**SUPPLEMENTARY MATERIAL**

**Model Equations**

**Homogenous Import Model**

Eqn S1.1

**Heterogenous Import Model**

**Data Manipulation**

We note the use of three curated datasets for this study. These datasets were used for three reasons: 1) Fitting the relationship between domestic livestock ampicillin usage and resistance, 2) Parameterising the relative share of import, contamination and resistance among importing countries and 3) UK-specific outcome measures for the Salmonella spp. in fattening pigs case study.

1. **Relationship between domestic ampicillin usage/resistance dataset**

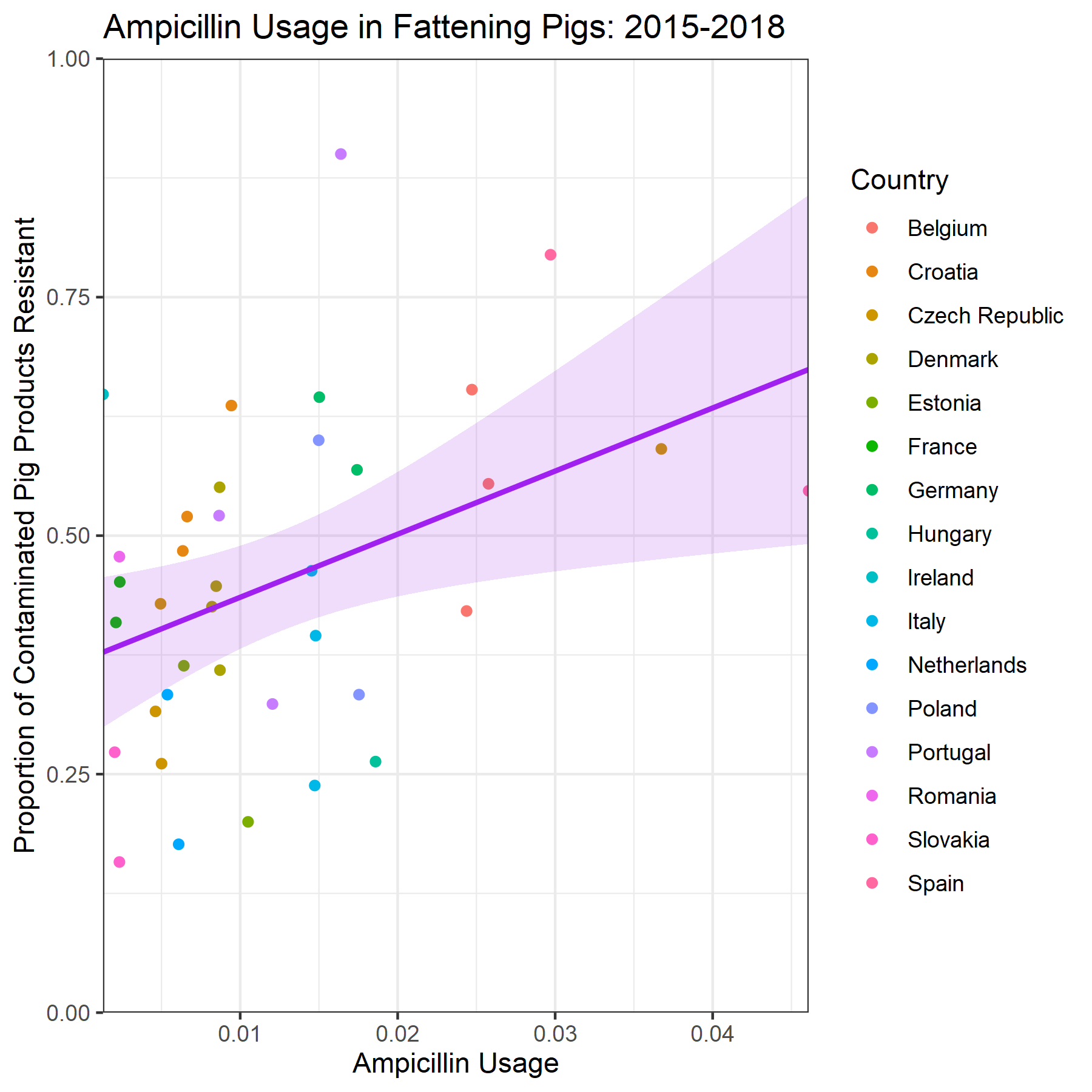
Ampicillin sales data from the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) from 2015-2018 was used in this study as a proxy for antibiotic usage. Rationale for the use of antibiotic sales data as a proxy for usage and details of scaling calculations used to scale general sales data for fattening pig biomass can be found in the **supplementary material** for chapter 2. The final unit of measurement used for ESVAC data was grams per population correctional unit (g/PCU). Yearly ESVAC sales data was paired with data on the proportion ampicillin-resistant isolates from fattening pig carcasses for different EU countries across 2015-2018 extracted from European Food Safety Authority (EFSA) summary reports. A linear regression was conducted to identify evidence of a relationship between

This data was paired with the proportion of ampicillin-resistant Salmonella spp. isolates identified from each country

As a key part of our model is to assess dynamics following a withdrawal in livestock antibiotic usage, it is critical that the model is able to reproduce the relationship between livestock antibiotic usage and resistance.

Therefore, this livestock portion of the model was fitted to this relationship between usage and resistance using surveillance data.

Resistance data was obtained from the European Food Safety Authority (EFSA) summary reports. The proportion of isolates resistant to the specific antibiotic class from carcasses of broiler poultry/fattening pigs was extracted from the respective EFSA dataset. Antibiotic sales data was obtained from European surveillance of veterinary consumption (ESVAC) reports ESVAC antibiotic sales data is found averaged for all livestock species in each country in the original surveillance report.



**Figure S1. Relationship between scaled ampicillin sales and the proportion of isolates ampicillin-resistant across different EU country/year pairs from 2015-2018.** Solid line and ribbon represent the best fitting linear regression between sales and resistance, with 95% CIs for model predictions. SHOW COEFFICIENTS

The relationship between am

* 1. Provide rationale for the datasets – why we picked ampicillin inf attending pigs etc
  2. Where we obtained the data from
  3. What stuff did we do to the data

1. **Import dataset**
   1. **How we calculated proportion of food usage from specific countries**
      1. **Using the different datasets**
      2. **Large amount of data and info here**
   2. Table – with each country and the contamiantion, share and resistance and with a avarege bottom row –
   3. also do a figure showing the distribution of the countries for contamiantion and resistance
   4. Level of contamination and resistance from these countries (mention what years we used)
      1. Contamination we specifically took data from carcasses – rather than fresh as this is more representative of imported food
      2. The details like making sure that the measurements were standardised and using competent authorities etc.
      3. Resistance we just took from the general fitting dataset
2. DEFRA has data on the relative share of Domestic vs EU vs nEU countries on the UK’s food supply.
3. However this is for general food products not specific to livestock origin food products – therefore it must be scaled for livestock food products (excluding things like vegetablexss and processed food imports)
   1. We note that two cases tudies were explored to explore the effect – general livestock food products (psi = 0.656) and pig carcasses (psi = 0.4545)
   2. It is important to note that while pigs are the case study chosen by this study – the general import proportions were used to have a fairer repsentation of nEU imports (perhaps need to justify this decision better)
4. We therefore generated the proportion of UK food supply for general livestock food products – including poultry, beef, pork and eggs – from EU and nEU countries (rest of the world) – by determiniung the dressed weight and using thgis to generate the propiortioons
5. We exclude milk
6. We also have data on the share of imports in the UKs EU trade partners – by lookinga tht eproportion of money spent on iumports for the UK
7. We can then use the difference between the official reportsz for all food products and the ones for livestock food products and scale these EU importing countries approiately.
8. **UK-specific Outcome Measure dataset**
9. UK specific outcome measures
   1. Livestock resistance
   2. Livestock contamination
      1. Mention here is where we figured we would need to have an extra parameter describing the reduction in caecum to carcass
   3. Human resistance
   4. Human fbd – mention that we missed the 2016 year so we only use a single year

Data was obtained from X paper which identified a prevalence of Salmonella spp. found in the caecum of pigs of 32.2%. We also identify a UK level of contamiantion on pig carcasses of 2.865%, representing a reduction in the proportion of 89%. We use this value to parameterise the eta parameter.

* Specifically the removal of certain datapoints because they were unrealistic (where it was just 45/45 resistant), the fact that we used 3 years worth of data (2015, 2016, 2017, 2018) – although one of these intermediate years aren’t available

**Supplementary Tables**

1. Homogenous model parameters – in the same table have columns for the prior distribution and the fitted mean model values after the fitting procedure

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Parameter | Description | Model (Fitted) Parameter Values  (Sum of squares from model fit in square brackets) | | References |
| **Ampicillin resistance in Broiler Poultry**  **(SS = 1.987)** | **Tetracycline resistance in Broiler Poultry**  **(SS = 5.473)** |
| ***βAA*** | Per Capita Rate of Transmission (Direct and Indirect) between the Infected Animal Fraction and Susceptible Animal Fraction | **0.116613 [0.004307,**  **0.227580] 1** | **0.091145**  **[0.001947,**  **0.206444] 1** | N/A |
| ***βHH*** | Per Capita Rate of Transmission (Direct and Indirect) between the Infected Human Fraction and Susceptible Human Fraction | 0.00001 | 0.00001 | N/A |
| ***βAH*** | Per Capita Rate of Transmission (Direct and Indirect) from the Infected Human Fraction to the Susceptible Animal Fraction | 0.00001 | 0.00001 | N/A |
| ***βHA*** | Per Capita Rate of Transmission (Direct and Indirect) from the Infected Animal Fraction to the Susceptible Human Fraction | **0.0001388**  **[0.000130,**  **0.000145] 1** | **0.000149**  **[0.000134,**  **0.000163] 1** | N/A |
| ***ζ*** | Background rate of transmission of foodborne bacteria to the livestock population | **0.8789726 [0.285250,**  **1.478116] 1** | **0.653686**  **[0.250350,**  **0.999701] 1** | N/A |
| ***τ*** | Per Capita Rate of Antibiotic Usage in Livestock (Baseline) in g/PCU | 0.0067 | 0.0067 | N/A |
| *κ* | Efficacy of antibiotic-mediated livestock recovery. | **1.144771 [0.251745,**  **1.995368] 1** | **0.682709**  **[0.006160,**  **1.459921] 1** | N/A |
| ***α*** | Transmission-related fitness costs associated with antibiotic-resistant strains (relative to antibiotic-sensitive strains). | **0.009010 [0.000461,**  **0.020193] 1** | **0.162060**  **[0.011241,**  **0.317247] 1** | N/A |
| ***φ*** | Per Capita Rate of Conversion from antibiotic-resistant to antibiotic-sensitive infection in animals | **0.030938**  **[0.024368,**  **0.036523] 1** | **0.021652 [0.011457,**  **0.031297] 1** | N/A |
| ***rA*** | Per Capita Rate of Natural Recovery from Animal Infection | 0 days-1 | 0 days-1 | (26) |
| ***rH*** | Per Capita Rate of Natural Recovery from Human Infection | 5.5 days-1 | 5.5 days-1 | (27) |
| ***µA*** | Per Capita Birth/Death Rate in Animals | 42 days-1 | 42 days-1 | (28) |
| ***µH*** | Per Capita Birth/Death Rate in Humans | 28835 days-1 | 28835 days-1 | (29) |
|  |  | - |  |  |
|  |  | - |  |  |
|  |  | - |  |  |

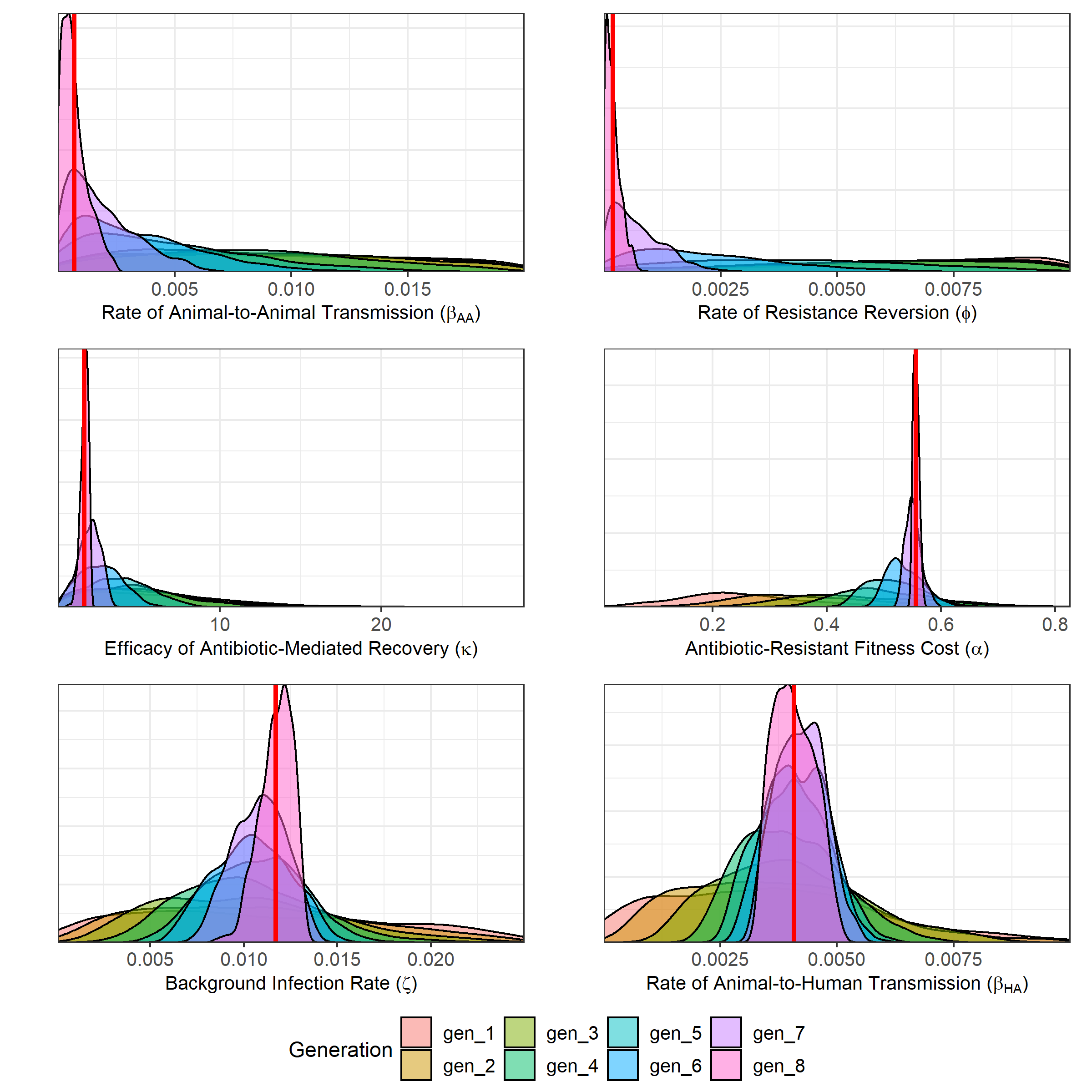
1. Thresholds used for each model fitting generation – homogenous model

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Summary Statistics | Model | Generation | | | | | | | |
| **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** |
| **Sum of squared errors** | Homogenous Import Model | 5 | 4 | 3.5 | 3.25 | 3 | 2.75 | 2.5 | 2.25 |
| Heterogenous Import Model | 10 | 8 | 7 | 6.5 | 6.25 | 6 | 5.9 | 5.8 |
| **Difference between modelled and observed overall prevalence of human salmonellosis** | Homogenous Import Model | 0.593 | 0.474 | 0.356 | 0.237 | 0.178 | 0.119 | 0.089 | 0.059 |
| Heterogenous Import Model | 0.593 | 0.474 | 0.356 | 0.237 | 0.119 | 0.059 | 0.047 | 0.412 |
| **Difference between modelled and observed proportion of resistant human salmonellosis** | Homogenous Import Model | 0.314 | 0.251 | 0.187 | 0.126 | 0.094 | 0.063 | 0.047 | 0.031 |
| Heterogenous Import Model | 0.316 | 0.253 | 0.189 | 0.126 | 0.063 | 0.032 | 0.025 | 0.022 |
| **Difference between modelled and observed overall prevalence of human salmonellosis** | Homogenous Import Model | 0.593 | 0.474 | 0.356 | 0.237 | 0.178 | 0.119 | 0.089 | 0.059 |
| Heterogenous Import Model | 0.593 | 0.474 | 0.356 | 0.237 | 0.119 | 0.059 | 0.047 | 0.412 |
| **Difference between modelled and observed overall prevalence of human salmonellosis** | Homogenous Import Model |  |  |  |  |  |  |  |  |
| Heterogenous Import Model |  |  |  |  |  |  |  |  |

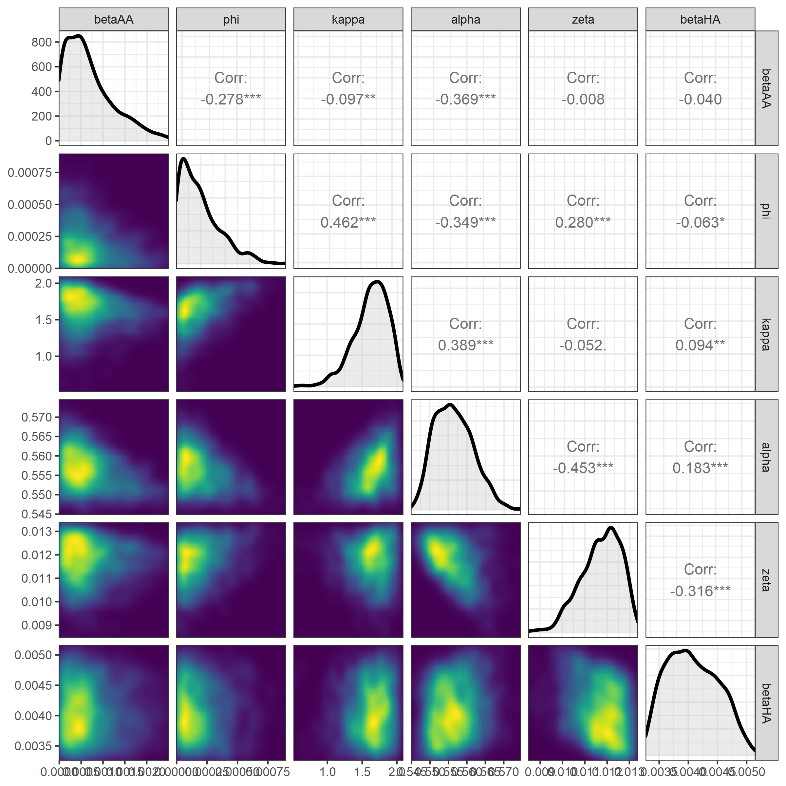
**Table S6. Fitted values for the primaryoutcome measures for the four modelcase studies.**

|  |  |  |
| --- | --- | --- |
| Outcome Measure | Model | |
| **Ampicillin Resistance in Broiler Poultry**  **[0.0049 g/PCU]** | **Tetracycline Resistance in Broiler Poultry**  **[0.0069 g/PCU]** |
| Daily incidence of human salmonellosis | 0.595 | 0.600 |
| Proportion of antibiotic-resistant human salmonellosis  (I\*RHProp) | 0.301 | 0.356 |
| Contamination Livestock |  |  |
| Resistance on Cracases |  |  |

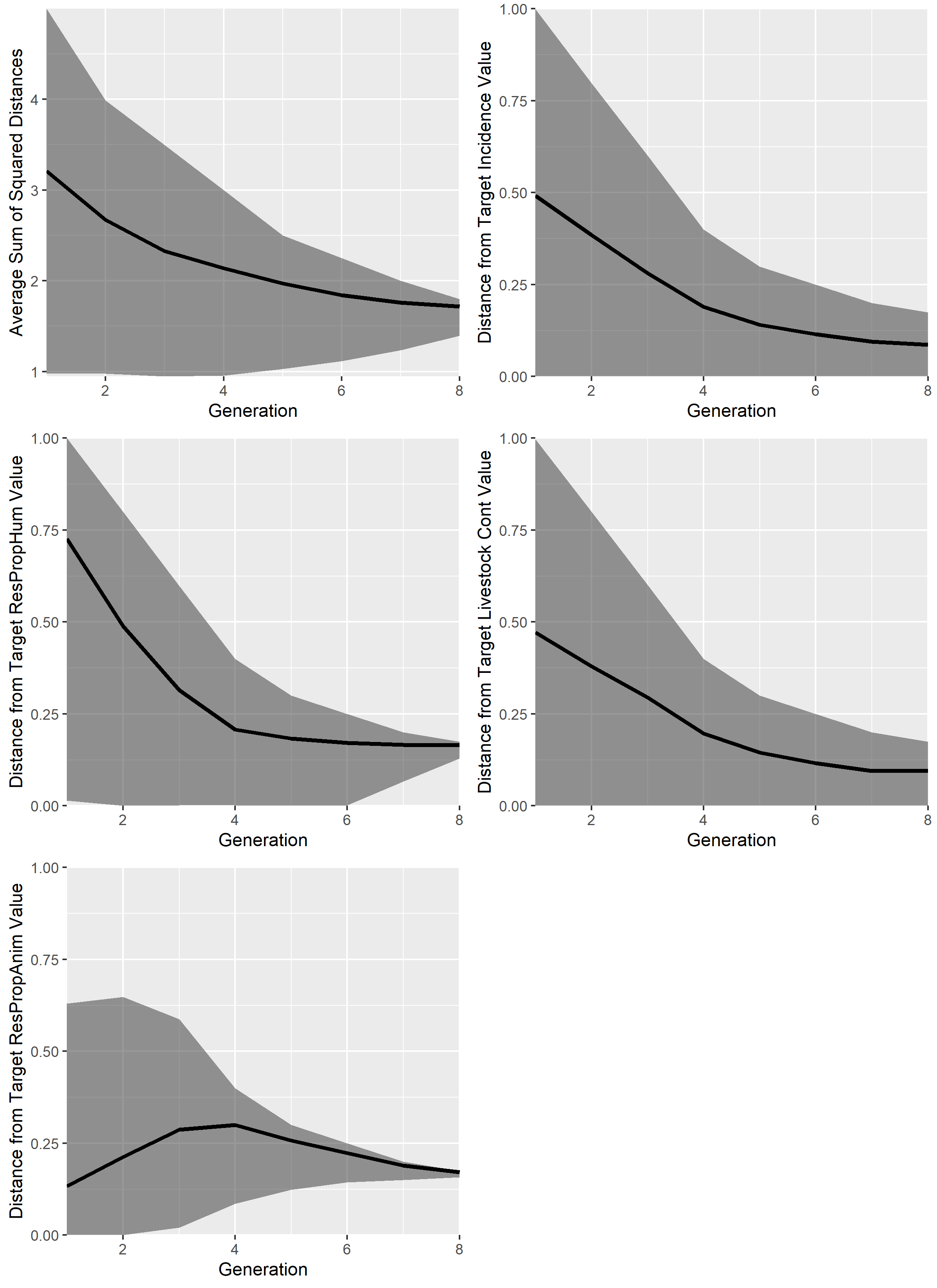
**Supplementary Figures**



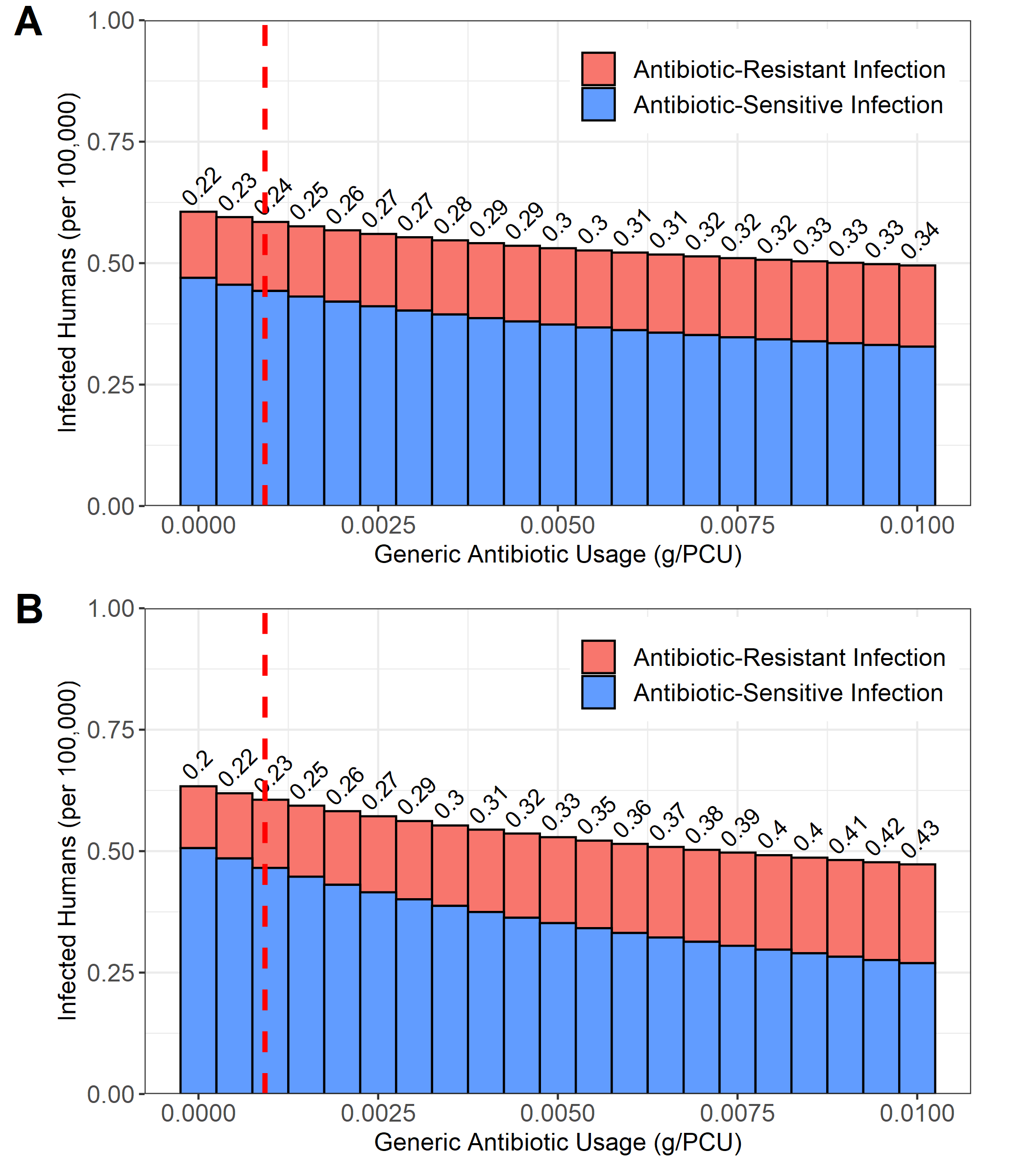
**Figure S2. Estimated posterior distributions for the rate of animal-to-animal transmission (βAA), efficacy of antibiotic-mediated recovery (κ), rate of antibiotic-resistant to antibiotic-sensitive reversion (φ), transmission-related fitness costs of resistance (α), background rate of transmission to animal populations (ζ) and the rate of animal-to-human transmission (βHA).** The estimated posterior distribution for each generation is highlighted by fill colours. Red line represents the mean from the 8th generation for each parameter.



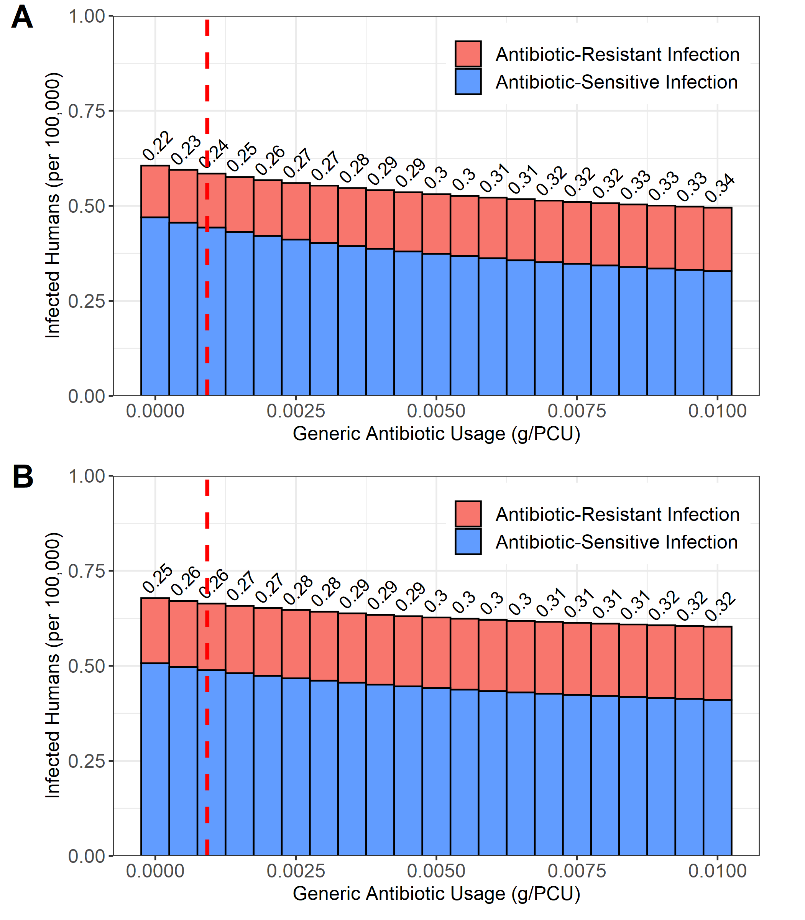
**Figure S3. Pairs plot for the approximated posterior distribution and the correlation coefficients for the homogenous import model fit.** The diagonals show the the approximated univariate posterior distribution. Kernel density estimation was used to identify the parameter space where a greater concentration of particles were accepted for the final tenth ABC-SMC generation (lighter colouring).



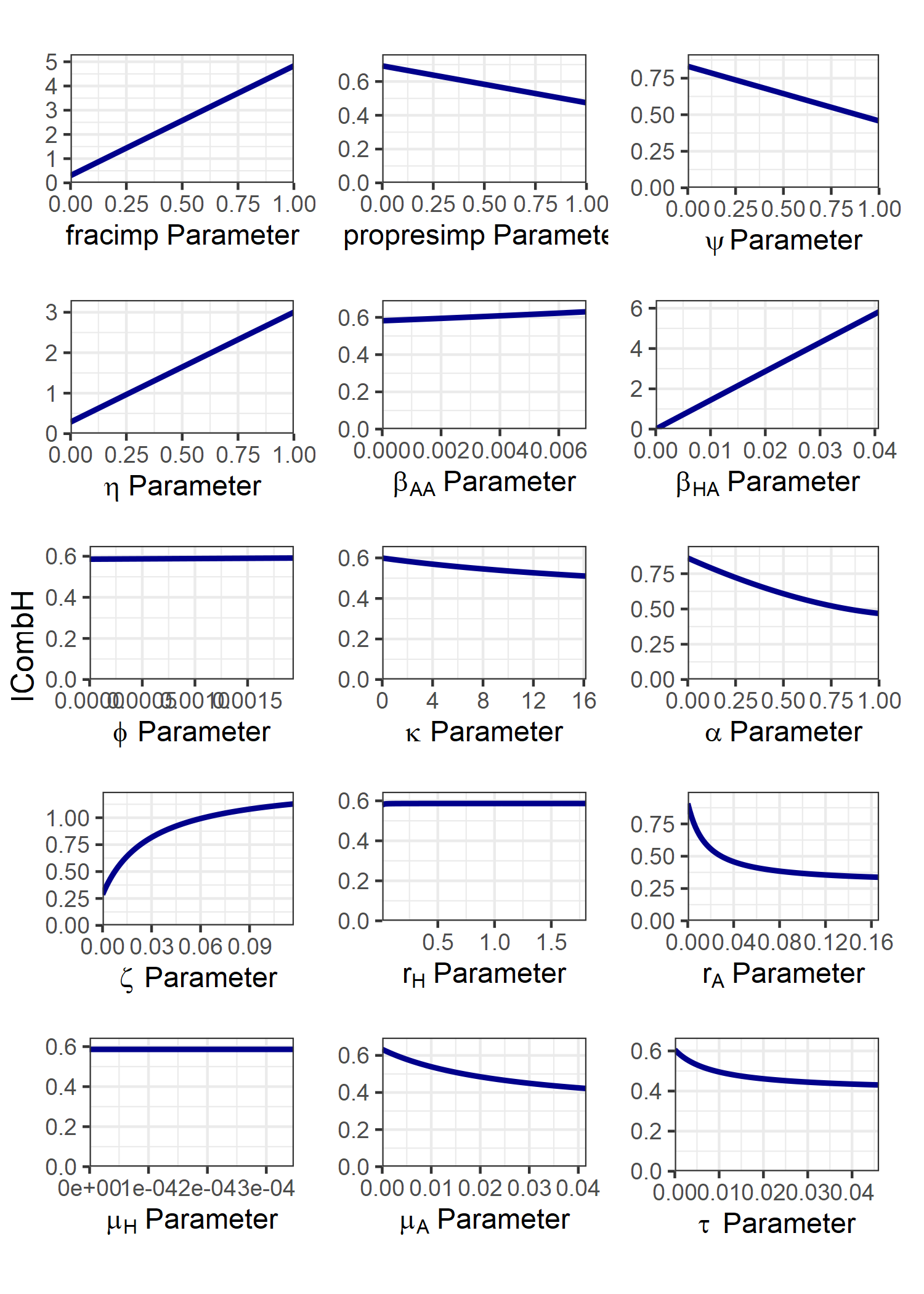
**Figure S4. Diagnostic plots showing the average sum of squared distance for each generation of the ABC-SMC model fit for the homogenous model.** Diagnostic plots were plotted for the average sum of square distances for the resistance/usage model fit, distance from the target incidence of human salmonellosis, distance from the target proportion of resistant human salmonellosis, distance from the target livestock contamination (ISA + IRA \* η) and the distance from the target proportion of antibiotic-resistant human salmonellosis.



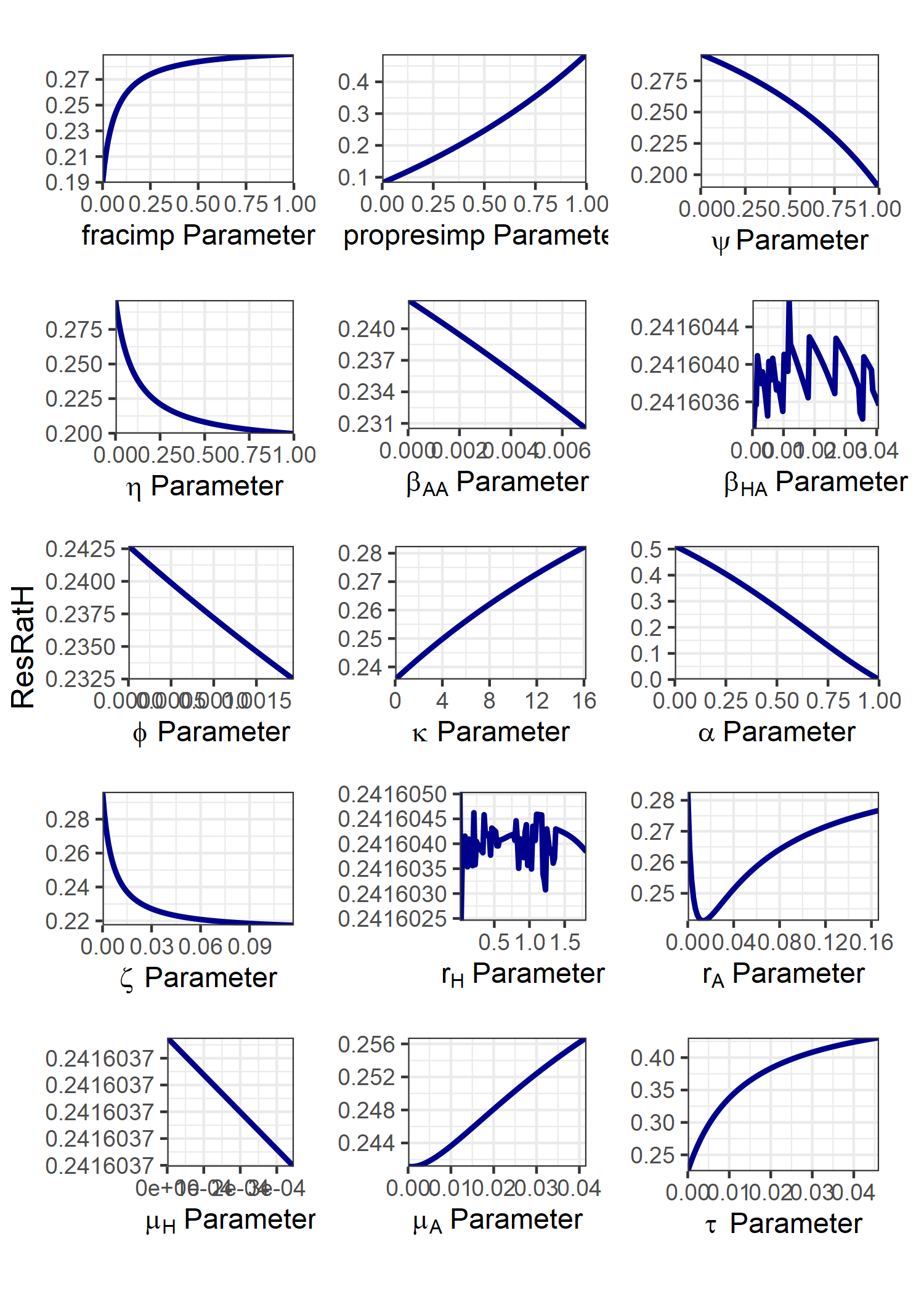
**Figure S5. Impact of alterations in livestock antibiotic usage on the daily incidence of salmonellosis and the proportion of resistant human infection for a model fitted to data with no import pressure (ψ = 1) and a model with homogenous import (ψ = 0.656).** The dotted red line denotes the baseline livestock ampicillin antibiotic usage. Numbers above the bars denote proportion of resistant human salmonellosis.



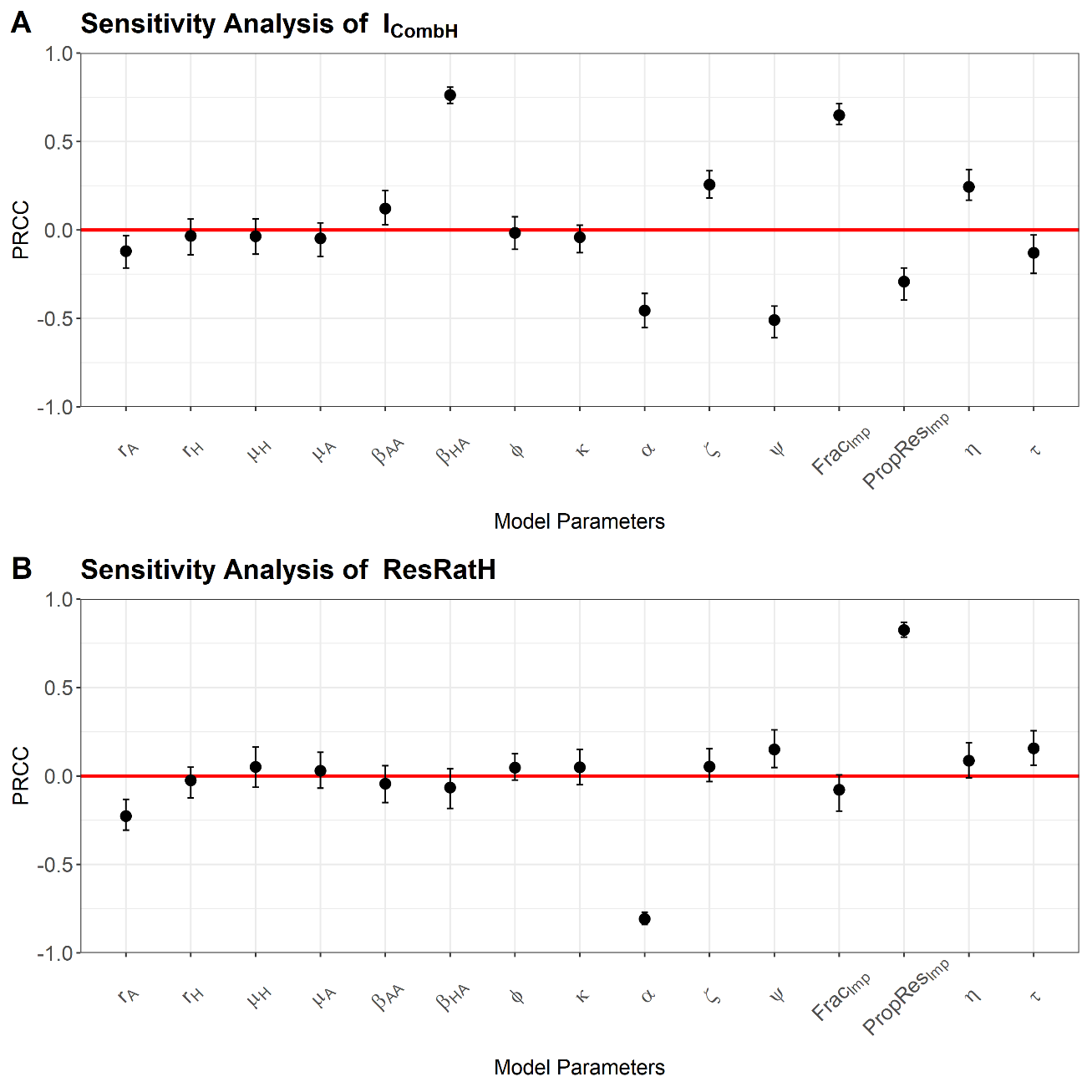
**Figure S6. Impact of alterations in livestock antibiotic usage on the daily incidence of salmonellosis and the proportion of resistant human infection for the homogenous model fitted to data with baseline levels (general livestock products) of import pressure (ψ = 0.656) and a pig food product specific import pressure (ψ = 0.4455).** The dotted red line denotes the baseline livestock ampicillin antibiotic usage. Numbers above the bars denote proportion of resistant human salmonellosis.



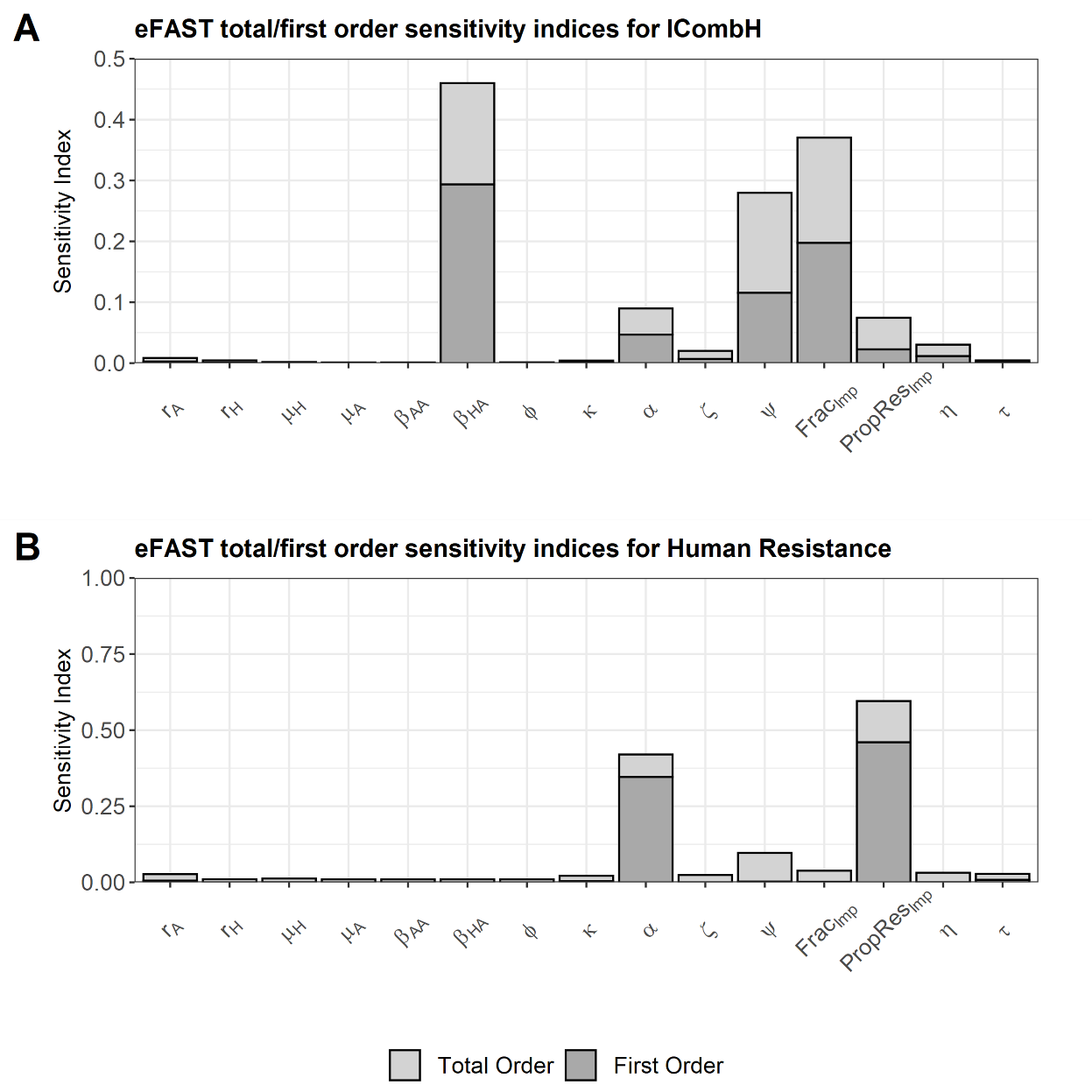
**Figure S7. Impact of varying each model parameter individually on the daily incidence of human salmonellosis for the homogenous import model.** The explored parameter range for each parameter was bounded at 0, to an order of magnitude above the parameterised model value. An exception was for *rH*, with *rH* ∈ [0.01, 0.55-1] to prevent the large relative changes in daily incidence at *rH* = 0 obscuring presented results. For fitted parameters this was taken as an order of magnitude above the mean fitted parameter value across all four case studies.



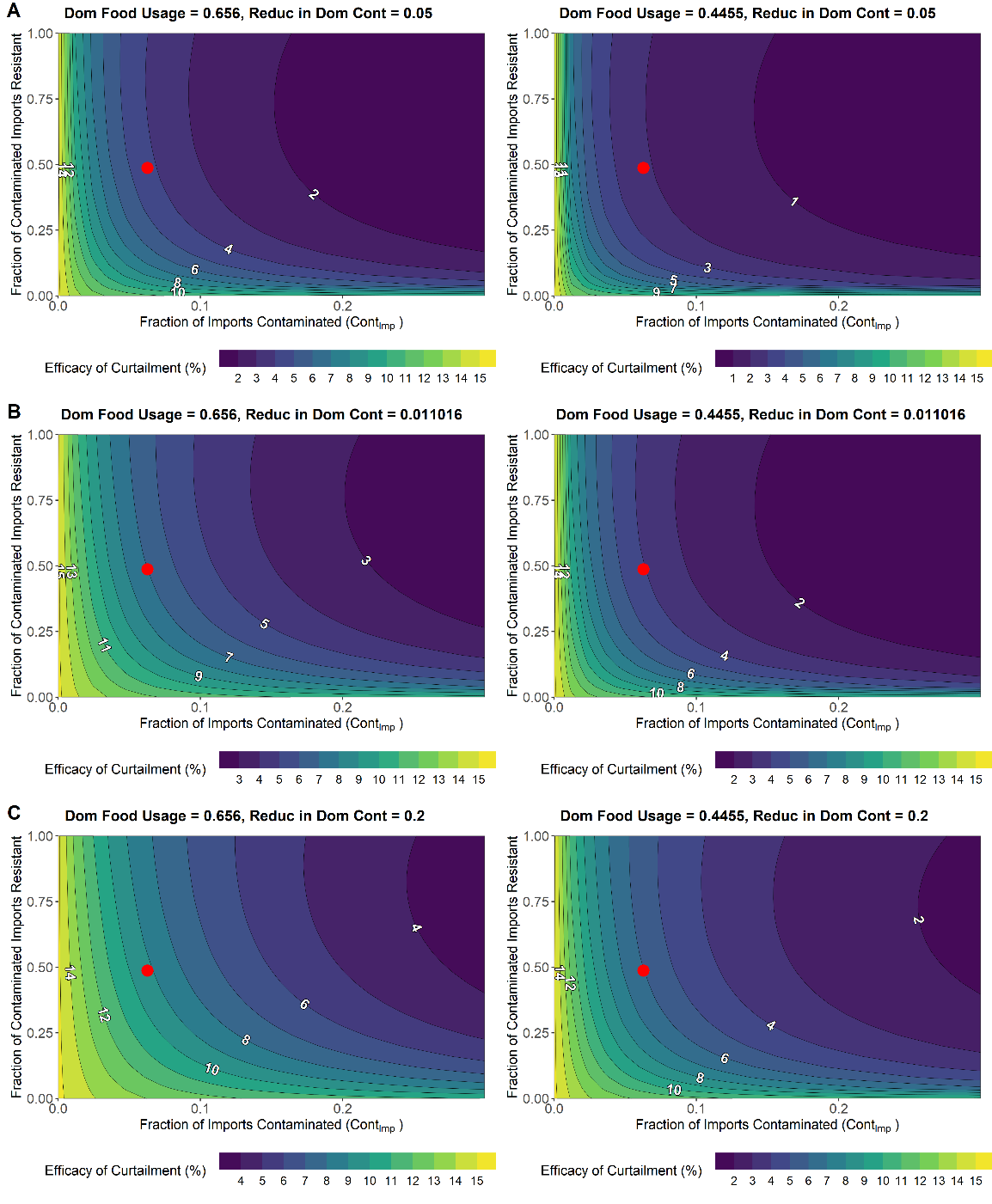
**Figure S8. Impact of varying each model parameter individually on the proportion of ampicillin-resistant human salmonellosis for the homogenous import model.** The explored parameter range for each parameter was bounded at 0, to an order of magnitude above the parameterised model value. An exception was for *rH*, with *rH* ∈ [0.01, 0.55-1] to prevent the large relative changes in daily incidence at *rH* = 0 obscuring presented results. For fitted parameters this was taken as an order of magnitude above the mean fitted parameter value across all four case studies. Note that rA displays a non-monotonic relationship with the outcome measure.



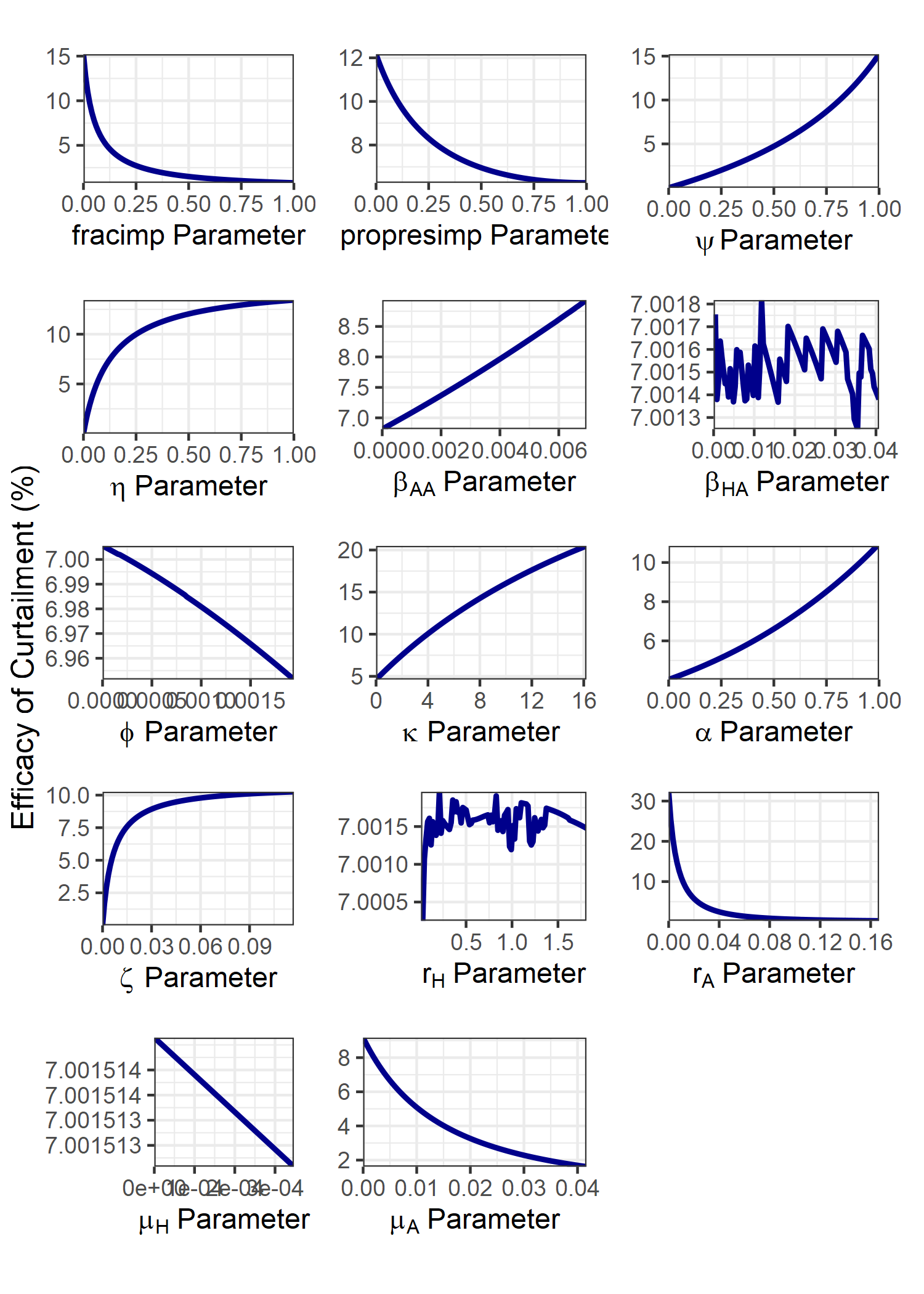
**Figure S9. Latin hypercube sampling partial rank correlation coefficient (LHS-PRCC) sensitivity analysis for the homogenous import model. A) Daily incidence of human salmonellosis. B) Proportion of human ampicillin resistant salmonellosis.** Note that 95% confidence intervals for each correlation coefficient was generated through generating n = 100 bootstrap replicates.



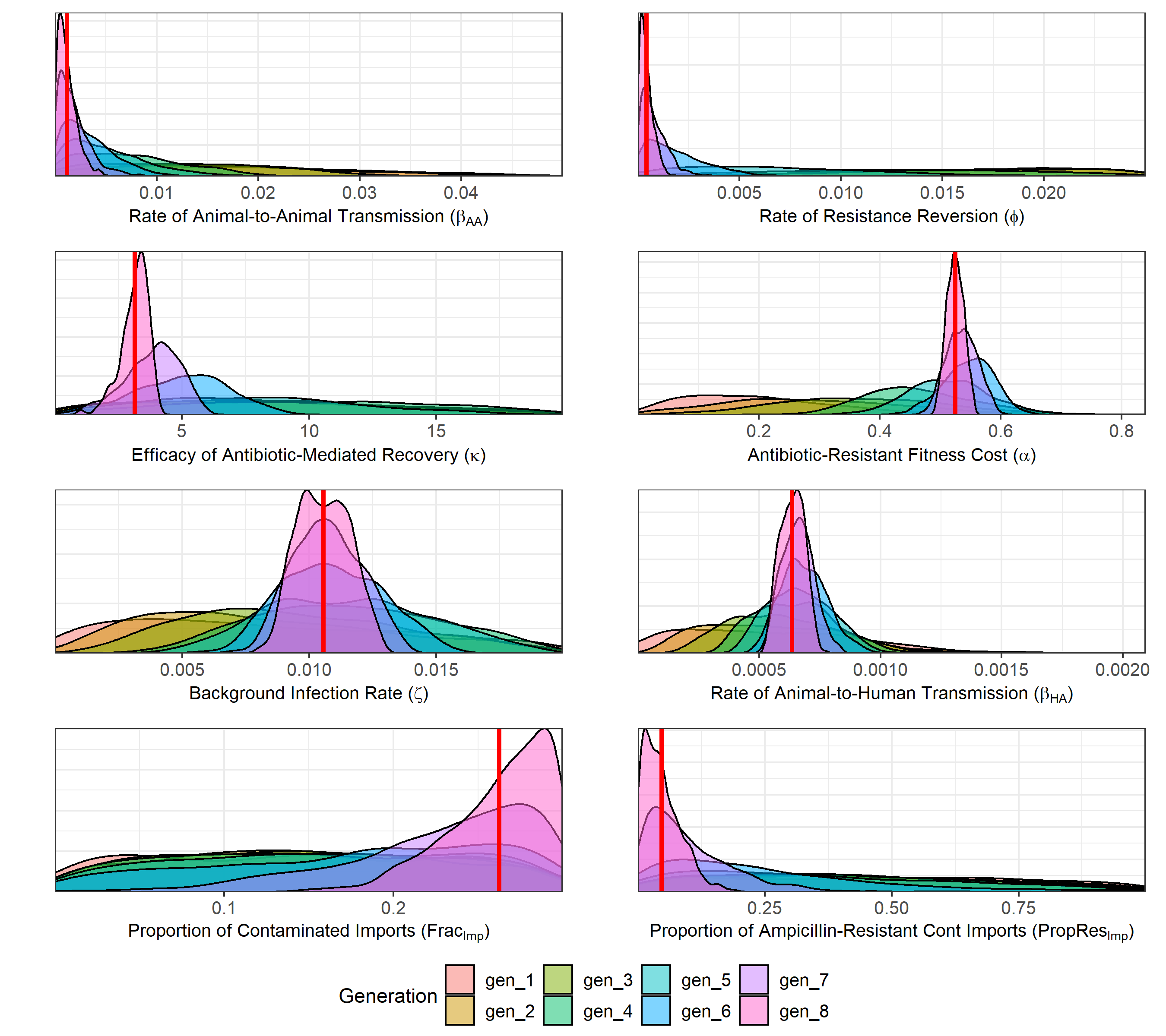
**Figure S9. Extended Fourier amplitude sensitivity analysis (eFAST) sensitivity analysis for the homogenous import model. A) Daily incidence of human salmonellosis. B) Proportion of human ampicillin resistant salmonellosis.** The remaining proportion of the total order effects after accounting for first order effects in the eFAST can be considered the second order effects for each explored model parameter.



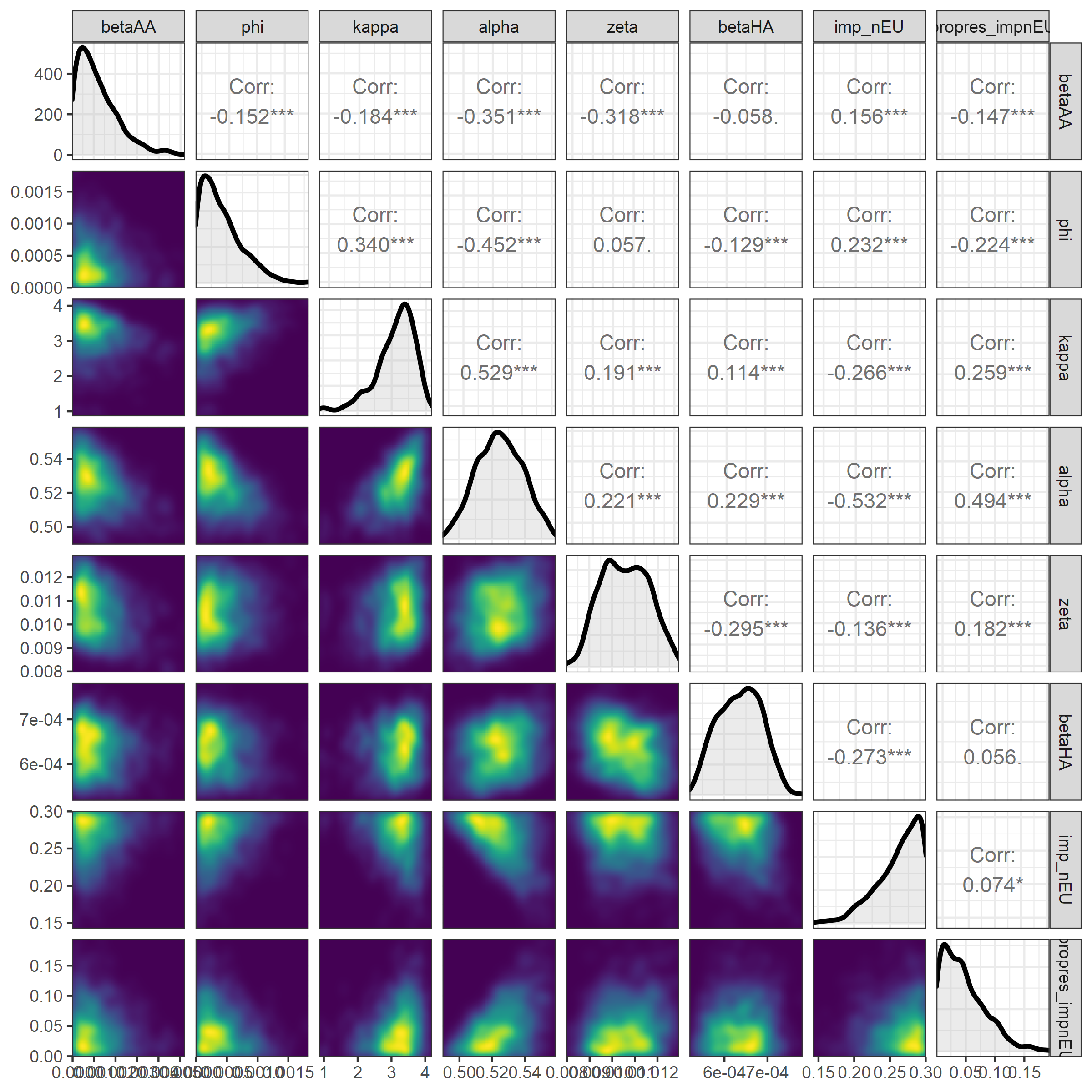
**Figure S10. Impact of altering FracImp and PropResImp import parameters on the efficacy of curtailment for the relative reduction in prevalence of Salmonella spp. from domestic livestock to carcasses. We explore two alternative scenarios relative to the baseline. A) Strong reductions to the level of contamination found in domestic livestock carcasses (η = 0.05). B) Baseline reductions to the level of contamination found in domestic livestock carcasses (η = 0.011). C) Weaker reductions to the level of contamination found in domestic livestock carcasses (η = 0.20).** For each value of η we explore a general livestock import case study (ψ = 0.656) and a scenario of import based on swine food products (ψ = 0.4455**).** Red dot represents the baseline parameterisation for FracImp and PropResImp parameters from ECDC data (FracImp = 0.0628; PropResImp = 0.487).



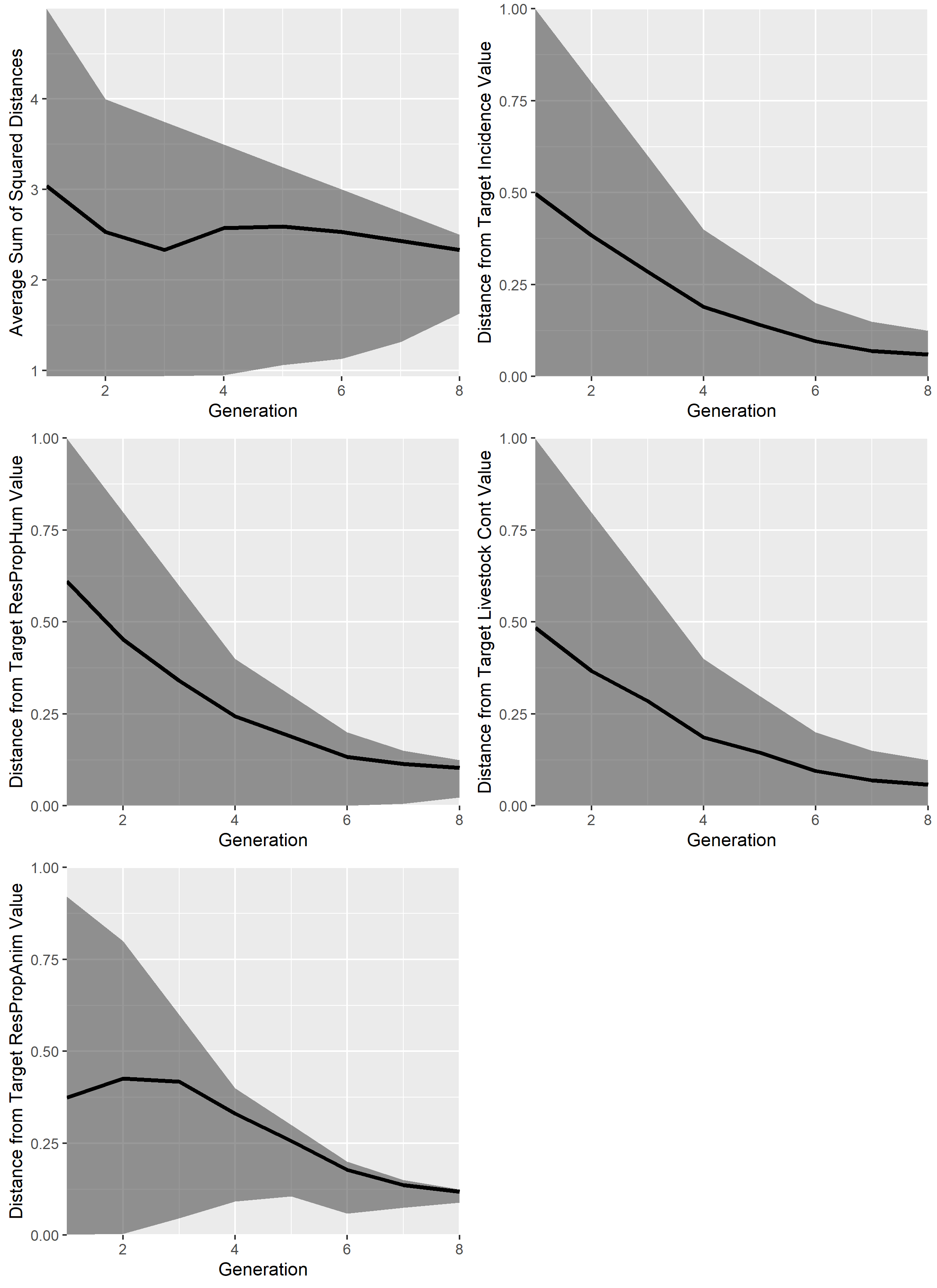
**Figure S11. Impact of varying each model parameter individually on the efficacy of curtailment outcome measure for the homogenous import model.** The explored parameter range for each parameter was bounded at 0, to an order of magnitude above the parameterised model value. An exception was for *rH*, with *rH* ∈ [0.01, 0.55-1] to prevent the large relative changes in daily incidence at *rH* = 0 obscuring presented results. For fitted parameters this was taken as an order of magnitude above the mean fitted parameter value across all four case studies. Note that rA displays a non-monotonic relationship with the outcome measure.



**Figure S12. Estimated posterior distributions for the rate of animal-to-animal transmission (βAA), efficacy of antibiotic-mediated recovery (κ), rate of antibiotic-resistant to antibiotic-sensitive reversion (φ), transmission-related fitness costs of resistance (α), background rate of transmission to animal populations (ζ), the rate of animal-to-human transmission (βHA), the proportion of imported food products contaminated with Salmonella spp. (FracImp) and the proportion of contaminated food products resistant to ampicillin (PropResImp).** The estimated posterior distribution for each generation is highlighted by fill colours. Red line represents the mean from the 8th generation for each parameter.



**Figure S13. Pairs plot for the approximated posterior distribution and the correlation coefficients for the homogenous import model fit.** The diagonals show the the approximated univariate posterior distribution. Kernel density estimation was used to identify the parameter space where a greater concentration of particles were accepted for the final tenth ABC-SMC generation (lighter colouring).



**Figure S14. Diagnostic plots showing the average sum of squared distance for each generation of the ABC-SMC model fit for the heterogenous model.** Diagnostic plots were plotted for the average sum of square distances for the resistance/usage model fit, distance from the target incidence of human salmonellosis, distance from the target proportion of resistant human salmonellosis, distance from the target livestock contamination (ISA + IRA \* η) and the distance from the target proportion of antibiotic-resistant human salmonellosis.

Chart, bar chart, histogram

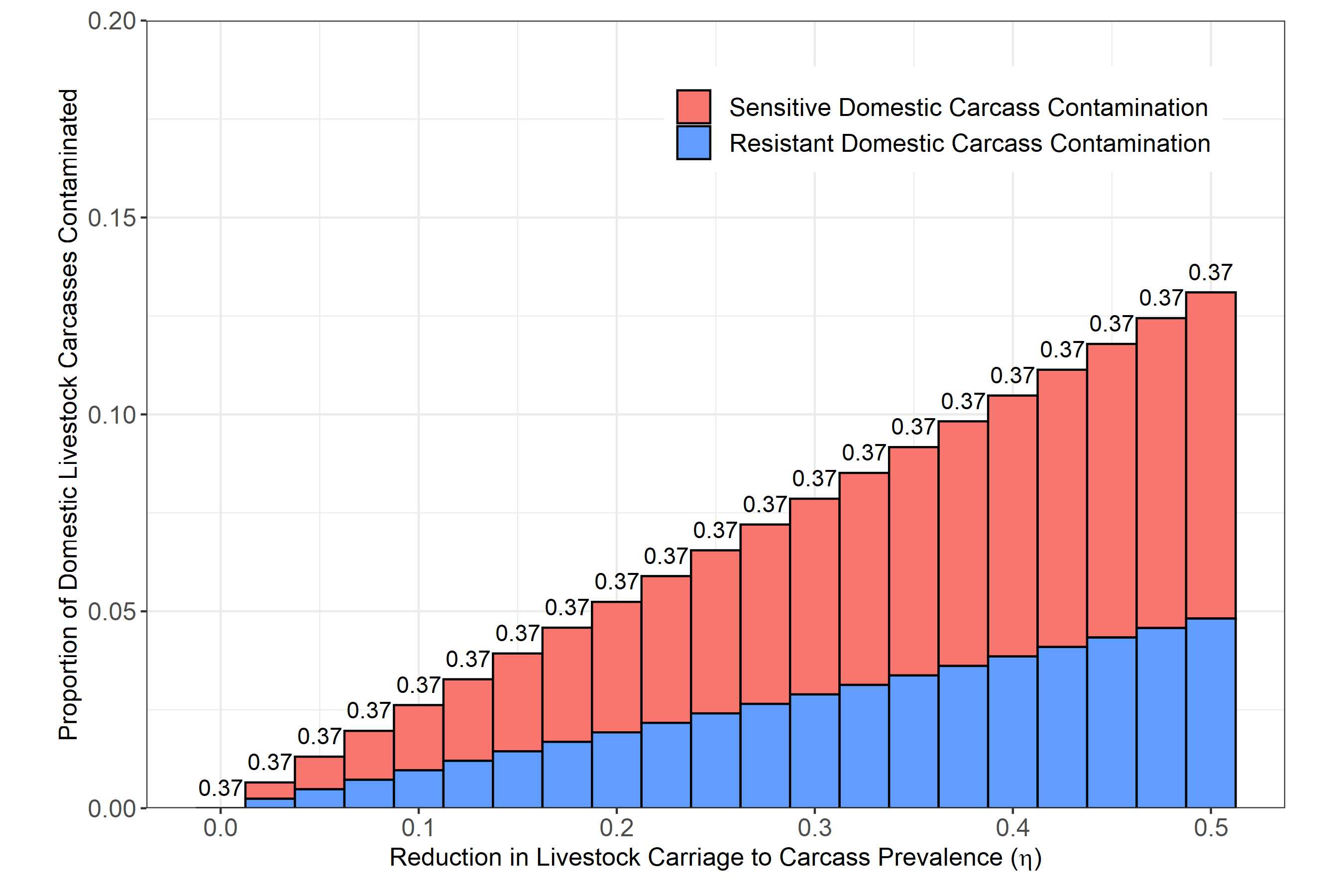
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**Figure S15. Impact of alterations in livestock antibiotic usage on the normalised proportion of resistant human infection for the heterogenous model attributable to domestic and non-domestic sources.** Normalisation was performed by dividing the proportion of ampicillin-resistant Salmonellosis attributable to each country by the sum attributable to all countries.

A picture containing diagram

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**Figure S16. Relationship between the proportion of UK food products (ψ) and the efficacy of curtailment (EoC) under different average parameterisation for the η parameter.** Baseline relationship between EoC/ψ is denoted by the red and dotted line.



**Figure S17. Relationship between the relative reduction in prevalence from domestic livestock carriage to carcass contamination (η) on both the proportion of domestic livestock carcasses contaminated with Salmonella spp. and the proportion of the ampicillin-resistant domestic carcasses.** Numbers above the bars denote proportion of resistant human salmonellosis.

1. **Heterogeneity analysis – with the effect on the average and the variation**