dynamics of recipient and transconjugant populations, as a function of the horizontal transfer rate from donors and transconjugants. We make the following assumptions: The plasmid can only be transferred to recipient cells. Five isogenic plasmid copies – each corresponding to one isogenic tag - exist, yielding 5 different transconjugant populations. The populations are well-mixed, and plasmid transfer is described by mass-action kinetics [48], i.e., the number of transfer events

is proportional to the product of plasmid-bearing (donors D or transconjugants T) and recipient cells (R). To account for the bounded resources in the gut, bacterial population growth is assumed to be logistic and reaches zero at carrying capacity K. The 5 donor populations in the gut epithelial tissues are assumed constant, and each transfers plasmids at a constant per-recipient rate η. The transconjugant populations transfer plasmids to recipients at a constant per-contact rate γ. The removal of bacteria, whether through death or efflux from the gut, is explicitly included in the model through the clearance rate *c*.

Let R denote the recipient population and T_j with $j \in \{1 \cdots N\}$ denote the transconjugant populations (N = 5 in the experiment). We simulate the population dynamics stochastically using a vector of state changes $\boldsymbol{\nu}$ (dimension $3N + 2$), and an associated vector of reaction rates **a**. To describe these reaction rates, we introduce two further parameters: *r* for the birth-rate, and r_K for the residual birth-rate at carrying capacity. These parameters are chosen such that birth and death balance each other out exactly once the population reaches carrying capacity, leading to the condition that $r_K = c$ (this is informed by experiments; see the parameter section further below). With these definitions, we obtain the following reaction rates:

Birth reactions:

$$\nu_1 : R \to R + 1$$

$$a_1 : (r + r_K)R$$

$k \in 2 \cdots N + 1$:

$$\nu_k : T_j \to T_j + 1; \quad j \in 1 \cdots N$$

$$a_k : (r + r_K)T_j; \quad j \in 1 \cdots N$$

i.e., new individuals are added to the population at a rate that reflects the joint contribution of the base birth-rate *r* and the residual birth-rate at carrying capacity r_K.

Death reactions:

$$\nu_{N+2} : R \to R - 1$$

$$a_{N+2} : cR + \mathrm{r}R\frac{R + \sum_{j \in 1 \cdots N} T_j}{K}$$

$k \in N + 3 \cdots 2N + 2$:

$$\nu_k : T_j \to T_j - 1; \quad j \in 1 \cdots N$$

$$a_k : cT_j + \mathrm{r}T_j\frac{R + \sum_{j \in 1 \cdots N} T_j}{K}$$

i.e., individuals are removed from the population at a constant clearance rate *c* and an additional population-size dependent term that reflects the increased killing as the populations size approaches the carrying capacity *K*.

Plasmid Transfer reactions, $k \in 2N + 3 \cdots 3N + 2$:

$$\nu_k : R \to R - 1 \text{ and } T_j \to T_j + 1; \quad j \in 1 \cdots N$$

$$a_k : (\eta + \gamma T_j)R; \quad j \in 1 \cdots N$$

i.e., a recipient is converted to a particular transconjugant population at a rate η that reflects the constant contribution from mucosa-associated donors of type *j*, as well as the transfer from transconjugants in the gut that carry this particular plasmid (γT_j).

The model was simulated using the tau-leaping stochastic simulation method from the R package *adaptivetau* (Philip Johnson (2016). adaptivetau: Tau-Leaping Stochastic Simulation. R package version 2.2-1. https://CRAN.R-project.org/package=adaptivetau).

Deterministic formulation of the stochastic model

In the limit of large numbers our stochastic model is equivalent to the following deterministic equations [53]:

$$\dot{R} = -\left(\eta N + \gamma \sum_{j\,\epsilon\,1\cdots N} T_j\right)R + (r + r_K)R - R\left(c + \mathrm{r}\frac{R+\sum_{j\,\epsilon 1\cdots N} T_j}{K}\right) \quad (1)$$

$$\dot{T}_j = \left(\eta + \gamma T_j\right)R + (r + r_K)T_j - T_j\left(c + \mathrm{r}\frac{R + \sum_{j\,\epsilon 1\cdots N} T_j}{K}\right) \quad (2)$$

Input parameters of the mathematical model

Parameters pertaining to Salmonella population growth in the mouse gut (*r, c, r_K, K)* were parametrized using previously published data from the same mouse model system (i.e., the streptomycin pre-treatment murine model for *Salmonella* colitis)[22,38]. Size of the recipient inoculum and number of distinguishable plasmid populations were set to mirror the experimental conditions in this paper.

In the common formulation of logistic growth, the population reaches a steady state at the carrying capacity K, where population clearance is balanced by birth. However, fixing the net growth rate to zero at this population size would exclude any dynamics, which is an inaccurate depiction of the (slowed) population turnover that takes place even at high densities. To correct this, we adapted the equations of logistic growth and parameterized them using previously published growth rate and population size estimates as detailed below.

If we assume a population free from transfer, i.e., if we set $\eta, \gamma = 0$ in equation (1), and study the limit where the recipient population is at carrying capacity, i.e. $R \to K$, we find:

$$\dot{R} \approx R(r_K - c)$$

The first term of this equation describes the growth. Previous experiments have shown that the "residual birth at carrying capacity" amounts to a doubling time of 6 hours (1/4 day) [22].

$$\Longrightarrow r_K = \frac{\ln(2)}{Doubling\ Time} = 4\ln(2) \text{ per day}$$

The removal rate of bacteria due to efflux from the gut balances this rate at the carrying capacity, and is otherwise independent of the population size.

$$\Longrightarrow c = 4\ln(2) \text{ per day}$$

On the other hand, in the limit where the recipient population is small, i.e. $R \to 0$, equation (1) simplifies to:

$$\dot{R} \approx R(r + r_K) - cR$$

Here, the growth rate is known to be 2 h^{-1} (i.e., the doubling time is 30 minutes or 1/48 day) [22]:

$$(r + r_K) = \frac{\ln(2)}{Doubling\ Time} = 48\ln(2) \text{ per day}$$

$$\Longrightarrow r = \frac{\ln(2)}{Doubling\ Time} - r_K = 44\ln(2) \text{ per day}$$

The carrying capacity was determined as 10^9 CFU/g feces, and the recipients were inoculated at a density of 5×10^7 CFU. Colonization of the intestine is not immediate, but after 8 hours bacteria are found at a density of 10^7 CFU/g feces [38]. Therefore, we used 10^7 CFU/g feces as our starting population size for the recipient population. Parameter values used in the model are summarized in **Supplementary table 3**.

Parameter estimation in the mathematical model

To infer the most likely rates of transfer η and γ, we use a simple Approximate Bayesian Computation (ABC) approach [40]. Both transfer rates were varied on a grid from 10^{-12} – 10^{-1} in 0.5 log increments, with 100 simulations per parameter combination. For each set of parameters, we compare the simulations to the experimental data of plasmid tag frequencies and the bacterial population counts, according to the summary statistics listed below. The likelihood of a given transfer parameter combination is given by the percentage of simulations that return all summary statistics within three standard deviations of the experimentally observed mean of these statistics.

i. The Evenness index E, defined as 1 – g where g is the Gini index [54], commonly used to describe the statistical dispersion of wealth distributions. Here, we use it to capture the skew of the plasmid tag abundance distribution.
ii. The probability p_0, defined as the fraction of plasmid tags with a relative abundance above the detection limit of 2.9×10^{-3} (on day 15).
iii. The size of the transconjugant population on day 15: $\sum T_j(t = 15)$.
iv. The time at which the transconjugant population size first exceeds 10^6 CFU/g feces.

Both transfer parameters η and γ are most strongly constrained by the timing of the rapid rise in transconjugant population size (summary statistic iv.). The rate at which donors introduce transconjugants (η) mostly determines the onset of the increase in transconjugants, whereas the rate of transconjugant-recipient conjugation (γ) dominates the slope of the increase in transconjugants. As a consequence, when η is high, γ must be low, otherwise the gut luminal population would be almost instantaneously overtaken by transconjugants. In addition, the summary statistics describing the plasmid tag distribution (i. and ii.) work to constrain η to low values. However, the exact slope of the transconjugants population increase is much less constrained by the experimental data than the timing of this increase, so when η is low enough, a wide range of γ values can explain the data almost equally well.

Dependence of conjugation on the donor re-seeding rate

In a separate analysis, we estimate the proportion of experiments with full-fledged conjugation, as a function of the donor re-seeding rate. We re-analyzed the stochastic simulation results focusing only on whether the simulation showed plasmid re-seeding, defined as a final transconjugant population size above 5×10^8 CFU/g feces. We considered only those simulations with the transconjugants-to-recipient transfer rate γ at its most likely value ($\gamma = 3.16\times10^{-8}$ per CFU/g feces per day), and plot the results as a function of the donor re-seeding rate η. For **Fig. 3d**, we estimated the fraction of simulations with plasmid re-seeding, defined as a final transconjugant population size above 5×10^8 CFU/g feces, as a function of η. Here γ is fixed at its most likely value $\gamma = 3.16\times10^{-8}$ per CFU/g feces

per day. The black vertical dotted line at $\eta = 3.16\times10^{-10}$ per day indicates the estimated most likely value (from **Fig. 3c**). The red vertical dotted line at $\eta = 3.16\times10^{-12}$ per day indicates a hypothetical 100-fold decrease of η (shown by a red arrow; e.g. accomplished by vaccination).

Estimating the number of transfer events per day

The estimated set of most likely parameters is ($\eta = 3.16\times10^{-10}$ per day; $\gamma = 3.16\times10^{-8}$ per CFU/g feces per day). These results can be translated into number of conjugation events per day by considering the part of equation (1) that pertains to plasmid dynamics:

$$\left(\eta N + \gamma \sum_{j \in 1\cdots N} T_j\right) R$$

If we assume the donor population is as in the experiment, and the lumen contains a population of naïve recipient cells at carrying capacity and a single transconjugant cell, then the number of donor seeding events associated with plasmid transfer is:

$$\eta N R = 3.16\text{x}10^{-10} \cdot 5 \cdot 10^{9} = 1.58 \text{ CFU/g feces per day}$$

In contrast, the number of transconjugant-to-recipient events is:

$$\left(\gamma \sum_{j \in 1\cdots N} T_j\right) R = 3.16\text{x}10^{-8} \cdot 1 \cdot 10^{9} = 31.6 \text{ CFU/g feces per day}$$

This number of transconjugant-to-recipient events will grow quickly (exponentially) once the first transconjugants enter the population.

The aim of this translation into number of conjugation events per day is to give an intuition for the magnitude of the η and γ parameters. Mathematically speaking, the ratio of 1:20 between donor re-seeding and transconjugant-to-recipient events will be the same also for smaller recipient populations (as is the case for our inoculum). Biologically speaking, η and γ may not be completely independent of recipient population density (as is assumed by our model). For example, ampicillin-sensitive donor bacteria are more likely to survive at higher recipient densities (that deplete ampicillin locally). This would result in even lower η, and thus a lower number of re-seeding events, at the start of the experiment. However, these population-size dependent effects will be balanced out quickly once the population grows to carrying capacity.

Simulation results in case of inflammation

In the case of inflammation, the increased bacterial killing can lead to a higher birth rate at the carrying capacity than 6 hours per generation. Therefore, we also simulated the case in which the residual birth-rate at carrying capacity is twice as high (a doubling time of 3 hours), i.e., $r_K = 8\ln(2)$ per day, and the corresponding clearance rate is $c = 8\ln(2)$ per day. The general birth rate r is fixed to its previous value $r = 44\ln(2)$ per day. As a result, the total birth rate at small population sizes is higher than before, but it is balanced by increased death, so the net growth remains the same.

The results of these simulations are shown in **Extended data Fig. 10a-b,** and listed in **Supplementary table 4**. The most likely parameter set is changed to ($\eta = 1\times10^{-9}$ per day; $\gamma = 3.16\times10^{-8}$ per CFU/g feces per day), i.e., η is estimated to be slightly higher than without inflammation. However, the qualitative results remain the same.

Simulation results on a finer parameter grid

We repeated the simulations on a more granular grid, with the rate of conjugation from donors η varying between 10^{-12}-10^{-6} (in 0.25 log increments) per day, and the rate of conjugation from transconjugants γ varying between 10^{-10}-10^{-1} (in 0.25 log increments) per CFU/g feces per day.

The parameter estimates of this simulation are listed in **Supplementary table 4**, and the results shown in **Extended data Fig. 10c-f**.

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