

Supplementary Tables

VERA: agent-based modeling transmission of antibiotic resistance between human pathogens and gut microbiota

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Supplementary Table 1 | Probabilities values used to build the model for *Shigella* sp.
Considering of the model probabilities values whereby agents pass between states.

Probability	Description	Value
p_1	to be hospitalized with other problems, non pathogen	0.002
p_2	to be infected (column "pGetInfectedTown" in the result table)	$p_2 = i_c * \frac{\mu_3 + \mu_4 + 0.5 * (\mu_6 + \mu_7)}{townHealthy + numInfectedTown}$
p_3	to be hospitalized with pathogen from incubation period	0.07
p_4	to be hospitalized with AB sensitive pathogen from home treatment	p_3
p_5	to be hospitalized with AB resistance pathogen from home treatment	$p_3 * r_c * 10$
p_6	to be infected in hospital	0.06
p_7	to become resistant pathogen	$r_i * r_c$
p_8	to get incorrect home treatment period	0.21
p_9	to be infected in hospital with resistant pathogen	r_h

Supplementary Table 2 | Characteristic of agent states. Agent states were characterized by: location, presence of the pathogen, resistance occurrence of pathogen, level of microbiota resistance, possible transits, treatment period, incubation period, group of antibiotic.

Name of state	Characteristics
<i>Healthy person</i>	location: town infection: no pathogen resistance: no microbiota resistance: reduce on r_- until r_l possible transits: into <i>Non Infected person in hospital</i> with p_1 , into <i>Person in incubation period</i> with p_2 number of agents: μ_1
<i>Non Infected person in hospital</i>	location: hospital infection: no pathogen resistance: no microbiota resistance: reduce on r_- until r_l treatment period: i_p possible transits: into <i>Healthy person</i> , into <i>Person in incubation period</i> with p_6 or p_9 number of agents: μ_2
<i>Person in incubation period</i>	location: town infection: yes pathogen resistance: can become resistant with the p_7 microbiota resistance: reduce on r_- until r_l incubation period: i_p possible transits: into <i>Infected person in hospital</i> with p_3 , into <i>Person in AB incorrect treatment period</i> with p_8 , into <i>Person in AB treatment period</i> with $1 - p_8$ number of agents: μ_3
<i>Person in incubation period 2</i>	location: town infection: yes pathogen resistance: yes microbiota resistance: reduce on r_- until r_l possible transits: into <i>Infected person in hospital</i> number of agents: μ_4
<i>Infected person in hospital</i>	location: hospital infection: yes therapy: Antibiotic-2 pathogen resistance: no microbiota resistance: reduce on r_- until r_l

	<p>treatment period: i_p</p> <p>possible transits: into a state <i>Healthy person</i>.</p> <p>number of agents: μ_5</p>
<i>Person in AB incorrect treatment period</i>	<p>location: town</p> <p>infection: yes</p> <p>therapy: Antibiotic-1</p> <p>pathogen resistance: can become resistant with p_7</p> <p>microbiota resistance: increase on r_+</p> <p>possible transits: into <i>Person in incubation period 2</i>, into <i>Infected person in hospital</i> with the p_4 or p_5.</p> <p>number of agents: μ_6</p>
<i>Person in AB treatment period</i>	<p>location: town</p> <p>infection: yes</p> <p>therapy: Antibiotic-1</p> <p>pathogen resistance: can become resistant with the p_7</p> <p>treatment period: i_p</p> <p>microbiota resistance: increase on r_+</p> <p>possible transits: into <i>Healthy person</i>, into <i>Infected person in hospital</i> with p_4 or p_5</p> <p>number of agents: μ_7</p>

Supplementary Table 3 | Input parameters values for *Shigella sp.* Estimation of the input parameters values. Name of parameters in table correspond to names in config.properties file (see Material and Methods).

Name of parameters	Note	Value	Description	Reference
N_INCUB_LIMIT	i_p	4	Maximal incubation period of pathogen (days)	Dekker and Frank (2015)
C_INFECTED_COEF	i_c	0.134	Pathogen infection potential	Hypothesis
C_PATHOGEN_RESIST_CHANGE_COEF	r_c	0.61	Pathogen susceptibility to receive antibiotic resistance	Sack et al. (2001)
P_INCUB_TO_HOSPITAL	p_3	0.07	Probability of being hospitalized during incubation period	Asseray et al. (2013)
P_WRONG_TREATMENT	p_8	0.25	Probability of incorrect antibiotic treatment	Based on public opinion polls
P_BE_INFECTED_IN_HOSPITAL	p_6	0.06	Probability of being infected by pathogen during hospitalization without current infection	D'Agata et al. (2007)
C_GROWTH_COEF	r_+	0.04	Growth rate of antibiotic resistance	Wu et al. (2016)
C_DECREASE_COEF	r_-	0.025	Decrease rate of antibiotic resistance	Hypothesis
P_HEALTHY_HOSPITALIZE	p_1	0.002	Probability of being hospitalized without current infection	Hypothesis
PERM_RESIST_LEVEL	r_l	$3.205 * 10^{-08}$	Persistent level of gut antibiotic resistance	Yarygin et al. (2017)
N_PEOPLE_IN_TOWN		10000	Agent count in all states	Hypothesis
N_HOSP_ANT_TR_PERSON	μ_5	10	Agent count in State5 (<i>Infected person in hospital</i>)	Hypothesis

Supplementary Table 4 | Parameter symbols and values used to build the model for *Shigella* sp. Considering of the model parameters values. Characteristic names in table correspond to names in config.properties file (see Material and Methods). Data are derived from the literature, estimated during model running (see Table 3).

Name of parameters	Note	Description	Value
N_INFECTED_PEOPLE_PER_YEAR	β_i	Number of pathogen infected people per year based on public opinion polls	19139
N_PEOPLE_IN_COUNTRY	β_c	number of country population, mn	142.8
C_INFECTED_COEF	i_c	coefficient of infection	$\frac{\beta_i * 10^3}{\beta_c * 10^6}$
C_GROWTH_COEF	r_+	coefficient of resistance growth	0.04
C_DECREASE_COEF	r_-	coefficient of resistance decrease	0.025
N_INCUB_LIMIT	i_p	number of incubation period days	4
C_PATHOGEN_RESIST_CHANGE_COEF	r_c	Pathogen's capacity of receiving resistance change	0.61
PERM_RESIST_LEVEL	r_l	Persistent level of gut antibiotic resistance	$3.205 * 10^{-08}$
	μ_i	Agent count in i -state	estimating in model running
	r_i	Microbiota resistance level in i -agent	estimating in model running
	r_t	Average pathogen resistance level in town	estimating in model running
	r_h	Average pathogen resistance level in hospital	estimating in model running
	r_m	Average microbiota resistance level in town	from result table after model running with column name <i>AvMicResistTown</i>
	r_p	Average pathogen resistance level in town	from result table after model running with column name <i>AvPathResistTown</i>

Supplementary Table 5 | Ranges for Input parameters. This parameters values was used for multiple model launches to investigate indicators variation (see Material and Methods).

Note	Description	Lower bound	Upper bound
i_p	Maximal incubation period of pathogen (days)	1	14
i_c	Pathogen infection potential	0.0001	1
r_c	Pathogen susceptibility to receive antibiotic resistance	0.0001	1
p_3	Probability of being hospitalized during incubation period	0.0001	1
p_8	Probability of incorrect antibiotic treatment	0.0001	1
p_6	Probability of being infected by pathogen during hospitalization without current infection	0.0001	1
r_+	Growth rate of antibiotic resistance	0.0001	1
r_-	Decrease rate of antibiotic resistance	0.0001	1
p_1	Probability of being hospitalized without current infection	0.0001	1
r_l	Persistent level of gut antibiotic resistance	0	1

Supplementary Table 6 | Grid of parameters. There are the input parameters, which was chosen by regression analysis as contributing to changes in indicator values. We name them *the control parameters*.

Model indicator	Parameter	p-value
The number of infected people	Pathogen infection potential, i_c	0
	Pathogen susceptibility to receive antibiotic resistance, r_c	0.008
	Maximal incubation period, i_p	0
	Probability of being hospitalized during incubation period, p_3	0
The average level of microbiota resistance	Pathogen infection potential, i_c	0
	Pathogen susceptibility to receive antibiotic resistance, r_c	$2 * 10^{-15}$
	Probability of being hospitalized during incubation period, p_3	0
	Probability of incorrect antibiotic treatment, p_8	$3 * 10^{-32}$
	Persistent level of gut antibiotic resistance, r_l	0
The average level of pathogen resistance	Pathogen infection potential, i_c	0
	Pathogen susceptibility to receive antibiotic resistance, r_c	$2 * 10^{-89}$
	Maximal incubation period, i_p	10^{-193}
	Probability of being hospitalized during incubation period, p_3	0
	Persistent level of gut antibiotic resistance, r_l	$4 * 10^{-81}$
The probability of being infected	Pathogen infection potential, i_c	0
	Maximal incubation period, i_p	0
	Probability of being hospitalized during incubation period, p_3	0
	Probability of incorrect antibiotic treatment, p_8	0.01

Supplementary Table 7 | Parameter values for the ESKAPE pathogens. Values of pathogen susceptibility to receive antibiotic resistance r_c , which corresponds to C_PATHOGEN_RESIST_CHANGE_COEF in config.properties file (see Material and Methods). Data are derived from the literature for the ESKAPE pathogens (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter* species).

Pathogen	Value	Reference
<i>Enterococcus faecium</i>	0.315	Seo and Lee (2013)
<i>Staphylococcus aureus</i>	0.46	Bishara et al. (2003)
<i>Klebsiella pneumoniae</i>	0.61	Taitt et al. (2017)
<i>Acinetobacter baumannii</i>	0.47	Roy et al. (2010), Armin et al. (2015)
<i>Pseudomonas aeruginosa</i>	0.5	Mulu et al. (2017)
<i>Enterobacter</i> sp.	0.183	Knudsen et al. (2017)

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