Supplementary Notes

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

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1	Parameter estimation for shigellosis.
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Supplementary Note 1 | Parameter estimation for shigellosis.

Shigellosis is a widespread disease in places of public catering, day-care centers, etc. Here we investigate Shigella spp. as a model pathogen. We consider that Antibiotic-1 is from the sulfonamide antibiotic family (i.e. co-trimoxazole) and Antibiotic-2 is from the fluoroquinolone or nitrofuran groups.

The values of reduction r_- and increase r_+ in microbiota resistance has been estimated based on the article by Wu et al., 2016. It was established that the abundance of sulfonamide resistance genes decreases after diet of 30 days. The constant microbiota resistance level r_l was estimated from data of ResistoMap (Yarygin et al., 2017). We set the value of a chance of a pathogen becoming antibiotic resistant r_c according to the WHO (World Health Organization) report saying that trimethoprim-sulfamethoxazole (TMP-SMZ) resistance has increased from 1% to 56% in all Shigella isolates over a period of 9 years (Sack, 2001). It was found that 7% of infected patients were hospitalized for reasons not connected to adverse drug reactions to self-administered medications (Asseray et al., 2013). Thus, the probability of being hospitalized during incubation period p_3 was assessed as 0.07. Self-medication with antibiotics is widespread and loosely controlled in Russia. Considering self-therapy statistics based on public opinion polls, we assume the probability of incorrectly prescribed antibiotic treatment to be p_8 equal to 0.25. The probability of being hospitalized without current infection p_1 is 0.002. In view of sanitary rules and the potential to be infected by a pathogen during hospitalization without a current infection, we assigned p_6 equal to 0.06 (D'Agata et al., 2000). A maximal incubation period of shigellosis i_p was determined from Dekker et al., 2015. Pathogen infection potential coefficient i_c was calculated basing on infection rates compared to population size. We assumed the possible case when infected persons in hospital μ_5 can be 10 persons per 10000 population in town.

The default values of input model parameters are reflected in additional materials and correspond to infection with *Shigella spp*. (see Supplementary Table 3 and Supplementary Table 4).

Supplementary Note 2 | Parameter estimation for cholera epidemic case in Yemen.

Cholera is a diarrheal illness caused by infection of the *Vibrio cholerae*. The infection has variable symptoms. It has been reported that approximately 10 percents of infected persons will have severe disease with rapid loss of body fluids leading to dehydration and shock. Transmission of cholera is mainly through contaminated food and water; thus, commonly it is a disease prevalent in the areas where clean water supply and sanitation systems are disturbed. Cholera outbreak has occurred in Yemen up to now, and we decided to validate our model on this case. We used information from WHO reports (www.emro.who.int/yem/yemeninfocus/situation-reports.html). As in the case of shigellosis, we consider that Antibiotic-1 is from the sulfonamide antibiotic family (i.e. co-trimoxazole) and Antibiotic-2 is from the fluoroquinolone or nitrofuran groups.

To estimate the value of *Vibrio cholerae* a chance of a receiving AR r_c we also used a WHO report, where it was noted that resistance has increased from 37% to 100% in all Shigella isolates over a period of 5 years (Sack, 2001). An incubation period of cholera was also assessed from this report. The values of the following parameters were estimated as in shigellosis case: $p_6 = 0.06$ (D'Agata et al., 2000), $p_1 = 0.002$, r_- and r_+ (Wu et al., 2016), and r_l from data of ResistoMap (Yarygin et al., 2017). Pathogen infection potential coefficient i_c was bounded based on infection rates compared to population size. Here the number of infected persons in hospital μ_5 can be 3 persons per 907000 population. According to WHO reports, there is deficient healthcare in Yemen, thus the probability of being hospitalized without current infection p_1 was established 0.00061. Based on WHO reports about the lack of education about adherence to prescribed treatment, we assume the probability of incorrect antibiotic treatment to be p_8 equal to 0.39.

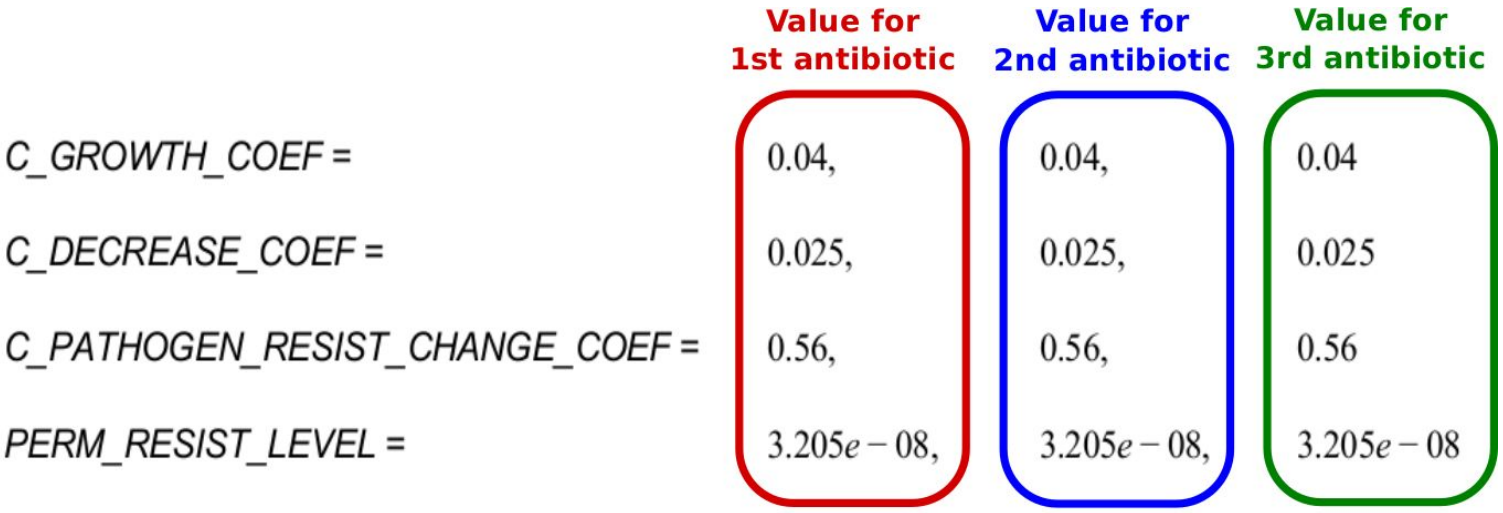
The values of input model parameters for *Vibrio cholerae* are stored in configure file on git repository.

Based on data about cholera outbreak in Yemen from 27 April to 12 June 2017 by WHO, we compared results after multiple runs of the model for *Vibrio cholerae* and real cholera cases. As a result we see high correlation between simulated data and data from report ($R = 0.895$, the Spearman's rank correlation coefficient, Supplementary Figure 4).

There is the additional option to investigate an infection spread in terms of multidrug resistance (Supplementary Notes 3).

Supplementary Note 3 | Multidrug resistance case.

We enhanced a facility to account pathogen infection spread taking into account the possibility of a pathogen becoming resistant to more than one antibiotic. For this, user should add values to the file with input parameters using comma as a delimiter in order to run the model, as shown below. Note that it is an example, and the values are equal for three antibiotic types. The user can add as many antibiotics as one needs. The example can be seen in *config.properties.Shigella.multi* file on git repository.



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