**Understanding the role of global food trade on the transmission dynamics of antibiotic-resistant foodborne bacteria**

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**ABSTRACT**

**INTRODUCTION**

1. Resistance is a big issue – specifically the resistance that might occur from livestock.
2. This is part of this one health issue – with studies often exploring the impact of transmission from livestock
3. However transmission from livestock is a multifaceted issue – transmission can come in the form of direct contact with domestic livestock, food products from domestic sources, but also from imported sources
4. Note some studies which have done this – the Ludden et al study as an example – which sampled food products from local supermarkets which obviously have food products from imported sources
5. But also mentioned that this often is not done – there needs to be more of an emphasis to explore the heterogeneity in terms of AMR transmission from livestock populations – to stratify the livestock population into both imported and domestic
6. This is important considering the implications of having heterogeneity in terms of transmission pressure – for example – give examples of other mathematical models showing that heterogeneity in terms of transmission pressure
7. This is therefore also the case in terms of AMR in a one health context – many reviews have stated that to understand AMR mechanistically from a modelling POV – we need to understand how the different sources of AMR might also contribute to AMR transmission
8. One such example is understanding how import of AMR on food products from different sources may also impact AMR transmission to humans – especially from livestock
9. This is an important aspect to consider considering a slow increase in food products over the next few years – the increase in the population requiring food to be imported
10. A likely reliance on imported food – and Brexit signing deals with countries with less than stellar food safety records
11. Means it makes sense to explore the impact of imported food products on the overall dynamics
12. We seek to explore the effect of heterogeneity in transmission pressure from livestock populations through the use of a compartmental metapopulation type model where we try to understand the impact of stratifying livestock antibiotic usage
13. We try to understand the impact on the impact of interventions such as the effect of curtailing livestock antibiotic usage when there is an import fraction.

**METHODS**

**Model Structure and Parameters**

A compartmental model was developed to describe the transmission of antibiotic-resistant and antibiotic-sensitive *Salmonella* spp. from domestic and imported livestock food products to humans (**Figure 1**). Salmonella transmission dynamics were modelled explicitly for domestic livestock and human populations, with each modelled population stratified based on their respective infection status: susceptible humans (SH), humans infected with antibiotic-sensitive bacteria (ISH), humans infected with antibiotic-resistant bacteria (IRH), susceptible livestock food-animals (SA), livestock food-animals infected with antibiotic-sensitive bacteria (ISA) and livestock food-animals infected with antibiotic-resistant bacteria (IRA).



**Figure 1. Model structure describing the transmission of foodborne pathogens between/within livestock and human populations.** Model equations and parameters can be found described in the supplementary material ().

The influence of imported food products was modelled as a constant transmission pressure to human populations. The proportion of imported food products contaminated with either antibiotic-resistant Salmonella spp. was modelled as a function of the proportion of contaminated food products that are antibiotic-resistant (PropResImp) and the proportion of food imports contaminated with Salmonella spp. (FracImp). The proportion of food imports contaminated with antibiotic-sensitive bacteria follows the same calculation bar the use of (1-PropResImp).

Two transmission routes of antibiotic-sensitive/resistant Salmonella spp. were modelled, with domestic livestock-to-livestock transmission (βAA) and transmission from contaminated domestic/imported livestock carcasses/food products modelled (βHA). This βHA parameter represents either direct transmission from the carcasses or through food borne transmission after further processing in the farm-to-fork pathway. Both human-to-human and human-to-animal transmission routes were not modelled due to the focus of the study on the transmission dynamics of foodborne transmission of Salmonella spp. and the negligible role of both pathways on the foodborne transmission of the pathogen ([Infection with Salmonella (cdc.gov)](https://www.cdc.gov/training/SIC_CaseStudy/Infection_Salmonella_ptversion.pdf)). A η scaling parameter was used to transform the proportion of antibiotic-sensitive/resistant carriage in livestock to the extent of Salmonella spp. contamination on livestock carcasses. This scaling parameter represents the decrease in the proportion due to processing steps in the farm-to-fork pathway.

A background rate of transmission in the livestock population was also modelled to represent infection of livestock hosts from non-livestock sources (ζ). This transmission rate was scaled by a factor of 0.5 to ensure an equal influence of ζ on both antibiotic-sensitive and resistant transmission routes. Natural recovery from antibiotic-sensitive/resistant infection occurs in both human/livestock populations at rate rH and rArespectively. Per capita birth/death rates are represented by µA in livestock and µH in human populations.

A parameter (τ) was used to describe the selective pressure and therapeutic effect of antibiotic usage in domestic livestock. The selective pressure of livestock antibiotics was modelled as a single transition rate, encompassing a range of evolutionary and biological phenomena that convert livestock between antibiotic-sensitive to resistant states. Similarly, a single reversion parameter (φ) was used to encompass a range of different biologically plausible phenomena that may cause reversion of antibiotic-resistant (IRA) to sensitive strains (ISA). **A description of these biologically plausible phenomena can be found in the methodology for chapter 2.** The relative proportion of human food usage from domestic sources was modelled as a ψ parameter, with 1-ψ representing the extent of human food products sources from imported non-domestic sources.

To explore the effects of import heterogeneity on antibiotic-sensitive/resistant Salmonella spp. transmission dynamics, the import pressure (FracImp, PropResImp) was stratified into separate transmission pressures, representing different countries that constitute the food trade network in the domestic country (**Figure 2**). Each of these transmission pressures from importing countries requires individual parameterisation with regard to the extent of contamination on imported food products (FracImpX ϵ [FracImp1, …, FracImpX]) and proportion of contaminated food products that are antibiotic-resistant (PropResImpX ϵ [PropResImp1, …, PropResImpX]).



Figure 2. **Model structure describing the transmission of foodborne pathogens between/within livestock and human populations in the model with increased import heterogeneity.** Model equations and parameters can be found described in the supplementary material ().

The increased heterogeneity in import pressure also requires the addition of another set of parameters detailing the relative share that each importing source contributes to the overall importation to the domestic country of interest (ShareX ϵ [ShareFRA, …, Share10]). The real world equivalent of this parameter can be conceptualised as the proportion/contribution of individual importing countries to the overall import of food products to a domestic country of interest.

**Ampicillin usage/resistance in Fattening Pigs Case Study**

The United Kingdom was chosen as the “domestic” country of interest for the model. Therefore, the compartmental model, including dynamic livestock and human populations were parameterised with regard to UK livestock/human outcome measures. The bug/drug/livestock population of interest was modelled as ampicillin usage/resistance in fattening pigs. This case study was chosen due to the high level of usage (both historical and current) of ampicillin in fattening pigs, and the availability of resistance data for this livestock species.

**Efficacy of Curtailment Outcome measure**

The primary outcome of interest for this study was the relative change in proportion of antibiotic-resistant human salmonellosis upon domestic livestock antibiotic. We term this percentage reduction in the proportion of antibiotic-resistant human salmonellosis as the efficacy of curtailment (EoC) (eqn 1.1).

Eqn 1.1

This outcome measure is calculated at the long-term model non-zero steady state. Studying the system at an equilibrium state is a useful indication of the long-term dynamics of antibiotic-resistant salmonella infection and the long-term trajectory of the system. However, we recognise that the “real-world” dynamics of AMR are not temporally stable and in flux.

**Data Sources and Model Fitting**

An approximate Bayesian computation sequential Monte Carlo (ABC-SMC) approach was used to fit the model to the ampicillin usage/resistance in fattening pigs case study, using the United Kingdom and the representative domestic livestock/human populations. This required the curation of three different datasets.

A usage/resistance dataset was curated to parameterise the relationship between livestock ampicillin usage and the proportion of ampicillin-resistant Salmonella spp. carriage. The proportion of isolates resistant to ampicillin from carcasses of fattening pigs was extracted from the respective European Food Safety Authority (EFSA) summary reports (**cite**). Ampicillin sales data was obtained from European surveillance of veterinary consumption (ESVAC) reports. A scaling calculation was required to convert the generic ampicillin sales for livestock to a value specific to fattening pigs with sales described as grams per population correction unit (g/PCU). **Details of this scaling calculation can be found in the supplementary information for chapter 2**. Note that due to a lack of accurate country-level antibiotic usage data, sales were assumed to be a proxy for usage.

A dataset was next curated using data from UK Department for Environment & Rural Affairs (DEFRA) data. The relative contribution of UK (domestic), EU and non-EU countries that contribute to the UK’s food product consumption was determined from DEFRA data to parameterise ψ and ShareX parameters. Data from DEFRA was used to stratify EU countries into the nine major EU livestock food product trade partners of the UK. This resulted in ten countries regions that require parameterisation with regard to the relative share of the UKs food product trade (ShareX), extent of food product contamination with Salmonella spp. (FracImpX) and the proportion of contaminated imports that are ampicillin-resistant (PropResImpX): Netherlands, Irish Republic, Germany, France, Spain, Italy, Belgium, Poland, Denmark, and general non-EU import. Scaling calculations were required to determine the relative contribution of ten of the UKs major food import trade partners for general livestock food products (ψ = 0.656) and swine-specific food products (ψ = 0.4455). **Details of these scaling calculations can be found in the supplementary material**. Note that data on the contribution of domestic, EU and nEU countries/regions for general livestock food products (ψ = 0.656) was used for baseline model parameterisation.

Data on the extent of contamination on fattening swine carcasses was obtained from ECDC surveillance reports, with contamination data obtained from 400cm2 swabs and competent authority (CA) surveillance prioritised in data collection. Data on the proportion of contaminated ampicillin-resistant isolates on fattening swine carcasses was obtained from EFSA surveillance reports.

**UK Dataset**

Data was obtained on UK specific livestock and human outcome measures to act as targets for model fitting. Baseline UK ampicillin usage/sales for the ampicillin-resistance in fattening pigs case study was considered the unweighted average ampicillin usage observed across 2015-2018 for the UK (τ = 0.0009 g/PCU). The observed ECDC daily EU incidence of human salmonellosis was used as a proxy for the baseline incidence of UK salmonellosis (0.593 per 100,000). This proxy was chosen due to the lack of multiplication factors available to scale UK-specific reported incidence of salmonellosis to community levels (**cite BCoDE**). The proportion of ampicillin-resistant UK human salmonellosis was obtained from 2015-2018 ECDC AMR summary reports (0.207). The proportion of ampicillin-resistant UK livestock Salmonella spp. carriage was parameterised from 2015-2018 EFSA surveillance reports (0.417). The extent of contamination in UK swine carcasses was calculated from 2015-2018 ECDC one health surveillance reports. Details of the calculations to determine these UK-specific outcome measures can be found in the supplementary material.

The η scaling parameter was also parameterised using UK specific epidemiological data, with a caecum carriage of Salmonella spp. in UK fattening pigs of 32.2% ([Abattoir-based study of Salmonella prevalence in pigs at slaughter in Great Britain | Epidemiology & Infection | Cambridge Core](https://www.cambridge.org/core/journals/epidemiology-and-infection/article/abattoirbased-study-of-salmonella-prevalence-in-pigs-at-slaughter-in-great-britain/3FDEA88F8CF084908FC34C7A6A57052E)). This information was combined with data on the extent of UK Salmonella spp. contamination on fattening pig carcasses (2.87%), to parameterise a 88.98% reduction from carriage to contamination in UK livestock (η = 0.1102).

**ABC-SMC Model Fitting**

A simulated dataset for the ampicillin usage/resistance in fattening pigs case study was generated by modelling the proportion of ampicillin-resistant livestock carriage for each country/year observation, for each of the observed levels of antibiotic sales included in the dataset. A sum of squared errors distance function was then used to calculate the distance between the simulated and observed fraction of antibiotic-resistant livestock infection for each country/year data point. In accordance with the EFSA methodology, countries with <10 isolates in the respective EFSA dataset for a particular year were omitted from the dataset

Four additional summary statistics were used in the fitting approach: 1) minimise the difference between the modelled daily EU incidence of human salmonellosis at baseline antibiotic usage and the observed ECDC daily EU incidence of human salmonellosis currently observed (0.593 per 100,000), 2) minimise the difference between the model estimated proportion of resistant human salmonellosis at baseline antibiotic usage and the EFSA averaged European proportion of resistant human salmonellosis specific for each case study, 2) minimise the difference between the model estimated prevalence of *Salmonella* spp. contamination on swine carcasses and the value observed in ECDC surveillance data and 4) minimise the difference between the model estimated proportion of *Salmonella* spp. livestock carriage that is ampicillin-resistant and the proportion observed in EFSA averaged data.

The ABC-SMC approach was used for both study models (Figure 1,2) to fit the model to available epidemiological data. For the first model, the ABC-SMC approach was used to estimate the marginal posterior probability distribution for six model parameters given the data, . Use of the second model required the estimation of the marginal posterior probability for nine model parameters. Other model parameters were not fitted as estimates with high levels of certainty were available (rH, rA, μA and μH). Prior distributions for each fitted parameter can be found in the supplementary material (Table S4).

The ABC-SMC model fit was run for eight generations, with each generation running until the acceptance of 1000 particles. Acceptance thresholds for each distance measure and summary statistic (ε) can be found in thesupplementary material (Table S5). A multivariate normal distribution was chosen for the ABC-SMC perturbation kernel. The randomly sampled mean and covariance matrix was calculated from the previously accepted generation of accepted particles. An intersection metric was used to ensure that accepted particles satisfied tolerance values set for the distance measure for each calculated for each summary statistic per generation.

Mean point estimates from the approximated marginal posterior probability distributions of the 8th accepted generation were used as the final parameter sets for each respective case study. Point estimates and calculated 95% HDIs from the marginal posterior distribution for each model parameter can be found in the supplementary material (Table S3).

**Sensitivity Analysis**

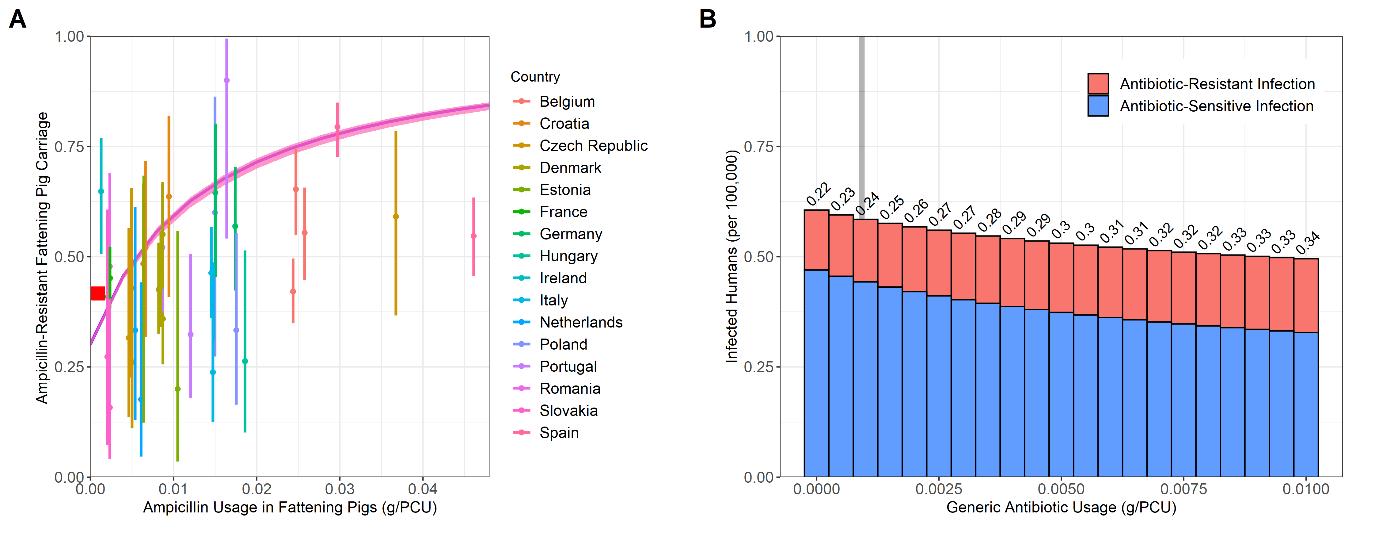
Latin-hypercube sampling partial rank correlation coefficient (LHS-PRCC) and extended Fourier amplitude sensitivity test (eFAST) approaches were used to conduct sensitivity analyses on both study models (Figure 1, 2) with regard to the efficacy of curtailment outcome measure. Supplementary sensitivity analyses were also conducted to identify important parameters regarding the incidence of human Salmonellosis and the proportion of ampicillin-resistant human salmonellosis outcome measures. Monotonicity analyses were performed for model parameters to identify potential non-monotonicities before conducting LHS-PRCC analyses. The parameter range chosen for the sensitivity analysis was limited to an order of magnitude above and below the fitted mean point estimate for each model parameter.

**RESULTS**

The basic import model was fitted to the UK case study and epidemiological data for ampicillin-resistance in fattening pigs (**Figure 1B**). Model fitting diagnostics can be found in the supplementary material (**SUPPLEMENTARY**). An **X** fold increase in the incidence of human salmonellosis was observed, with an increase from **X** per 100,000 population under baseline antibiotic usage (τ = 0.0009 g/PCU) from **X** per 100,000 population when antibiotics are curtailed (τ = 0 g/PCU) (**Figure 4**). The proportion of ampicillin-resistant human salmonellosis displayed a decrease from **X** to **X** when antibiotics were curtailed. This represents an efficacy of curtailment of **X**% (supplementary material).

Increasing the proportion of food from imported sources from a value consistent with general livestock produce (ψ = 0.656), to a value more consistent with swine livestock produce (ψ = 0.4455), resulted in an overall increase in the incidence of foodborne disease () and the proportion of ampicillin-resistant human salmonellosis () at baseline antibiotic usage (τ = 0.0009 g/PCU) (**SUPPLEMENTARY**).

* It is important to note that under baseline parameterisation, the FracImp is generally higher than the level of contamination in domestic livestock carcasses, and the level of ampicillin resistance amongst isolates is also higher in imports relative to domestic livestock.

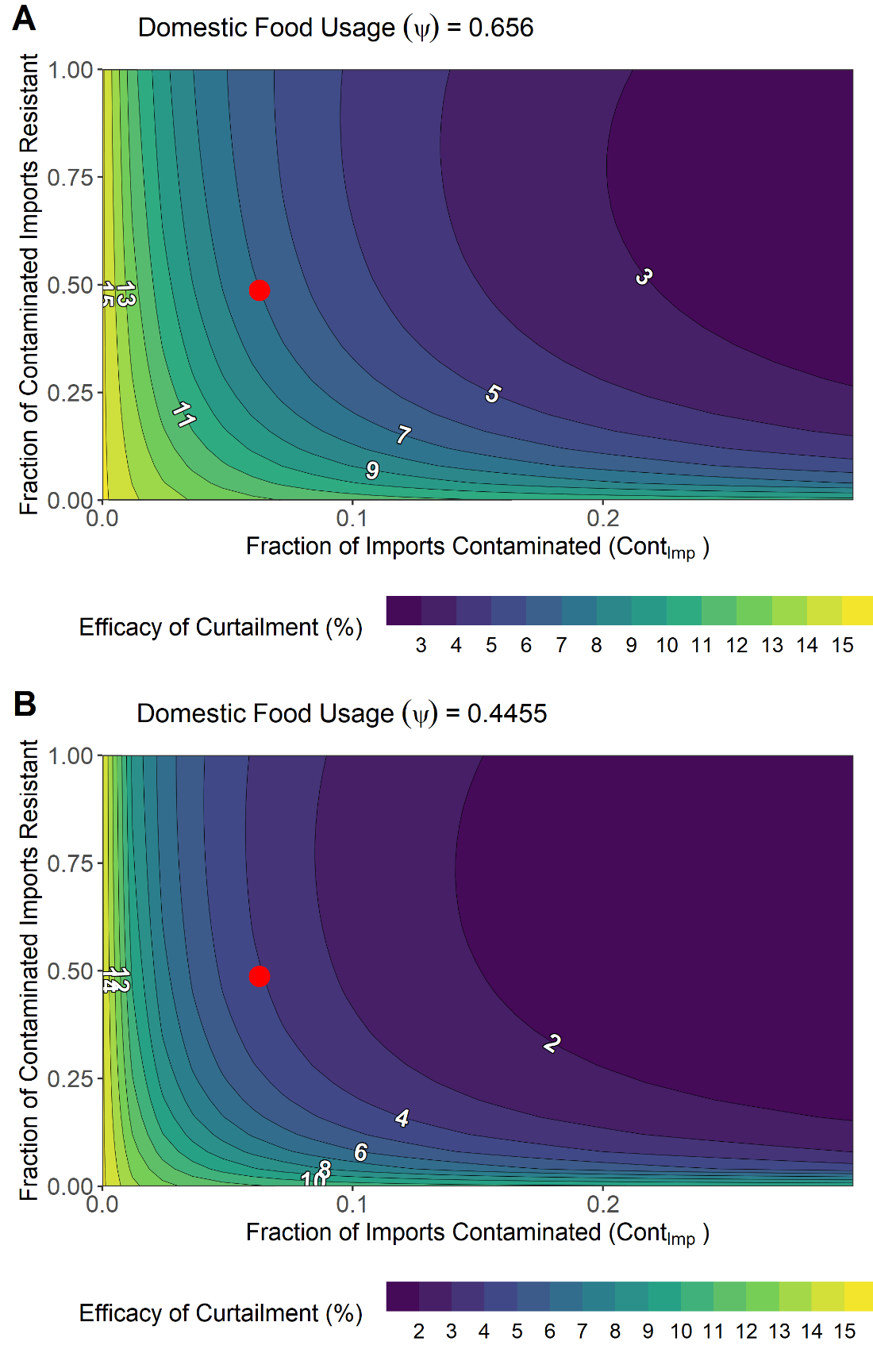


**Figure 4. A) Observed and estimated relationship between livestock ampicillin usage and ampicillin-resistant salmonellosis in humans using the simple model. B) Impact of alterations in livestock ampicillin usage (τ) on the daily incidence of salmonellosis and the proportion of ampicillin-resistant human infection (I\*RHProp).** Solid red lines and ribbons represent model fit resulting from the approximated posterior distribution using ABC-SMC and the corresponding 95% HDI. Country-specific 95% confidence intervals for the observed data (dots) were calculated for each case study using a 1-sample proportion test with continuity correction. Red square denotes the target level of ampicillin-resistance (0.4167) for baseline levels of UK ampicillin usage (τ = 0.0009 g/PCU).

* What the model fit looks like without import – fit the model without import and identify the model fits and the closeness to the outcome measure – see if there are qualitative differences when we change antibiotic usage

A sensitivity analysis using LHS-PRCC and eFAST approaches identified the proportion of contaminated imports that are ampicillin-resistant (PropResImp) and the transmission-related antibiotic resistance fitness cost (α) as the most important parameters for determining the proportion of proportion of ampicillin-resistant human salmonellosis. The animal-to-human transmission rate (βHA), the proportion of imports contaminated (FracImp) and the proportion of UK food supply from domestic sources (ψ) were important for determining the incidence of human salmonellosis (**SUPPLEMENTARY**). Approximated marginal posterior probability distributions for the fitted model parameters from the ABC-SMC approach, respective model diagnostics and monotonicity plots for the LHS-PRCC can be found in the supplementary material (**SUPPLEMENTARY**).

We next identified the effect of import parameters in a scenario analysis by altering the proportion of imported food products contaminated (FracImp) and the proportion of ampicillin-resistant contaminated imported food products (PropResImp) and observing the effect on the efficacy of curtailment outcome measure. Parameter alterations were limited to FracImp ϵ [0, 0.3] and PropResImp ϵ [0, 1], with these ranges observed in ECDC datasets (**SUPPLEMENTARY**).



**Figure 5. Impact of altering FracImp and PropResImp import parameters on the efficacy of curtailment for two values of the proportion of UK food supply from domestic sources (ψ). A) General livestock import case study (ψ = 0.656). B) Swine-food product import case study (ψ = 0.4455).** Red dot represents the baseline parameterisation for FracImp and PropResImp parameters from ECDC data (FracImp = 0.0628; PropResImp = 0.487).

Increasing the extent of contamination of import food products with Salmonella spp. and the proportion of ampicillin-resistant contaminated imported food products (FracImp = ; PropResImp = ) decreased the efficacy of curtailment relative to baseline parameterisation, with EoC being reduced from 7% to 2%. This suggests that increasing the extent of contamination and resistance on imports can decrease the efficacy of local interventions. Reductions to FracImp () and PropResImp () from baseline levels had the opposite effect, with increases to the EoC from X%, to X%. A related phenomenom can also be observed with decreases to the extent of domestic food product usage from baseline levels (ψ= 0.4455), with equivalent reductions to fracimp and propresimp compared to baseline ψ () resulting in greater reductions to EoC (). Supplementary analyses also explored the effect of altering the relative reduction in prevalence from carriage to contamination on carcasses, with increases in the η parameter (poorer clearance)., resulting in equivalent changes to FracImp and PropResImp increasing the EoC. Decreases to η (greater clearance) resulted in a less efficacious intervention, with lower a EoC for equivalent changes to FracImp and PropResImp (**SUPPLEMENTARY**).

An LHS-PRCC and eFAST sensitivity analysis was next conducted to assess the importance of model parameters on the efficacy of curtailment. Monotonicity plots were used to identify any potential non-monotonic behaviour between explored model parameters and the efficacy of curtailment outcome measure (**SUPPLEMENTARY**). Among export parameters (), the proportion of UK food products from domestic sources (ψ) and the relative reduction in prevalence from carriage to contamination on carcasses () had a strong effect of increasing the efficacy of curtailment () under higher parameter values. The proportion of ampicillin-resistant contaminated food imports had a strong effect of reducing the efficacy of curtailment, with the extent of contamination on imported food products () having a small effect of reducing the EoC (). The importance of these import parameters is corroborated by the relative height of the sensitivity indices for the first order effects in the eFAST analysis. Interestingly, the second order effects comprised the majority of the variation in EoC explained by the PropResImp parameter, suggesting that interactions with other model parameters are necessary for PropResImp to affect EoC.

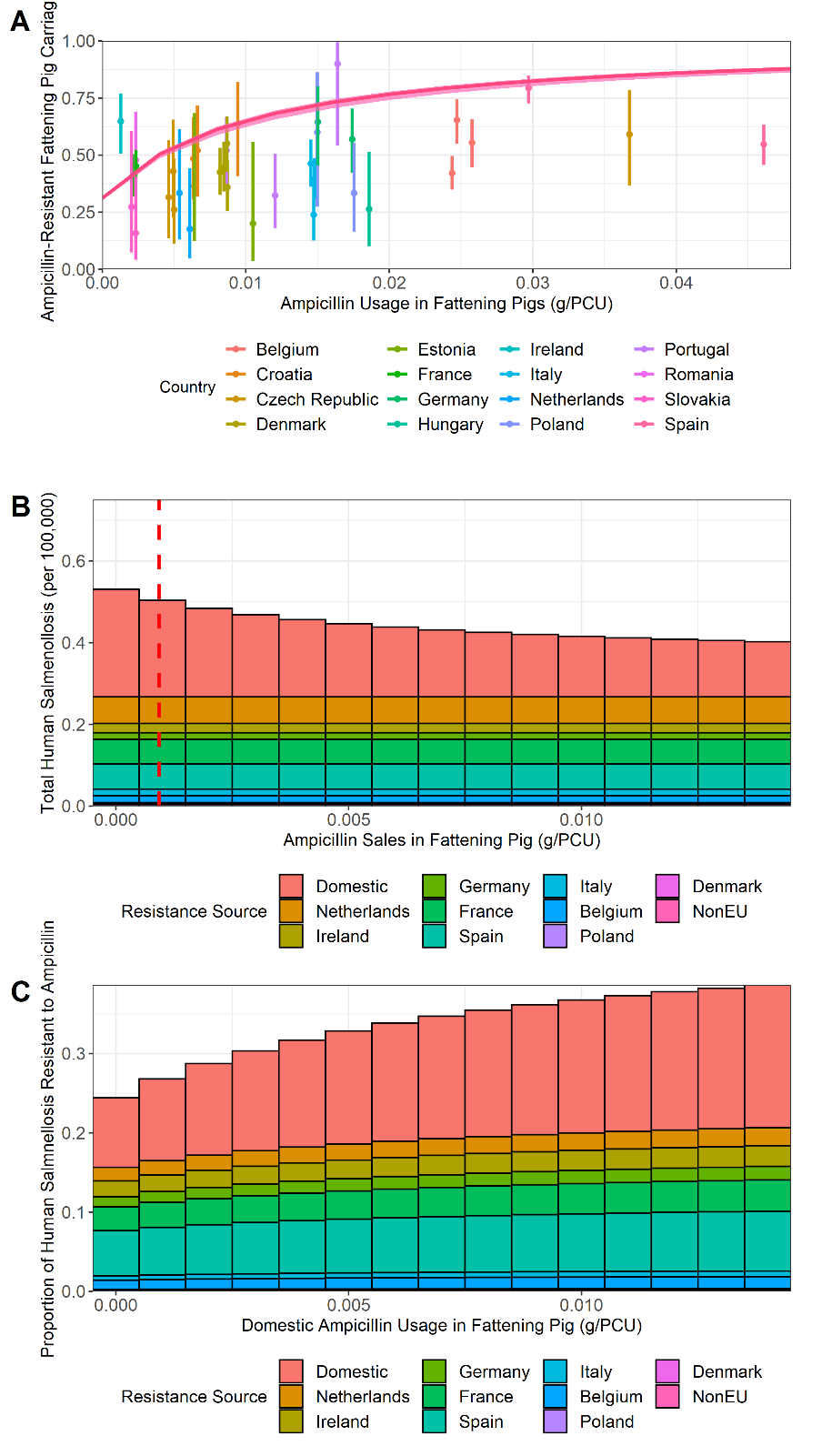


**Figure 6. Sensitivity analyses for the efficacy of curtailment (EoC) outcome measure. A) Latin hypercube sampling partial rank correlation coefficient test (LHS-PRCC). B) Extended Fourier amplitude sensitivity test (eFAST).** Note that 95% confidence intervals for each correlation coefficient was generated through generating n = 100 bootstrap replicates. 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.

Among non-import related parameters, the rate of livestock recovery from Salmonella spp. carriage () had a strong effect of reducing the efficacy of curtailment when increased (). The efficacy of antibiotic-mediated livestock recovery (κ), transmission related fitness costs associated with antibiotic-resistance (α), the per capita rate of background transmission to livestock populations (ζ) had moderate effects on increasing the EoC ().

**Section 2**

To assess the effect of heterogeneity in food product/AMR import and AMR import on AMR dynamics, we fit an adapted model with stratified importation to the study datasets (**Figure** ). The key difference between the adapted model and the previously described model is stratification of the previously homogenous importation transmission pressure into 10 distinct importing countries based on the UKs major trading partners for livestock food products: Netherlands, Irish Republic, Germany, France, Spain, Italy, Belgium, Poland, Denmark, and general non-EU import. Each country required specific parametrisation with regards to the extent of contamination on import products (FracImpX) and the proportion of ampicillin-resistant contaminated import food products (PropResImpX). Approximated marginal posterior probability distributions for the fitted model parameters from the ABC-SMC approach and the respective diagnostics can be found in the supplementary material (**SUPPLEMENTARY**).



**Figure 7. A) Observed and estimated relationship between livestock ampicillin usage and ampicillin-resistant salmonellosis in humans using the complex model. B) Impact of alterations in domestic livestock ampicillin usage (τ) on the daily incidence of human salmonellosis. C) Impact of alterations in domestic livestock ampicillin usage (τ) on the proportion of ampicillin-resistant human infection.** Solid red lines and ribbons represent model fit resulting from the approximated posterior distribution using ABC-SMC and the corresponding 95% HDI. Country-specific 95% confidence intervals for the observed data (dots) were calculated for each case study using a 1-sample proportion test with continuity correction. Red square denotes the target level of ampicillin-resistance (0.4167) for baseline levels of UK ampicillin usage (τ = 0.0009 g/PCU).

* Need a red line and dot for resistance and the first plot

We note similar X-fold increases in the overall incidence of salmonellosis () and X-fold decreases proportion of ampicillin-resistant human salmonellosis () compared to the previously described model (). Under baseline livestock ampicillin usage (), the majority of overall and ampicillin-resistant human salmonellosis was attributed to domestic livestock (), with x% attributed to EU countries and x% attributed to non-EU countries. The level attributable to domestic livestock decreased in both outcome measures () when ampicillin usage was curtailed in domestic livestock. The level of overall salmonellosis and ampicillin-resistant human salmonellosis attributable to non-domestic sources did not change significantly when domestic livestock antibiotic usage was curtailed.

Alterations to the proportion of UK food supply from domestic sources () were next explored in relation to the efficacy of curtailment (EoC) outcome measure. We term increases in ψ as “decreases to import” and decreases to ψ as “increases to import”. Decreases to import under baseline parameterisation resulted in less than proportionate increases to the EoC, roughly equal to an exponential or quadratic growth curve. EoC under baseline levels of import was 7% and reached a maximum value of X% when no importation is utilised ().

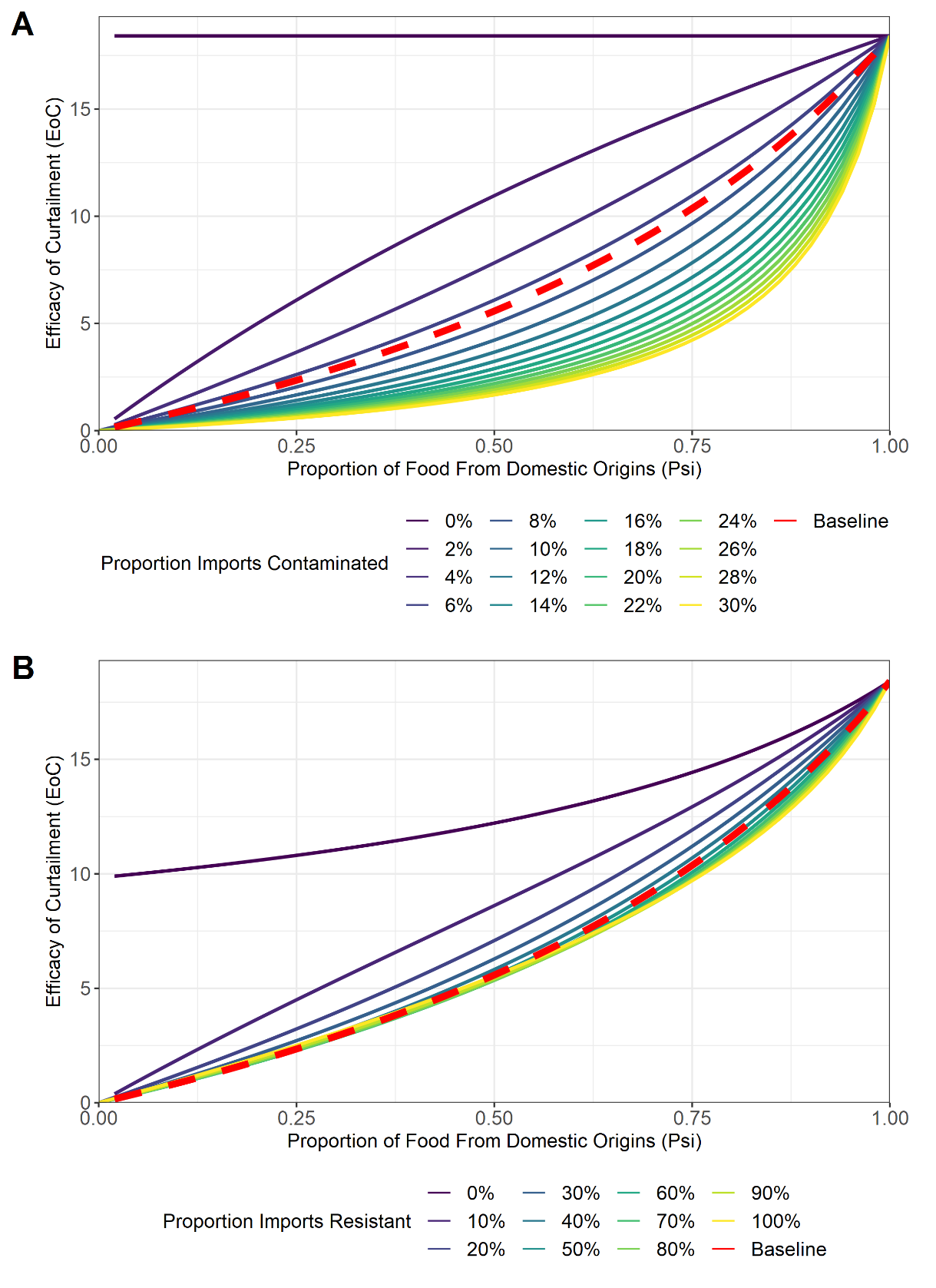
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**Figure 8. Relationship between the proportion of UK food products (ψ) and the efficacy of curtailment (EoC) for baseline parameterisation.** Using the values of EoC for the maximum and minimum values of ψ, we can split the figure into two sections: **XXX**

Using the maximum EoC value of x% when ψ = 1, we can define two areas: one where the rate of change in EoC is inversely proportionate to the current rate of change (top left of plot), resulting in a high EoC at relatively high levels of import (), but which plateaus as import is decreases. This results in the EoC/ψ relationship having a shape akin to logarithmic growth and we can denote this area as “lower impact of import”. The second area occurs where the rate of change in EoC is directly proportionate to the current rate of change in EoC (bottom right of plot). This results in a low EoC for a large range of import values, with EoC increasing rapidly when import is at low levels. This has a EoC/ψ curve with a shape similar to an exponential growth curve and we can denote this area as “greater impact of import”. It is important to note that the baseline relationship between EoC/ψ can be found in this latter area of the plot. We note that the former curve shape is qualitatively better for import, as high values of EoC can still be obtained despite the saturating effect of import on local interventions.

We next explored the effect of changing the average characteristics of import across impoirting countries on the relationship between the proportion of UK food supply from domestic sources () and the effiacy of curtailment (). Explored parameters included the extent of contamination of import food products with Salmonella spp. and the proportion of ampicillin-resistant contaminated imported food products. The average level of contamination on imports was ranged from FracImp ϵ [0, 0.3], in accordance with the range of values observed in ECDC reports.

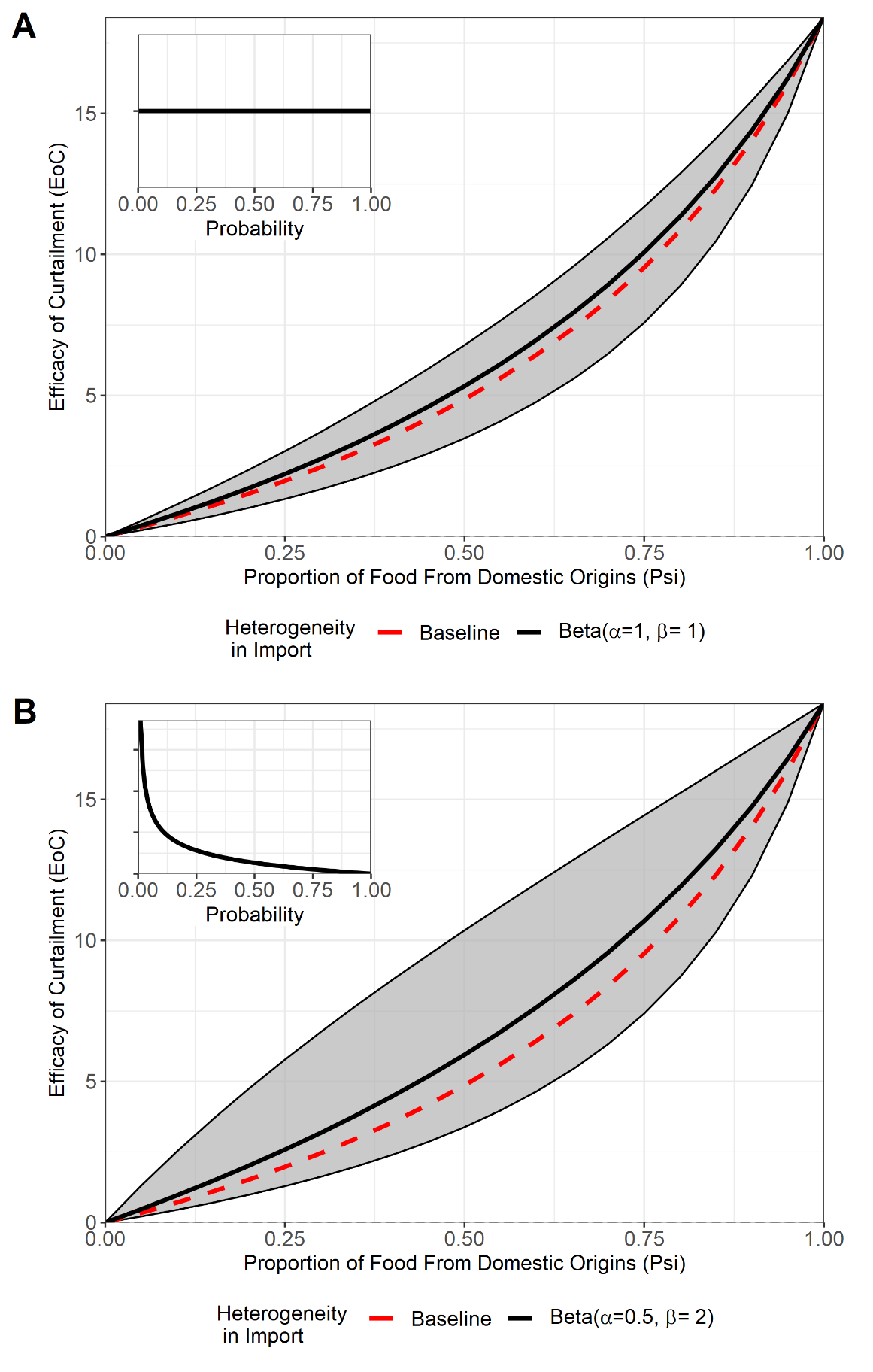


**Figure 9. Relationship between the proportion of UK food products (ψ) and the efficacy of curtailment (EoC) under different average parameterisation for FracImp and PropResImp across importing countries. A) Changes to the proportion of Salmonella spp. contaminated food imports across importing countries (FracImp). B) Changes to the proportion of ampicillin-resistant Salmonella spp. contaminated food imports across importing countries (PropResImp).** Baseline relationship between EoC/ψ is denoted by the red and dotted line.

Decreasing the average overall proportion of contaminated import food products (FracImp) to 0-6% resulted in a large shift in relationship between EoC/ψ, where increases to importation has a lower effect on reducing the EoC. The opposite phenomenon was observed with increases to the average FracImp above 8% with the relationship between EoC/ψ rapidly reaching a state where EoC is low across a large range of import values. We also note a “saturation” type effect with increases in average FracImp above low-moderate values having no further alterations on the relationship between EoC/ψ, stabilising at a relationship where import () has a significant effect on the EoC. Intuitively, changes to import where the level of contamination on imported food products is X% had no impact on the EoC.

Changes to the average proportion of ampicillin resistant contaminated food imports (PropResImp) had a qualitatively different effect to changes to FracImp, with all changes to PropResImp resulting in EoC/ψ relationships having a curve akin to an exponential growth curve. Removing ampicillin-resistant contamination on imports (PropResImp = 0) resulted in changes in imports still having an impact on EoC. Similarly, to FracImp, we also note a saturation effect occurring, with increases to PropResImp above ~40% having minor effects on the shape of the relationship between EoC/ψ. Increases to the relative reduction in prevalence from carriage to contamination on carcasses (η) (lower levels of contamination on domestic carcasses) resulted in EoC/ψ relationship where EoC is low across a large range of values of ψ (**Supplementary**). This is due to human foodborne disease being less attributable to domestic sources under high values of η, therefore domestic livestock interventions having less of an effect on EoC.

We next explored the effect of heterogeneity in the relative contribution to import across importing countries (ShareX) on the relationship between importation and the efficacy of curtailment. The ShareX parameter was sampled ten times, corresponding to the ten importing countries/regions in the model, from two different beta distributions, Beta(α = 1, β = 1) and Beta(α = 0.5, β = 2). These represent two hypotheses about importation, with the relative share of import being distributed equally across importing countries or import being prioritised from a select few countries. Note that the total sum of ShareX must sum to 1, therefore each group of ten samples was scaled by the sum of the samples, . Sampling was performed n = 1000 for each Beta distribution, and the average, minimum and maximum value of EoC for each explored values of ψ was identified.



**Figure 10.** **Relationship between the proportion of UK food products (ψ) and the efficacy of curtailment (EoC) under different assumptions regarding the heterogeneity of import from importing countries. A) ShareX samples from a uniform sampling distribution, Beta(α = 1, β = 1). B) ShareX samples from a “skewed” sampling distribution, Beta(α = 0.5, β = 2).** Note that the average, minimum and maximum value of EoC for each value of ψ, is denoted by the middle-black line, lower bound, and upper bound of the grey shaded area respectively.Baseline relationship between EoC/ψ is denoted by the red and dotted line.

Sampling from either Beta distribution resulted in minor changes to the average relationship between the proportion of UK food supply from domestic sources and the efficacy of curtailment, with minor increases in the EoC across explored values of ψ relative to baseline. However, sampling from the Beta distribution promoting more heterogeneity in the relative share of importation, Beta(α = 0.5, β = 2) (Figure 10B), resulted in a greater heterogeneity in the minimum and maximum EoC values observed for each value of Psi compared to the distribution promoting a more uniform share of import, Beta(α = 1, β = 1). As an example, the minimum and maximum value for baseline values of Psi were X and X with Beta(α = 0.5, β = 2), compared to X and X for Beta(α = 0.5, β = 2). This suggests that if import is distributed more heterogeneously across importing countries, then there is the potential for greater uncertainty concerning the effects of changing import on the EoC compared to importing uniformly from different countries.

**DISCUSSION**