Foot and mouth disease: the risks of the international trade in live animals

This paper (No. 01112017-00114-EN) has been peer-reviewed, accepted, edited, and corrected by authors. It has not yet been formatted for printing. It will be published in December 2017 in issue 36 (3) of the *Scientific and Technical Review*

D.W. Shanafelt [1, 2]* & C.A. Perrings [2]

(1) Centre for Biodiversity, Theory and Modelling, Theoretical and Experimental Ecology Station, CNRS and Paul Sabatier University, 2 Route du CNRS, 09200 Moulis, France

(2) School of Life Sciences, Arizona State University, P.O. Box 874501, Tempe, AZ 85287-4501, United States of America

*Corresponding author: dshanafe@asu.edu

Summary

The growth in world trade has generated significant benefits to humankind, but it has also generated costs. Among these is an increase in the dispersal of pests and pathogens across the globe. International trade has been implicated in outbreaks of several re-occurring livestock diseases. This paper is focused on the risk of foot and mouth disease (FMD) associated with the international trade in live animals. A model was used to estimate FMD risk as a function of the international trade in live animals, controlling for the biosecurity measures undertaken by importing and exporting countries, and for the presence of endemic FMD reservoirs. It was found that the indirect risks associated with exports may be as great as the direct risks associated with imports. For countries where livestock production occurs in disease-free zones (with or without vaccination) the trade risks vary with both species and trading partner. These findings may assist the targeting of disease risk mitigation activities.

Keywords

Foot and mouth disease – International trade – Risk.

Introduction

The growth in world trade has delivered significant benefits to consumers worldwide. At the same time it has dramatically increased the rate at which pests and pathogens are dispersed. Indeed, the increased spread of human, animal and plant diseases has been argued to be among the most important side effects of the growth of international trade (1). Research on the general problem of invasive species has revealed strong positive relationships between the development of new trade routes and the introduction of new species, and between the growth in trade volumes and the probability that introduced species will establish and spread (2, 3, 4, 5, 6, 7, 8, 9, 10, 11). The spread of many emerging zoonotic and epizootic diseases has been facilitated through local, regional or international trade in livestock and wildlife products. The list of emerging zoonoses spread this way includes monkeypox, severe acute respiratory syndrome (SARS) and H5N1 avian influenza (8, 12, 13, 14, 15), though for the latter two trade likely plays a larger role in local and regional rather than international spread. Epizootic diseases spread through trade include H9N2 avian influenza and re-emerging livestock diseases such as foot and mouth disease (FMD), bovine spongiform encephalopathy (BSE) and a range of swine viral diseases (16, 17, 18, 19).

This paper is focused on the epizootic disease risks of trade, and in particular on the FMD risks of the trade in live animals. Live animals are not the only source of FMD risk. The trade in animal products is also implicated. What makes the trade in live animals particularly interesting, however, is that trade vessels may be as much a source of risk as the animals themselves. Therefore, an empirical model of FMD risk is estimated that incorporates both the import and export risks of the international trade in live animals, while controlling for the presence of endemic reservoirs and how well a country manages disease within its borders. Import risks correspond to risks associated with import of potentially infected animals. Export risks correspond to risks associated with the export of animals to locations where the disease may be present. These risks are largely associated with contaminated material returning in trade vessels.

Previous research has shown that the probability that animal or plant pathogens will be transmitted from one location to another via the movement of goods depends on direct exposure to infected materials (4, 5), and on the biosecurity measures undertaken by those who produce and transport the goods (20, 21, 22, 23, 24, 25). However, there are concerns that focusing only on imports and generic biosecurity can be misleading. Current trade-related animal disease risk assessments are argued to understate risk when they ignore indirect trade linkages (26, 27, 28) and to overstate risk when they treat all commodities as equal (29, 30). For example, African swine fever in the Russian Federation continues to pose a serious risk to the European Union (EU) swine industry even though trade in pigs and pig products from the Russian Federation has been banned since June 2007. One reason for this is that infection may occur via contaminated waste or infected vehicles used to trade goods not subject to the ban (26). This is equivalent to invasive species being unintentionally imported into countries as ‘passengers’ on cargo or transport vessels, a good example of which is the large number of aquatic species transported via ballast water (31).

Two sets of disease risk models were estimated that incorporate the two-way effects of imports and exports in the international trade in livestock. One set of models captures the disease risks associated with national imports and exports of all susceptible animals into all countries of a given disease status. The World Organisation for Animal Health (OIE) recognises five states: disease-free everywhere in a country (with and without vaccination), disease-free in specified zones within a country (with and without vaccination), and not disease-free anywhere in a country (32). The disease-free categories used by the OIE are also trade categories since they determine which countries have access to what markets. The other set of models captures the disease risks associated with national exports and imports of different animals into all countries in a given geographical region, using the Food and Agriculture Organization of the United Nations (FAO) regions. This enables evaluation of the relative significance and strength of the different risk factors identified, including the impact of imports from/exports to groups of countries.

Two current trends in international trade are important. One is a long-term but still accelerating growth in the volume of trade relative to output. Since 1950, world merchandise exports have increased at more than three times the rate of gross domestic product (GDP) growth (33). The second is a more recent change in the regional structure of exports. Export growth has been more rapid in emerging markets and developing economies than in developed economies – a trend that has accelerated since the 2007–2009 recession (34). In the first decade of this century the world trade in live animals increased by over 50%. While it is recognised that this has implications for the spread of FMD (35), there are relatively few attempts to quantify the associated risks (36, 37, 38, 39, 40, 41). This paper reports on the estimation of a model of the FMD risks of the live animal trade, and especially the risks associated with the increasing live animal trade into and out of emerging markets and developing economies.

Background

The biology of the FMD virus is well understood (see Alexandersen *et al.* [42], Arzt *et al.* [43, 44], and Sutmoller *et al.* [45] for reviews of this literature). Transmission may occur via a number of pathways such as airborne droplets, entry through cuts and abrasions in the skin, and consumption of contaminated fodder (42). The virus is also able to persist in a variety of materials including hay, soil, fodder, milk, hair, machinery and clothing, although the length of time it persists varies with environmental conditions and the type of material (42, 45, 46, 47, 48, 49, 50). Persistence time ranges from several days to six months or more (47, 48, 50).

Virtually every cloven-hoofed animal is susceptible to FMD, but susceptibility and infectivity vary with the virus strain and host species (42, 51). In livestock, the disease causes the formation of lesions within and around the mouth and feet, lameness, fever, depression, loss of appetite, reduction in milk yields and reproductive potential, but causes mortality only in rare cases (42, 52).

The primary cost of the disease lies more in the trade response it induces rather than its clinical effects. The primary response to an

FMD disease outbreak in disease-free zones is to ban the export of risky goods until satisfactory animal health conditions have been restored, and to slaughter infected and potentially infected livestock (32, 53). The economic damage caused by FMD outbreaks due to this response may be very large (52, 54). The 2001 United Kingdom (UK) outbreak, for example, resulted in the culling of over 2 million head of livestock (55), and in costs for the national government, farmers, agriculture, the food chain and tourist revenues of around £6.5 billion (56). That is, the cost of the outbreak comprised both the loss of a substantial proportion of standing stock, and the loss of trade in both agriculture and related industries. Similarly, the 1997 Taiwan FMD outbreak caused US$ 378 million in damages to the livestock industry, but also led to the loss of over 65,000 jobs spanning pharmaceutical, animal fodder, meat packaging, equipment manufacture and supply, and transportation industries (57). Indeed, FMD outbreaks in disease-free countries frequently induce additional expenditures on disease monitoring, vaccination and the isolation of disease-free areas as conditions for restoring trade, while trade restrictions imposed in response to an outbreak frequently affect sectors other than agriculture (41, 52, 54).

The international management of trade-related animal disease risks is governed by the Sanitary and Phytosanitary (SPS) Agreement, which regulates the trade interventions allowed to protect animal and plant health under Article 20 of the General Agreement on Tariffs and Trade. Three bodies fix the sanitary standards applied: the OIE, the Codex Alimentarius and the International Plant Protection Convention. The former includes health standards for international trade in animals and animal products. The SPS Agreement permits trade interventions to protect animal health, but also requires those interventions to be informed by a scientific assessment of risk. The risk assessment methodology developed by the OIE aims to establish the likelihood of the introduction, establishment and spread of disease within the territory of an importing country, and to assess its biological and economic consequences (29).

Typically, risk assessments for both pests and pathogens transmitted through trade assume that risk is a function of direct exposure to risk material (often referred to as 'propagule pressure' [58, 59], approximated by the volume of imports) and biosafety measures (the sanitary capabilities of exporting countries). For FMD, the OIE applies the principles specified in the OIE *Terrestrial Animal Health Code*, which requires the geographical separation of production zones from areas where FMD is present (32). Permitted policy responses include trade restrictions that either ban exports from areas where no separation has been established, or allow exports only from particular zones or compartments within a country that is recognised as applying acceptable biosecurity standards (42, 45, 53, 60, 61, 62).

Data description

The dataset used in this study spans 216 countries over the period between 1996 and 2011. It reports the number of monthly outbreaks published by the OIE (www.oie.int). The OIE itself includes 180 Member Countries, 24 having joined since 2002, but reports outbreaks in both Member and non-member countries. Beginning in 1996, participating countries filed both annual and monthly reports of the number of new outbreaks within their borders. Because trade data were, until recently, reported on an annual basis, outbreak data were aggregated to the annual level. In order to test two different aggregations of trade data, two sets of dependent variables were constructed: a count of the number of outbreaks reported in each country, and a binary outbreak(s)/no outbreak measure for each country. These are the primary dependent variables in the analysis.

To identify the value at risk during outbreaks, proxies were secured for the economic consequences of outbreaks. Three measures of the potential economic losses due to an FMD outbreak or 'value at risk' were considered: agriculture value added, livestock production index, and the standing stock of livestock. The first is agriculture value added or agricultural GDP, as reported by FAO. This is a measure of value added in the agricultural sector – the annual income the sector yields to farmers, farm workers and associated industries. Since it is not possible to isolate the livestock sector within agriculture, this is an overestimate of the value at risk. While the value added by the livestock sector alone would be a better measure of value at risk, these data were not available for most of the countries in our study. The second is a measure of the growth trajectory of the livestock sector: the FAO livestock production index (LPI) calculated as a country's aggregate volume of production compared with a base period (in this case, between 2004 and 2006). It includes meat and milk, dairy products, eggs, honey, raw silk, wool and animal hides and skins, and is a proxy for the development of a country's livestock industry. The third is a measure of the assets that might be destroyed during efforts to control an outbreak – the standing stock of cattle, sheep and pigs in a country. It was hypothesised that all three measures would be positively correlated with *ex ante* risk mitigation measures, and hence negatively correlated with the likelihood that the disease will be reported to the OIE.

The authors are interested in two sets of risk factors: those relating to the structure and volume of international trade in live animals, and those relating to the biosecurity measures taken within importing countries and along trade routes. The trade dataset includes the volume of imports and exports of all cloven-hoofed animals reported to FAO between 1996 and 2011 (http://faostat3.fao.org/home/E). While FAO makes available data on the trade of other risk materials (e.g. meats, milk, hides, skins and genetic material) these are beyond the scope of the analysis.

Country imports and exports were aggregated in two different ways. The first was by the disease-free categories recognised by the OIE (Fig. 1). Using this aggregation the authors explored country risks in terms of the volume of imports from and exports to all countries in each designation. The number of countries in each disease-free category and the aggregate number of annual outbreaks per category are presented in Figure 2. While countries with disease-free designations tend to trade with countries with the same designation, they also import from and export to countries with FMD. This suggests that while disease history plays a role in trade decisions, it is not the only driving factor.

Insert Figures 1 and 2

The second aggregation was by geographically defined regions. More particularly, imports from and exports to each of the 22 geographical regions of the FAO were aggregated (Fig. 3). Owing to low trade volumes, Melanesia, Polynesia and Micronesia were combined into a single 'Pacific Islands' region. While resolution is lost by aggregating the data into regions as opposed to individual countries, not aggregating causes significant collinearity in the trade data among members of particular regional groups.

Insert Figure 3

Certain countries and regional groups of countries are regarded as safer trading partners than others (Figs 1–4). For example, India, Iran, Thailand, Turkey and Vietnam are known to be high-risk areas for FMD (mean annual number of outbreaks 1,555, 1,130, 69, 436 and 822, respectively). Other countries, such as the United States of America (USA), France, Germany, the UK, Australia and New Zealand, are known to be FMD disease-free.

Insert Figure 4

It was assumed that the volume of livestock imports captures the import risk – the probability that imports of infected animals will lead to an outbreak in the importing country. It was also assumed that the volume of livestock exports captures the export risk – the probability that exports into a risky port will lead to an outbreak in the exporting country. The authors do not have data on the specific mechanisms involved in export risks, but these would include mechanisms similar to those reported for African swine fever (26). That is, there is some probability that FMD contaminated material is 'picked up' and transported back to the exporting country in livestock containers/vessels, as occurs with many pest species (31).

With regard to biosecurity measures, FMD spread is affected by how well a country manages disease within its borders (40, 41, 63). A number of proxies were employed for this. One is the density of veterinarians registered with the OIE. This measure includes veterinarians in both private and public sectors, but does not include associated personnel such as veterinary technicians. A second is binary data on control measures reported to the OIE, including:

– inspection and interception at the border

– disease monitoring and surveillance of livestock

– the control of wild reservoirs and

– the presence of measures, such as veterinary cordon fences, that isolate disease-free regions within the country (www.oie.int).

The last three may also be interpreted as indirect proxies for the existence of endemic disease reservoirs within countries. For example, zoning isolates the quarantined zone areas where FMD is present. It was hypothesised that these measures will be positively related to the likelihood that an FMD outbreak will be reported as ‘present’ in the national herd. Their inclusion helps control for the presence of endemic, non-commercial livestock reservoirs that may potentially affect commercial disease incidence rates by providing sources of disease that may spread to commercial livestock (36, 45, 64).

Since the trading status of a country depends on a commitment to certain management practices prior to and in response to an outbreak (32), a second set of binary data were included on the practice of and prohibition of vaccination within a country. These contribute to the ‘disease-free’ designation given by the OIE, and serve as proxies both for the trading behaviour of a country, and for the presence of endemic disease reservoirs. A country that practises (or prohibits) vaccination will be more (or less) likely to possess an endemic disease reservoir. A country that prohibits vaccination will be more cautious of what they trade, and with whom, than a country that vaccinates its entire national herd. International market prices of meat are closely tied to a country's OIE disease-free designation, with the lowest risk designation fetching the highest market price. Countries that meet the requirements for a high disease-free designation will behave in ways that maintain that designation.

Table I reports the summary statistics of the data included in the analysis. Table II presents pairwise correlation coefficients for all non-trade variables.

Insert Tables I and II

Methods

In order to evaluate the effect of trade on relative disease risk, the impact of various risk factors on the probability that an FMD outbreak was reported in the national herd in a given period was first considered using each of the two models. The dependent variable in the first model is the number of new outbreaks reported in a country per year in the study period. Traditionally, both Poisson and negative binomial regression analyses have been used to analyse count data of this sort (65). While Poisson regression models are more robust to model misspecification than negative binomial models, the data are highly overdispersed (μ = 40.15, σ = 316.20), making a Poisson regression model inappropriate. A zero-inflated Poisson with scaled variances also proved inadequate. Therefore a negative binomial model was estimated, of the form:

[1] $y_{it} \sim NegativeBinomial(\theta_{it}, \kappa)$

[2] $$\theta_{it} = \exp\left[\alpha_{it} + \sum_{j=1}^{9} Z'_{jit}\beta_j + \sum_{k=1}^{5} M'_{ikt}\beta_{k+9} + \sum_{k=1}^{5} X'_{ikt}\beta_{k+14} + \varepsilon_{it}\right]$$

for country *i* in year *t*, where the dependent variable is the probability that a number of FMD outbreaks were reported to the OIE by a country, conditional on the linear predictors. The elements of *Z* include the following: value at risk, veterinarian density and binaries for disease control measures and management factors contributing to a country's disease-free designation. Owing to the non-linear nature of the negative binomial model, its estimation is sensitive to binary data and correlations between independent variables (66). Given the correlation between standing stocks of species, stocks of cattle, pigs and sheep were summed into a single measure of value at risk. Because of the correlation between border precautions and the prohibition of vaccination, the presence of border precautions was also dropped from the analysis. The elements of M and X are aggregate imports and exports, respectively, of all cloven-hoofed livestock between the country i and all other countries within each OIE disease-free designation category. Intercept and error terms are represented by α and ε respectively. The overdispersion parameter, κ, is estimated automatically in the regression.

Since the authors did not have observations for all countries for all years the data comprise an unbalanced panel. The model was estimated as a fixed effects negative binomial, using the method of maximum likelihood with standard errors, in Stata 14.0 (StataCorp, 2015, College Station, TX, USA). Non-linearity in model structure prevented specification tests for fixed versus random effects. While independence between the fixed effect (country) and other covariates is a strong assumption, relaxation of this assumption is left for future work.

The dependent variable in the second model is the presence or absence of a reported FMD outbreak in a country in particular year. That is, a binary outbreak/no outbreak measure was used for each country in each year (μ = 0.34, σ = 0.47). The trade data in this case refer to imports to and exports from each of the 20 FAO regions. This is meant to capture differences among regional risks for the main species traded internationally. Owing to non-linearity in the model structure, estimation of the negative binomial by maximum likelihood methods is difficult, particularly when dummy variables are used in the analysis (66).

Linear regression, logit/probit and tobit models are frequently used for binary data (65). The data in this study do not fit the assumptions for ordinary least squares regression, nor are the data truncated. A logistic model was therefore chosen, of the form:

[3] $\Pr(y_{it}=1) \sim \left[1+\exp(-\theta_{it})\right]^{-1}$

[4] $$\theta_{it} = \alpha_{it} + \sum_{j=1}^{12} Z'_{jit}\beta_j + \sum_{s=1}^{3}\sum_{k=1}^{20} M'_{ikt}\beta_{20s+k-8} + \sum_{s=1}^{3}\sum_{k=1}^{20} X'_{ikt}\beta_{20s+k+52} + \varepsilon_{it}$$

for country *i* in year *t*. The left-hand side of equation [3] is a binary indicator that an FMD outbreak was/was not reported to the OIE, conditional on the linear predictors. Specifically, $y_{it}=1$ when a country reported an outbreak; $y_{it}=0$ when no outbreaks were reported to the OIE. The elements of *Z* include the values at risk, veterinarian density and a set of binary biosecurity variables. Elements of *M* and *X* include aggregate imports and exports of cattle, pigs and sheep between the region containing country *i* and all regions *k*. Although trade data are available on other species that may transmit FMD, far fewer countries are involved and there is a high degree of collinearity between the data on other species. The constant intercept and error terms are represented by α and ε, respectively. The logistic model was estimated using the method of maximum likelihood with robust standard errors in Stata 14.0 (StataCorp, 2015), explicitly treating country as a random effect.

The logistic model was estimated with and without a one-year lag in trade. The reason for this is that disease spread, particularly through trade, is not instantaneous. Like an invasive species, a virus must be physically transported to a new location and establish a large enough population to be detected. However, there is uncertainty about the mean length of the lag. The FMD virus may persist in animals, animal products and the environment from days to months (48, 50). Once introduced, spread and detection will vary by species and biosecurity in the new location (42).

The estimates were then used to calculate the relative economic risks associated with trade. The authors took the trade-related relative economic risk of FMD outbreak as the product of the relative probability of disease occurrence from trade and the magnitude of potential damage caused by an FMD outbreak. The former was calculated directly from the odds ratio (OR), the exponential of the betas generated from the logistic regression (above) (67). By subtracting 1 from the OR we calculated the change in the odds for a one-unit change (1,000 head) in the importation (exportation) of livestock from (to) a particular region. Although it is generally understood that ORs overestimate relative risk (RR) when greater than 1 and underestimate it when less than 1, the degree of deviation between the two is more severe at high ORs and when the event is very likely to occur (68, 69, 70). Using the UK in 2001 as an example, two values of the potential economic damage of an FMD outbreak are presented: the aggregate dollar value of exports of cattle, sheep and pigs, and the dollar value of the agriculture sector. The former is a lower bound representing the short-term losses due to a time-lapse in trade in response to an FMD outbreak. This is an alternative to the long-term losses due to the culling of the standing stock. The latter provides an upper bound as value added by the agricultural sector to GDP.

Results

The results on the relative disease risks of trade, and the impacts of risk factors, are summarised in Tables III to VII. These report significance at the 10% level. The results of the disease-free designation trade aggregation model (negative binomial, explicit panel, fixed effects and standard errors) are reported in Table III. The results of the disaggregated regional trade model (logistic, explicit panel, random effects and robust standard errors) are reported in Tables IV through VI. Estimates of non-trade explanatory variables are reported in Table IV. Estimates of imports and exports are reported in Tables V and VI. Since this more disaggregated model has a large number of trade variables, only trade results that are statistically significant at the 10% level are presented. Detailed lists of all trade results may be found in Appendix A.

Insert Tables III to VII

Of the measures of value at risk, the livestock production index was selected as a measure of the development of a country's livestock industry. This was found to be negatively correlated with the probability of reporting disease outbreaks, in both models. Countries in which agricultural productivity was rapidly increasing were less likely to experience FMD outbreaks than countries in which agricultural output was stagnating. The other measures of value at risk were either uncorrelated with or did not significantly alter the odds of reporting an outbreak.

Of the measures that serve as proxies for the existence of endemic reservoirs of FMD in a country – monitoring and surveillance, the existence of control measures for wild reservoirs, and zoning – all were positively correlated with the probability of reporting an outbreak in the disaggregated model. However, in the aggregated model only monitoring and surveillance was positively correlated with the probability of reporting an outbreak. The existence of control measures for wild reservoirs and zoning were not statistically significant.

The authors had hypothesised that precautionary biosecurity measures would be negatively correlated with disease outbreaks. A strong negative correlation was found between the density of veterinarians and FMD outbreaks, significant at the 5% level in the disaggregated model but not significant in the aggregated model. In the disaggregated model, border precautions (which were removed from the aggregated model) were uncorrelated with FMD outbreaks. Also, it was found that the prohibition of vaccination was statistically associated with a reduction in the probability of a country reporting an outbreak, while the practice of vaccination did not have a significant effect in either model.

The authors' primary interest in the study was the relationship between trade and disease risk. The disease-free categories used by the OIE are also trade categories, since they are used in regulating which countries have access to what markets. To get an overview of the impact of the OIE trade structure on disease risk, the aggregated model reported in Table III was considered. These estimates showed the association between the RR of reported FMD outbreaks and the volume of trade into and out of countries belonging to each of the OIE's main disease-free categories:

– disease-free without vaccination

– disease-free with vaccination

– disease-free zones without vaccination

– disease-free zones with vaccination

– not disease-free.

The authors had hypothesised that the disease risks of imports and exports would be lower for countries having disease-free status, and higher for those where the disease is endemic. It was found that imports from countries in the disease-free, no vaccination category were indeed risk reducing, and that imports from the disease-free zones with vaccination and not disease-free categories were risk increasing. Exports into countries in disease-free zones without vaccination were risk reducing, but exports into disease-free zones with vaccination were risk increasing.

The disaggregated model reported in Tables IV to VI provided an alternative perspective on the relation between trade and disease risks in the intermediate OIE disease categories. The two aggregations are presented alongside each other in Tables VIII and IX.

Insert Tables VIII and IX

For the disaggregated model the results turned out to be more mixed. The authors had expected the probability of outbreaks to be increasing in imports of animals from regions in which FMD is known to be endemic, and the results generally confirm this (see Figs 3 and 4). Imports from regions experiencing no outbreaks were generally negatively correlated with the probability of reported outbreaks (and vice versa). Interestingly, in both the lagged and unlagged models, imports from the North America and Eastern Asia regions were positively correlated with the likelihood of FMD outbreaks in the importing country.

A number of region-specific differences within species were also found. For imports in the unlagged model, cattle brought in from Southern Asia were positively correlated with the probability of reported FMD outbreaks in importing countries, but cattle brought in from Central America and Western Europe were negatively correlated with reported outbreaks. Among pigs, imports from Western Asia were positively correlated with reported outbreaks, but imports from North America, Southern Europe, Australia and New Zealand were all negatively correlated with reported outbreaks. For sheep, imports from Southern Africa, Southeast Asia and Southern Europe were all negatively correlated with reported FMD outbreaks.

The authors had less well-defined assumptions about the indirect effect of exports on disease risks. For some regions, exports were negatively correlated with FMD outbreaks in the exporting country. In the unlagged model, examples include cattle to Central and Southeast Asia; pigs to Eastern Africa; sheep to Central America and Southeast Asia. However, exports of cattle to Southern Africa, North America and Eastern Asia were also found to be positively associated with reported outbreaks. Similarly, exports of pigs to Western Asia and sheep to Eastern and Southern Asia and the Pacific Islands were also all positively correlated with FMD outbreaks in the exporting country.

In general, a greater number of trade variables were found to be associated with FMD outbreaks in the lagged than the unlagged model. This is particularly true for imports and exports of pigs and sheep. Nonetheless, with the exception of some regions/species, the estimates of risk were consistent between the two models. See, for example, imports of sheep from Southeast Asia and Southern Europe, or exports of pigs to Southeast and Western Asia.

Based on these results, the trade-related FMD risk for the UK in 2011 was calculated according to regions of importation or exportation. The results are reported in Figures 5 and 6 and Table VII. In this context, negative risk implies that, all else being equal, an increase in trade by a country with a particular region will be statistically associated with a reduction in the likelihood of disease outbreaks in that country. By contrast, positive risk implies that, all else being equal, an increase in trade by a country with a particular region will be statistically associated with an increase in the likelihood of disease outbreaks in that country. The risk as measured by expected forgone live animal export earnings (lower bound) was found to be relatively minor. The risk as measured by expected output in the whole agriculture sector (upper bound) was found to be quite large. High relative economic risks of trade were found in low-income regions where biosecurity tends to be lax, but also in high-income regions where trade volumes are high (e.g. North America and Eastern Asia).

Insert Figures 5 and 6

Discussion

The disease risks of the trade in live animals depend on the structure and volume of trade, the biosecurity measures undertaken by trading partners, and on interactions between the two. As expected, the authors found a generally positive relationship between the quantity of live animals imported from riskier countries and the probability of reported disease outbreaks. Globally, trade with disease-free countries is negatively associated with reported outbreaks; trade with countries experiencing outbreaks or where the disease is endemic amongst wild populations is positively associated with reported outbreaks. These are the most intuitive and transparent trade-related risks revealed by the models.

At the international scale, the findings on imports in this study are broadly consistent with those of others (37, 38, 39, 40, 41, 63), even though the methods are different. Berentsen *et al.* (40), Garner & Lack (41) and Schoenbaum & Disney (63), for example, used simulations in a coupled epidemiological–economic framework. Hartnett *et al.* (38), Martínez-López *et al.* (37) and Miller *et al.* (39), grounded their analysis in data, as in this study, but relied on stochastic simulation to determine the probability of introduction using a much smaller range of trading partners. Nevertheless, the estimates of import risk often reach the same conclusions.

Somewhat counter-intuitively, this study also found that imports of cattle (pigs) from the North American (Eastern Asia) region were positively correlated with the probability of FMD outbreaks. Yet, with the exception of a 2011 outbreak in Bermuda and the 1997 Taiwan outbreak, North America and Eastern Asia were free of FMD over the study period. Indeed, the USA has not experienced an FMD outbreak since 1929 (71), and Canada has not experienced an outbreak since 1952 (72). Others have reached similar findings. Miller *et al.* (39), for example, found the probability of FMD introduction to the USA from Canada to be positive (0.048%). A potential explanation for this is that infected countries seeking to improve their biosecurity and/or their trading position have an incentive to import livestock from uninfected countries such as the USA. That is, the causality runs not from imports to outbreaks, but from outbreaks to imports.

In two other respects the findings of this study differ from those in the wider literature. The first is that the authors found exports to be as strongly correlated with disease risk as imports. This is consistent with findings on African swine fever by Mur *et al.* (26) that identified trade vehicles returning from infected areas as a source of risk. However, few other studies have explored the relationship between exports and disease risk. This study did not include explicit measures of the risk factors associated with exports, nor did the authors have data on vessel itineraries. However, it is noted that the risks of trade into regions characterised by high trade volumes and a complex trade network – North America and East Asia (Figures 5 and 6, Table VIII) – are frequently positive. This suggests that treating trade flows as unidirectional (considering only the propagule pressure associated with imports) overlooks a significant source of disease risk.

The second difference concerns countries with intermediate disease status according to the OIE. At the extremes of the OIE spectrum, the conclusions from the disease status and regional models coincide. Higher-risk geographical regions often have disease endemic status, and lower-risk regions often have disease-free status (see Figures 1 and 3). The estimates of the risk of trade into and out of both geographical regions and OIE zones are consistent with this observation (Tables VIII and IX). At intermediate disease designations, the ability of the disease-free grouping model to estimate risk is less clear. Although the direction of impact is as expected, the *p*-values of the incidence rate ratio (IRR) estimates are not sufficiently precise to determine the sign of the effect. When aggregating trading partners by geographical region two notable differences were found between regions with intermediate designations: Southern Africa and Southeast Asia. While trade with countries carrying intermediate designations was positively associated with FMD outbreaks in the disease-free grouping model, imports (exports) of sheep from Southern Africa and Southeast Asia (Southeast Asia) were negatively correlated with outbreaks (Tables VIII and IX). Many of the countries within these regions implemented vaccination protocols and had few or no outbreaks during the study period (e.g. Botswana, Namibia and South Africa; Malaysia and the Philippines). It is possible that there are unobserved spatial effects captured by the regional aggregation that are not accounted for when grouping trade by disease-free status (though this should be at least partially accounted for by country-level fixed/random effects).

Nor does the disease-free grouping capture the effect of different species or differences in regional trade volumes on risk. Different species have different degrees of susceptibility to and infectivity with FMD (42, 45), and animal husbandry standards and biosecurity measures would be expected to differ among types of livestock production. For example, pigs tolerate proportionately larger dosages of virus compared with cattle and sheep before contracting the disease but infected pigs proportionately excrete the virus in larger quantities than cattle and sheep (42). At the same time, while cattle may have a lower excretion of the virus per unit body mass than pigs, their greater size may make them excrete greater quantities of the virus and so pose a larger risk (45). In this respect there is added value in using a regional trade aggregation to evaluate the risks of trade.

The findings on the relation between disease outbreaks and biosecurity measures were largely as expected. To interpret these, however, recall that several of the measures tested are themselves evidence for the existence of endemic FMD reservoirs in the country. Monitoring and surveillance, the presence of controls for wild reservoirs, and zoning are all activities that take place in countries where the disease is endemic in wild and/or domesticated populations. In countries that implement disease-free zones alongside wild reservoirs, the control and isolation of wild animals in which the disease is endemic is the primary goal of management (36). Participation in the international live animal trade is conditional on maintaining disease-free compartments. Since the existence of wild reservoirs increases the risks to a country's trading partners, it is not surprising that these activities are positively and significantly related to disease outbreaks.

The two biosecurity measures tested, the density of veterinarians and precautions at the borders, were both expected to be increasing in the value at risk, and so to be negatively related to the probability of disease outbreaks. While, for the density of veterinarians, the IRR and the OR were indeed significantly below 1, it was found that the existence of protective measures at the border was uncorrelated with the probability of FMD outbreaks. Similarly, the practice of vaccination was not a significant factor in FMD disease risk. The prohibition of vaccination, on the other hand, was negatively correlated with the probability of reported outbreaks. There are two possible explanations for this. First, the prohibition of vaccination generally indicates the lack of (or strict isolation of) an endemic disease reservoir. The absence of an endemic population removes one potential avenue of disease transmission to commercial livestock. Prohibition of vaccination is also required for the highest disease-free status, and binds countries to particular sets of management practices and particular responses to FMD outbreaks. Since these responses carry a high cost, countries that prohibit vaccination are likely to be more cautious about what they trade and with whom.

The analysis used in this study does have its limitations. While the authors identify an association between observed outbreaks and factors that may be implicated in their occurrence, the models are correlative and are not able to assign causality. Indeed, it is difficult to establish causality outside of controlled experiments (65) (Appendix B). Nor can the authors exclude the possibility that certain explanatory variables are biased, which creates a potential problem in identifying their true effect. The most likely sources of bias are: unobserved heterogeneity in the sample, omitted variables bias and simultaneity (73). Each of these is addressed in turn.

There is potential in both models that the errors are spatially correlated due to unobserved, time-varying events affecting the animal movement across borders of adjacent countries (e.g. conflict, famine, smuggling, natural disasters, etc.). This would lead to spatially correlated effects on reporting and/or the outcomes themselves. If present, however, this should be at least partially captured by country-level fixed/random effects. Nor do the models account for bias in reporting outbreaks between countries, often termed 'endogenous stratification' (74, 75, 76). While differences in measurement and reporting between countries are expected, the local involvement of the OIE in its Member Countries should help to alleviate potential sampling bias.

While the authors believe that they have accounted for the most relevant factors in the international spread of FMD, they cannot exclude the possibility that there are others. Live animals are not the only source of risk, and detailed data on shipping routes and trade volumes in other risk materials, such as products of animal origin, were lacking. The FMD virus is capable of persisting in the environment for extended periods of time, ranging from weeks to months, depending on the nature of the contaminated material (manure, bedding, fodder, clothing, equipment) and environmental conditions (temperature, humidity, pH) (42, 45, 46, 47, 48). Therefore, it would be useful to consider the trade in other risk materials that may potentially spread FMD, including meat, milk, hides and skins.

Simultaneity, also known as reverse causation, occurs when an explanatory variable (in this case, the trade response) and a dependent variable (disease outbreaks) are jointly determined at the same moment in time (73). To address this, the trade data were time-lagged. This should have helped to alleviate the problem, although there is a degree of uncertainty about the mean length of the lag. Resistance, persistence and infectivity vary significantly across species and environments (42) and there are likely to be differences in the conditions in which species are transported. Each of these will affect the length of time between infection and detection. Time-lagging the data should also partially account for potential autocorrelation of the dependent variable. Specifically, the logistic model assumes that the 'choice' of the dependent variable is independent over time (77). That is, past states have no influence on the current state and there is no lag in the response of the dependent to the independent variables.

Several other issues are worth mentioning. For the more disaggregated model the odds ratios provide less reliable approximations of relative risk as incidence rates increase or as the OR deviates from 1 (68, 70). Odds ratios less than 1 tend to underestimate RR; ORs greater than 1 overestimate it (70). It is likely that the proxies for wild reservoirs (veterinarian density) overestimate (underestimate relative) risk, though the authors believe that they have correctly identified the direction of the effect.

Aggregating trade by disease status or region loses a certain degree of spatial resolution and may pose a potential source of bias. The estimates in this study are, from a global perspective, the change in probability that a country will have reported an outbreak given that it engaged in a particular biosecurity measure. This is different from an analysis of the effect of biosecurity on the probability of an outbreak within a single country. This potentially matters if the sanitary conditions and regulations pertaining to the surveillance and monitoring for disease are very different between the countries in a particular region. The risks undertaken by an importing or exporting country depend on biosecurity measures at the point of entry, which vary from country to country. For example, Botswana, Namibia and

South Africa – all countries that achieved a status of disease-free zones with no vaccination during the study period – would be expected to behave differently from other countries in the Southern Africa region (e.g. Lesotho and Swaziland). In this case, the trade risks for each country are averaged together to estimate the global risk of trade for the region. The risk of importing infected livestock is likely to be overestimated for countries such as the USA or those of the BRICS (Brazil, Russia, India, China and South Africa), which have stringent protocols at the border, and underestimated for countries whose border security is more lax.

It would be helpful to have precise estimates of the different risks associated with biosecurity and trade for individual countries. Indeed, the Global FMD Disease Control Strategy relies heavily on increasing biosecurity, particularly the development of veterinary services and vaccination, in transitioning endemic countries to disease-free with vaccination status (54).

The results of this study represent long-term average estimates of risk. This will be appropriate for countries whose conditions remain relatively constant over the study period, but less appropriate for countries that experience short-term fluctuations in disease or trade. For instance, Eastern Asia, Northern Europe and South America are generally low risk areas, but some countries of these regions experienced a large number of reported outbreaks during the 1997 Taiwan and 2001 UK/Uruguay epidemics (see Fig. 4). Marked changes in trade volumes were also observed around the 2007–2009 recession, when patterns of disease risk paralleled those of trade (Fig. 4).

In the future, the authors hope to explicitly account for changes in trade networks. The 'natural' response by an importing country to an FMD outbreak is to impose trade bans on high-risk products from the exporting country with FMD (53), i.e. to cut off 'propagule pressure' of risk materials. The World Trade Organization (WTO) makes available information on the initialisation, length and termination of trade sanctions between countries in response to FMD outbreaks.

However, the authors were unable to exploit such information in this paper.

Conclusions

To conclude, it is worth repeating the central finding that export risks may be as large as or greater than import risks, and that high-risk regions may be characterised as much by high trade volumes and complex trade networks as by lax biosecurity measures. Current risk assessments that consider only the risk posed by direct 'propagule pressure' – the one-way threat posed by imports – may therefore overlook a potentially significant risk factor for the spread of FMD. Ignoring the indirect effects of exports means that the 'natural' trade response to disease – banning imports – may prove less effective at mitigating risk than the many countries would like to believe. It was also found that a country's disease-free status provides a reasonable approximation of the riskiness of trading with that country, but a regional grouping captures finer-scale and species-specific characteristics of risk. This can potentially inform targeting of trade actions to mitigate disease.

Acknowledgements

This work was funded by NSF grant 1414374 as part of the joint NSF-NIH-USDA Ecology and Evolution of Infectious Diseases program, and by UK Biotechnology and Biological Sciences Research Council grant BB/M008894/1.

References

1. Perrings C. (2014). – Our uncommon heritage: Biodiversity change, ecosystem services, and human wellbeing. Cambridge University Press, Cambridge, United Kingdom, 522 pp. doi:10.1017/CBO9781107338913.

2. Cassey P., Blackburn T.M., Russel G.J., Jones K.E. & Lockwood J.L. (2004). – Influences on the transport and establishment of exotic bird species: An analysis of the parrots (Psittaciformes) of

the world. *Global Change Biology*, **10** (4), 417–426. doi:10.1111/j.1529-8817.2003.00748.x.

3. Semmens B.X., Buhle E.R., Salomon A.K. & Pattengill-Semmens C.V. (2004). – A hotspot of non-native marine fishes: Evidence for the aquarium trade as an invasion pathway. *Marine Ecology Progress Series*, **266**, 239–244. doi:10.3354/meps266239.

4. Dalmazzone S. (2000). – Economic factors affecting vulnerability to biological invasions. *In* The economics of biological invasions (C. Perrings, M. Williamson & S. Dalmazzone, eds). Edward Elgar, Cheltenham, United Kingdom, 17–30. doi:10.4337/9781781008645.00010.

5. Vila M. & Pujadas J. (2001). – Land-use and socio-economic correlates of plant invasions in European and North African countries. *Biol. Conserv.*, **100** (3), 397–401. doi:10.1016/S0006-3207(01)00047-7.

6. Dehnen-Schmutz K., Holdenrieder O., Jeger M.J. & Pautasso M. (2010). – Structural change in the international horticultural industry: Some implications for plant health. *Scientia Horticulturae*, **125** (1), 1–15. doi:10.1016/j.scienta.2010.02.017.

7. Pavlin B., Schloegel L.M. & Daszak P. (2009). – Risk of importing zoonotic diseases through wildlife trade, United States. *Emerg. Infect. Dis.*, **15** (11), 1721–1726. doi:10.3201/eid1511.090467.

8. Smith K.F., Behrens M., Schloegel L.M., Marano N., Burgiel S. & Daszak P. (2009). – Reducing the risks of the wildlife trade. *Science*, **324** (5927), 594–595. doi:10.1126/science.1174460.

9. Tatem A.J., Rogers D.J. & Hay S.I. (2006). – Global transport networks and infectious disease spread. *Adv. Parasitol.*, **62**, 293–343. doi:10.1016/S0065-308X(05)62009-X.

10. Tatem A.J., Hay S.I. & Rogers D.J. (2006). – Global traffic and disease vector dispersal. *Proc. Natl Acad. Sci. USA*, **103** (16), 6242–6247. doi:10.1073/pnas.0508391103.

11. Tatem A.J. (2009). – The worldwide airline network and the dispersal of exotic species: 2007–2010. *Ecography*, **32** (1), 94–102. doi:10.1111/j.1600-0587.2008.05588.x.

12. Karesh W.B., Dobson A., Lloyd-Smith J.O., Lubroth J., Dixon M.A., Bennett M., Aldrich S., Harrington T., Formenty P., Loh E.H., Machalaba C.C., Thomas M.J. & Heymann D.L. (2012). – Ecology of zoonoses: Natural and unnatural histories. *Lancet*, **380** (9857), 1936–1945. doi:10.1016/S0140-6736(12)61678-X.

13. Xu R.H., He J.F., Evans M.R., Peng G.W., Field H.E., Yu D.W., Lee C.K., Luo H.M., Lin W.S., Lin P., Li L.H., Liang W.J., Lin J.Y. & Schnur A. (2004). – Epidemiologic clues to SARS origin in China. *Emerg. Infect. Dis.*, **10** (6), 1030–1037. doi:10.3201/eid1006.030852.

14. Li W.D., Shi Z.L., Yu M., Ren W.Z., Smith C., Epstein J.H., Wang H.Z., Crameri G., Hu Z.H., Zhang H.J., Zhang J.H., McEachern J., Field H., Daszak P., Eaton B.T., Zhang S.Y. & Wang L.F. (2005). – Bats are natural reservoirs of SARS-like coronaviruses. *Science*, **310** (5748), 676–679. doi:10.1126/science.1118391.

15. Kilpatrick A.M., Chmura A.A., Gibbons D.W., Fleischer R.C., Marra P.P. & Daszak P. (2006). – Predicting the global spread of H5N1 avian influenza. *Proc. Natl Acad. Sci. USA*, **103** (51), 19368–19373. doi:10.1073/pnas.0609227103.

16. Rweyemamu M.M. & Astudillo V.M. (2002). – Global perspective for foot and mouth disease control. *Rev. Sci. Tech. Off. Int. Epiz.*, **21** (3), 765–773. doi:10.20506/rst.21.3.1378.

17. Karesh W.B., Cook R.A., Bennett E.L. & Newcomb J. (2005). – Wildlife trade and global disease emergence. *Emerg. Infect. Dis.*, **11** (7), 1000–1002. doi:10.3201/eid1107.050194.

18. Fevre E.M., Bronsvoort B., Hamilton K.A. & Cleaveland S. (2006). – Animal movements and the spread of infectious diseases. *Trends Microbiol.*, **14** (3), 125–131. doi:10.1016/j.tim.2006.01.004.

19. Drew T.W. (2011). – The emergence and evolution of swine viral diseases: to what extent have husbandry systems and global trade contributed to their distribution and diversity? *In* The spread of pathogens through international trade (S.C. MacDiarmid, ed.). *Rev. Sci. Tech. Off. Int. Epiz.*, **30** (1), 95–106. doi:10.20506/rst.30.1.2020.

20. Whittington R.J. & Chong R. (2007). – Global trade in ornamental fish from an Australian perspective: The case for revised import risk analysis and management strategies. *Prev. Vet. Med.*, **81** (1–3), 92–116. doi:10.1016/j.prevetmed.2007.04.007.

21. Scott A., Zepeda C., Garber L., Smith J., Swayne D., Rhorer A., Kellar J., Shimshony A., Batho H., Caporale V. & Giovannini A. (2006). – The concept of compartmentalisation. *Rev. Sci. Tech. Off. Int. Epiz.*, **25** (3), 873–879. doi:10.20506/rst.25.3.1702.

22. Brasier C.M. (2008). – The biosecurity threat to the UK and global environment from international trade in plants. *Plant Pathol.*, **57** (5), 792–808. doi:10.1111/j.1365-3059.2008.01886.x.

23. Perrings C., Burgiel S., Lonsdale M., Mooney H. & Williamson M. (2010). – International cooperation in the solution to trade-related invasive species risks. *Ann. N.Y. Acad. Sci.*, **1195** (1), 198–212. doi:10.1111/j.1749-6632.2010.05453.x.

24. Perrings C., Mooney H., Lonsdale M. & Burgeil S. (2010). – Globalization and invasive species: Policy and management options. *In* Bioinvasions and globalization: Ecology, economics, management and policy (C. Perrings, H. Mooney & M. Williamson, eds). Oxford University Press, Oxford, United Kingdom, 235–250. doi:10.1080/19390459.2011.604558.

25. Hardstaff J.L., Häsler B. & Rushton J.R. (2015). – Livestock trade networks for guiding animal health surveillance. *BMC Vet. Res.*, **11**, 82. doi:10.1186/s12917-015-0354-4.

26. Mur L., Martínez-López B. & Sánchez-Vizcaíno J.M. (2012). – Risk of African swine fever introduction into the European

Union through transport-associated routes: returning trucks and waste from international ships and planes. *BMC Vet. Res.*, **8**, 149. doi:10.1186/1746-6148-8-149.

27. Barker I., Brownlie J., Peckham C., Pickett J., Stewart W., Waage J., Wilson P. & Woolhouse M. (2006). – Foresight. Infectious diseases: Preparing for the future. A vision of future detection, identification, and monitoring systems. Office of Science and Innovation, London, United Kingdom, 118 pp. Available at: www.gov.uk/government/publications/infectious-diseases-preparing-for-the-future (accessed on 1 September 2015).

28. King D.A., Peckham C., Waage J.K., Brownlie J. & Woolhouse M.E.J. (2006). – Infectious diseases: Preparing for the future. *Science*, **313** (5792), 1392–1393. doi:10.1126/science.1129134.

29. MacDiarmid S.C. (2011). – Introduction. *In* The spread of pathogens through international trade (S.C. MacDiarmid, ed.). *Rev. Sci. Tech. Off. Int. Epiz.*, **30** (1), 13–17. doi:10.20506/rst.30.1.2015.

30. Brückner G.K. (2011). – Managing the risks of disease transmission through trade: A commodities-based approach? *In* The spread of pathogens through international trade (S.C. MacDiarmid, ed.). *Rev. Sci. Tech. Off. Int. Epiz.*, **30** (1), 289–296. doi:10.20506/rst.30.1.2030.

31. Hulme P.E. (2009). – Trade, transport and trouble: managing invasive species pathways in an era of globalization. *J. Appl. Ecol.*, **46** (1), 10–18. doi:10.1111/j.1365-2664.2008.01600.x.

32. World Organisation for Animal Health (OIE) (2016). – Terrestrial Animal Health Code. OIE, Paris. Available at: www.oie.int/en/international-standard-setting/terrestrial-code/access-online/ (accessed on 5 May 2017).

33. World Trade Organization (WTO) (2013). – International trade statistics. WTO, Geneva. Available at:

www.wto.org/english/res_e/statis_e/its2012_e/its12_appendix_e.htm (accessed on 8 May 2017).

34. International Monetary Fund (IMF) (2013). – World economic outlook: Global prospects and policies. IMF, Washington D.C. Available at: www.imf.org/external/pubs/ft/weo/2013/01/ (accessed on 1 September 2015).

35. Di Nardo A., Knowles N.J. & Paton D.J. (2011). – Combining livestock trade patterns with phylogenetics to help understand the spread of foot and mouth disease in sub-Saharan Africa, the Middle East and Southeast Asia. *In* The spread of pathogens through international trade (S.C. MacDiarmid, ed.). *Rev. Sci. Tech. Off. Int. Epiz.*, **30** (1), 63–85. doi:10.20506/rst.30.1.2022.

36. Jori F., Vosloo W., Du Plessis B., Bengis R., Brahmbhatt D., Gummow B. & Thomson G.R. (2009). – A qualitative risk assessment of factors contributing to foot and mouth disease outbreaks in cattle along the western boundary of the Kruger National Park. *Rev. Sci. Tech. Off. Int. Epiz.*, **28** (3), 917–931. doi:10.20506/rst.28.3.1932.

37. Martínez-López B., Perez A.M., De la Torre A. & Sánchez-Vizcaíno Rodriguez J.M. (2008). – Quantitative risk assessment of foot-and-mouth disease introduction into Spain via importation of live animals. *Prev. Vet. Med.*, **86** (1–2), 43–56. doi:10.1016/j.prevetmed.2008.03.003.

38. Hartnett E., Adkin A., Seaman M., Cooper J., Watson E., Coburn H., England T., Marooney C., Cox A. & Wooldridge M. (2007). – A quantitative assessment of the risks from illegally imported meat contaminated with foot and mouth disease virus to Great Britain. *Risk Analysis*, **27** (1), 187–202. doi:10.1111/j.1539-6924.2006.00869.x.

39. Miller G.Y., Ming J., Williams I. & Gorvett R. (2012). – Probability of introducing foot and mouth disease into the United States via live animal importation. *Rev. Sci. Tech. Off. Int. Epiz.*, **31** (3), 777–787. doi:10.20506/rst.31.3.2154.

40. Berentsen P.B.M., Dijkhuizen A.A. & Oskam A.J. (1992). – A dynamic model for cost–benefit analyses of foot-and-mouth disease control strategies. *Prev. Vet. Med.*, **12** (3–4), 229–243. doi:10.1016/0167-5877(92)90052-H.

41. Garner M.G. & Lack M.B. (1995). – An evaluation of alternate control strategies for foot-and-mouth disease in Australia: A regional approach. *Prev. Vet. Med.*, **23** (1–2), 9–32. doi:10.1016/0167-5877(94)00433-J.

42. Alexandersen S., Zhang Z., Donaldson A.I. & Garland A.J.M. (2003). – The pathogenesis and diagnosis of foot-and-mouth disease. *J. Comp. Pathol.*, **129** (1), 1–36. doi:10.1016/S0021-9975(03)00041-0.

43. Arzt J., Juleff N., Zhang Z. & Rodriguez L.L. (2011). – The pathogenesis of foot-and-mouth disease I: Viral pathways in cattle. *Transbound. Emerg. Dis.*, **58** (4), 291–304. doi:10.1111/j.1865-1682.2011.01204.x.

44. Arzt J., Baxt B., Grubman M.J., Jackson T., Juleff N., Rhyan J., Rieder E., Waters R. & Rodriguez L.L. (2011). – The pathogenesis of foot-and-mouth disease II: Viral pathways in swine, small ruminants, and wildlife; myotropism, chronic syndromes, and molecular virus–host interactions. *Transbound. Emerg. Dis.*, **58** (4), 305–326. doi:10.1111/j.1865-1682.2011.01236.x.

45. Sutmoller P., Barteling S.S., Casas Olascoaga R. & Sumption K.J. (2003). – Control and eradication of foot-and-mouth disease. *Virus Res.*, **91** (1), 101–144. doi:10.1016/S0168-1702(02)00262-9.

46. Ryan E., Mackay D. & Donaldson A. (2008). – Foot-and-mouth disease virus concentrations in products of animal origin. *Transbound. Emerg. Dis.*, **55** (2), 89–98. doi:10.1111/j.1865-1682.2007.01004.x.

47. Callis J.J. (1996). – Evaluation of the presence and risk of foot and mouth disease virus by commodity in international trade.

Rev. Sci. Tech. Off. Int. Epiz., **15** (3), 1075–1085. doi:10.20506/rst.15.3.974.

48. Paton D.J., Sinclair M. & Rodríguez R. (2010). – Qualitative assessment of the commodity risk for spread of foot-and-mouth disease associated with international trade in deboned beef. *Transbound. Emerg. Dis.*, **57** (3), 115–134. doi:10.1111/j.1865-1682.2010.01137.x.

49. Sutmoller P. & Casas Olascoaga R. (2003). – The risks posed by the importation of animals vaccinated against foot and mouth disease and products derived from vaccinated animals: a review. *Rev. Sci. Tech. Off. Int. Epiz.*, **22** (3), 823–835. doi:10.20506/rst.22.3.1435.

50. Cottral G.E. (1969). – Persistence of foot-and-mouth disease virus in animals, their products and the environment. *Bull. Off. Int. Epiz.*, **71** (3-4), 549–568. Available at: http://doc.oie.int/dyn/portal/index.seam?page=alo&aloId=29758&fonds=&menu=&cid=586 (accessed on 8 May 2017).

51. Alexandersen S. & Mowat N. (2005). – Foot-and-mouth disease: Host range and pathogenesis. *Curr. Top. Microbiol. Immunol.*, **288**, 9–42. doi:10.1007/3-540-27109-0_2.

52. Knight-Jones T.J.D. & Rushton J. (2013). – The economic impacts of foot and mouth disease – What are they, how big are they and where do they occur? *Prev. Vet. Med.*, **112** (3–4), 161–173. doi:10.1016/j.prevetmed.2013.07.013.

53. Grubman M.J., Moraes M.P., Segundo F.D.-S., Pena L. & De Los Santos T. (2008). – Evading the host immune response: How foot-and-mouth disease virus has become an effective pathogen. *FEMS Immunol. Med. Microbiol.*, **53** (1), 8–17. doi:10.1111/j.1574-695X.2008.00409.x.

54. World Organisation for Animal Health (OIE) and Food and Agriculture Organization (FAO) (2012). – The global foot and mouth disease control strategy – Strengthening animal health systems

through improved control of major diseases. OIE, Paris, FAO, Rome, 253 pp. Available at: www.oie.int/doc/ged/D11886.PDF (accessed on 8 May 2017).

55. Sobrino F. & Domingo E. (2001). – Foot-and-mouth disease in Europe. *Eur. Molec. Biol. Org. (EMBO) Rep.*, **2** (6), 459–461. doi:10.1093/embo-reports/kve122.

56. Thompson D., Muriel P., Russell D., Osborne P., Bromley A., Rowland M., Creigh-Tyte S. & Brown C. (2002). – Economic costs of the foot and mouth disease outbreak in the United Kingdom in 2001. *Rev. Sci. Tech. Off. Int. Epiz.*, **21** (3), 675–687. doi:10.20506/rst.21.3.1353.

57. Yang P.C., Chu R.M., Chung W.B. & Sung H.T. (1999). – Epidemiological characteristics and financial costs of the 1997 foot-and-mouth disease epidemic in Taiwan. *Vet. Rec.*, **145** (25), 731–734. Available at: http://veterinaryrecord.bmj.com/content/145/25/731.short (accessed on 30 May 2017).

58. Williamson M. (1999). – Invasions. *Ecography*, **22** (1), 5–12. doi:10.1111/j.1600-0587.1999.tb00449.x.

59. Williamson M. (1996). – Biological invasions. Chapman and Hall, London, 244 pp.

60. Sugiura K. & Murray N. (2011). – Risk analysis and its link with standards of the World Organisation for Animal Health. *In* The spread of pathogens through international trade (S.C. MacDiarmid, ed.). *Rev. Sci. Tech. Off. Int. Epiz.*, **30** (1), 281–288. doi:10.20506/rst.30.1.2031.

61. Ratananakorn L. & Wilson D. (2011). – Zoning and compartmentalisation as risk mitigation measures: An example from poultry production. *In* The spread of pathogens through international trade (S.C. MacDiarmid, ed.). *Rev. Sci. Tech. Off. Int. Epiz.*, **30** (1), 297–307. doi:10.20506/rst.30.1.2029.

62. Leforban Y. (1999). – Prevention measures against foot-and-mouth disease in Europe in recent years. *Vaccine*, **17** (13–14), 1755–1759. doi:10.1016/S0264-410X(98)00445-9.

63. Schoenbaum M.A. & Disney W.T. (2003). – Modeling alternative mitigation strategies for a hypothetical outbreak of foot-and-mouth disease in the United States. *Prev. Vet. Med.*, **58** (1–2), 25–52. doi:10.1016/S0167-5877(03)00004-7.

64. Thomson G.R., Vosloo W. & Bastos A.D.S. (2003). – Foot and mouth disease in wildlife. *Virus Res.*, **91** (1), 145–161. doi:10.1016/S0168-1702(02)00263-0.

65. Cameron A.C. & Trivedi P.K. (2005). – Microeconometrics: Methods and applications. Cambridge University Press, Cambridge, 1034 pp. doi:10.1017/CBO9780511811241.

66. Allison P.D. & Waterman R.P. (2002). – Fixed-effects negative binomial regression models. *Sociol. Methodol.*, **32** (1), 247–265. doi:10.1111/1467-9531.00117.

67. Gelman A. & Hill J. (2007). – Data analysis using regression and multilevel/hierarchical models. Cambridge University Press, New York, 625 pp. doi:10.1017/CBO9780511790942.

68. Cohen M.P. (2000). – Note on the odds ratio and the probability ratio. *J. Educ. Behav. Stat.*, **25** (2), 249–252. doi:10.3102/10769986025002249.

69. Davies H.T.O., Crombie I.K. & Tavakoli M. (1998). – When can odds ratios mislead? *Br. Med. J.*, **316**, 989–991. doi:10.1136/bmj.316.7136.989.

70. Zhang J. & Yu K.F. (1998). – What's the relative risk? A method of correcting the odds ratio in cohort studies of common outcomes. *J. Am. Vet. Med. Assoc.*, **280** (19), 1690–1691. doi:10.1001/jama.280.19.1690.

71. Metcalf H.E. & McElvaine M.D. (1995). – Risk of introducing exotic disease through importation of animals and animal products. *In* Risk assessment for veterinary biologicals (E.G.S. Osborne & J.W. Glosser, eds). *Rev. Sci. Tech. Off. Int. Epiz.*, **14** (4), 951–956. doi:10.20506/rst.14.4.907.

72. Sellers R.F. & Daggupaty S.M. (1990). – The epidemic of foot-and-mouth disease in Saskatchewan, Canada, 1951–1952. *Can. J. Vet. Res.*, **54** (4), 457–464. Available at: www.ncbi.nlm.nih.gov/pmc/articles/PMC1255693/ (accessed on 1 September 2015).

73. Kennedy P. (2008). – A guide to econometrics. 6th Ed., Wiley-Blackwell, Malden, United States of America, 598 pp. doi:10.1017/CBO9780511753930.

74. Shaw D. (1988). – On-site samples' regression: Problems of non-negative integers, truncation, and endogenous stratification. *J. Econometrics*, **37** (2), 211–223. doi:10.1016/0304-4076(88)90003-6.

75. Englin J. & Shonkwiler J.S. (1995). – Estimating social welfare using count data models: An application to long-run recreation demand under conditions of endogenous stratification and truncation. *Rev. Econ. Stat.*, **77** (1), 104–112. doi:10.2307/2109996.

76. Richards T.J., Shanafelt D.W. & Fenichel E.P. (2014). – Foreclosures and invasive insect spread: The case of Asian citrus psyllid. *Am. J. Agric. Econ.*, **96** (3), 615–630. doi:10.1093/ajae/aat099.

77. Train K.E. (2009). – Discrete choice methods with simulation. 2nd Ed., Cambridge University Press, Cambridge, 388 pp. doi:10.1017/cbo9780511805271.

Table I

Summary of outbreak data and independent variables

Variable	Units	Mean	St. Dev.	Min.	Max.	Source
FMD outbreak	Count	40.15	316.20	0	10,625	OIE
FMD outbreak	Binary	0.34	0.47	0	1	Authors
Agriculture value added	Current US$	110.97E8	369.2E8	2,802,446	734.9E9	FAO
Livestock production index	–	99.07	17.04	36.15	236.08	FAO
Stocks, cattle	# heads	8256939	2.49E7	5	2.13E8	FAO
Stocks, pigs	# heads	5673672	3.43E7	0	4.76E8	FAO
Stocks, sheep	# heads	6591824	1.70E7	420	1.78E8	FAO
Veterinarian density	#/km^2	0.29	2.12	8.58E–7	53.03	Authors
Existence of wild reservoirs	Binary	0.06	0.23	0	1	OIE
Monitoring and surveillance	Binary	0.26	0.44	0	1	OIE
Precautions at the border	Binary	0.60	0.49	0	1	OIE
Vaccinations practised	Binary	0.31	0.47	0	1	OIE
Vaccinations prohibited	Binary	0.27	0.44	0	1	OIE
Zoning	Binary	0.19	0.40	0	1	OIE

#: number

FAO: Food and Agriculture Organization of the United Nations

FMD: foot and mouth disease

OIE: World Organisation for Animal Health

St. Dev.: standard deviation

US: United States

The livestock production index is a unit-less index of the aggregate volume of production of a country's livestock sector compared to a baseline (in this case, the production between 2004 and 2006). Count and binary outbreaks are the dependent variables. Agriculture value added, the livestock production index and stocks of cattle, sheep and pigs are taken as proxies for 'value at risk'. The remaining variables are proxies for biosecurity measures undertaken by countries and the presence of an endemic disease population. Sources of data include the World Organisation for Animal Health, Food and Agriculture Organization and author calculations ('authors'). See text for details

Table II

Pairwise correlation coefficients for independent variables

	FMD outbreak	Ag Val Ad	LPI	Vet density	Existence of wild	Monitoring	Border precautions	Vacc. practised	Vacc. prohibited	Zoning	Stocks, cattle	Stocks, pigs	Stocks, sheep
FMD outbreak	1												
Ag Val Ad	0.105*	1											
LPI	−0.085*	0.074*	1										
Vet density	−0.071*	−0.032	0.025	1									
Existence of wild	0.109*	0.151*	0.066*	−0.004	1								
Monitoring	0.228*	0.085*	0.214*	−0.007	0.266*	1							
Border precautions	−0.005	0.099*	0.203*	−0.014	0.168*	0.341*	1						
Vacc. practised	0.434*	0.112*	−0.015	−0.078*	0.170*	0.296*	0.203*	1					
Vacc. prohibited	−0.313*	−0.010	0.134*	−0.042*	0.037*	−0.009	0.411*	−0.361*	1				
Zoning	0.125*	0.106*	0.130*	−0.009	0.332*	0.292*	0.345*	0.258*	0.158*	1			
Stocks, cattle	0.165*	0.652*	−0.028	−0.059*	0.048*	0.057*	0.091*	0.199*	−0.066*	0.098*	1		
Stocks, pigs	0.066*	0.786*	−0.004	−0.021	0.143*	0.054*	0.019	0.055*	−0.008	0.082*	0.415*	1	
Stocks, sheep	0.142*	0.684*	−0.001	−0.077*	0.121*	0.087*	0.064*	0.130*	−0.098*	0.045*	0.521*	0.720*	1

Ag Val Ad: agriculture value added

FMD: foot and mouth disease

LPI: livestock production index

Vacc: vaccination

Correlation coefficients were rounded to three decimal places. A single asterisk denotes significance at the 10% level

Table III
Negative binomial estimates of exogenous variables

	Variable	IRR	*P*-value
	Agriculture value added	1.000*	0.071
	Livestock production index	0.993*	0.042
	Veterinarian density	0.001	0.191
	Existence of wild reservoirs	1.326	0.136
	Monitoring and surveillance	1.377*	0.006
	Vaccination practised	1.200	0.152
	Vaccination prohibited	0.568*	0.014
	Zoning	0.895	0.429
	Stocks (cattle, sheep, pigs)	1.000	0.752
Importing from:	Disease-free, no vaccination	0.999999*	0.054
	Disease-free, vaccination	1.000000	0.909
	Disease-free zones, no vaccination	1.000004	0.706
	Disease-free zones, vaccination	1.000003*	0.075
	Not disease-free	1.000002*	0.007
Exporting to:	Disease-free, no vaccination	0.999998*	0.088
	Disease-free, vaccination	0.997832*	0.014
	Disease-free zones, no vaccination	0.999997	0.190
	Disease-free zones, vaccination	1.000023*	0.047
	Not disease-free	1.000000	0.446
	Constant	−0.570	0.112
	N	761	
	Log-likelihood	−1875.90	
	AIC	3789.81	
	BIC	3877.86	

AIC: Akaike information criterion

BIC: Bayesian information criterion

IRR: Incidence rate ratio

N: number of observations

Note that the dependent variable is the number of new outbreaks. Estimates are reported as incidence rate ratios. Owing to non-linearity in the maximum likelihood function, convergence of the negative binomial model is sensitive to correlation between independent variables and binary data (66). Therefore, stocks of cattle, pigs and sheep were aggregated into a single variable and the presence of border precautions was dropped from the analysis. Non-trade data and *p*-values are rounded to three decimal places; trade data are rounded to six. A single asterisk denotes significance at the 10% level

Table IV

Logistic regression estimates of exogenous variables

	No trade lag		One-year trade lag	
Variable	Odds ratio	*P*-value	Odds ratio	*P*-value
Agriculture value added	1.000*	0.036	1.000*	0.031
Livestock production index	0.970*	0.035	0.951*	0.001
Veterinarian density	0.000*	0.020	0.000*	0.014
Existence of wild reservoirs	5.794*	0.002	5.282	0.111
Monitoring and surveillance	2.601*	0.027	3.801*	0.004
Precautions at the border	0.607	0.404	0.586	0.316
Vaccination practised	2.083	0.181	0.922	0.895
Vaccination prohibited	0.226*	0.024	0.197*	0.009
Zoning	10.004*	0.000	21.734*	0.000
Stocks, cattle	1.000	0.810	1.000	0.344
Stocks, pigs	1.000*	0.069	1.000*	0.000
Stocks, sheep	1.000	0.623	1.000*	0.005
Constant	2.903	0.441	14.540	0.103
N	1307		1298	
Pseudo log-likelihood	–290.194		–245.528	
AIC	800.039		707.057	
BIC	1369.343		1265.263	

AIC: Akaike information criterion

BIC: Bayesian information criterion

N: number of observations

Note that the dependent variable is a binary outbreaks/no outbreaks indicator. Odds ratios are rounded to three decimal places. A single asterisk denotes significance at the 10% level. The associated trade variables are reported in Tables V and VI

Table V
Logistic regression trade estimates from imports

		No trade lag		One-year trade lag	
	Variable	Odds ratio	*P*-value	Odds ratio	*P*-value
Importing from:	*Cattle*				
	Eastern Africa	–	–	1.0003	0.055
	Northern Africa	–	–	0.9965	0.033
	Southern Africa	–	–	0.9999	0.048
	Western Africa	0.9992	0.062	1.0022	0.005
	North America	1.0006	0.000	–	–
	Central America	0.9993	0.096	–	–
	Eastern Asia	0.9999	0.002	1.0003	0.001
	Southern Asia	1.0003	0.057	–	–
	Western Europe	0.9999	0.024	–	–
	Pacific Islands	1.0294	0.002	1.0734	0.005
	Pigs				
	Eastern Africa	–	–	1.0074	0.062
	North America	0.9991	0.014	–	–
	Caribbean	–	–	1.0934	0.047
	Central Asia	–	–	1.0160	0.015
	Eastern Asia	–	–	1.0001	0.000
	Southern Asia	–	–	1.3422	0.035
	Western Asia	1.0181	0.000	–	–
	Northern Europe	–	–	0.9997	0.054
	Southern Europe	0.9996	0.022	0.9984	0.095
	Western Europe	–	–	1.0002	0.024
	Australia and New Zealand	0.9907	0.039	0.9846	0.005
	Sheep				
	Eastern Africa	–	–	0.9999	0.019
	Southern Africa	0.9991	0.060	–	–
	South America	–	–	0.9999	0.060
	Central Asia	–	–	1.0035	0.053
	Southeast Asia	0.9961	0.001	0.9898	0.005
	Eastern Europe	–	–	1.0001	0.042
	Northern Europe	–	–	1.0007	0.033
	Southern Europe	0.9996	0.049	1.0009	0.079

P-values are rounded to three decimal places; trade data to four places. Imports of cattle from Australia and New Zealand and South America (no lag), and imports of sheep from Western Europe (trade lag) were significant at the 10% level and possessed odds ratios equal to 1 (rounding to five decimal places). A dash indicates an estimate not significant at the 10% level

Table VI

Logistic regression trade estimates from exports

	Variable	No trade lag		One-year trade lag	
		Odds ratio	*P*-value	Odds ratio	*P*-value
	Cattle				
	Eastern Africa	1.0000	0.032	–	–
	Southern Africa	1.0006	0.068	–	–
	North America	1.0214	0.000	–	–
	Central Asia	0.9989	0.000	0.9978	0.004
	Eastern Asia	1.0001	0.032	–	–
	Southeast Asia	0.9999	0.002	0.9997	0.007
	Western Asia	1.0000	0.024	–	–
	Pigs				
	Eastern Africa	0.9979	0.005	–	–
	Southern Africa	–	–	0.9888	0.010
	Western Africa	–	–	1.0014	0.069
	Eastern Asia	–	–	0.9999	0.000
Exporting to:	Southern Asia	–	–	2.1892	0.041
	Southeast Asia	1.0000	0.030	1.0001	0.026
	Western Asia	1.0011	0.075	1.0021	0.059
	Southern Europe	–	–	0.9998	0.009
	Australia and New Zealand	–	–	0.1329	0.015
	Sheep				
	Southern Africa	1.0000	0.064	–	–
	Western Africa	–	–	1.0000	0.069
	Central America	0.9859	0.005	0.9604	0.037
	Caribbean	–	–	1.0288	0.035
	Central Asia	–	–	1.0011	0.079
	Eastern Asia	1.0004	0.012	0.9984	0.018
	Southern Asia	1.0006	0.000	1.0010	0.002
	Southeast Asia	0.9989	0.029	–	–
	Western Asia	–	–	1.0000	0.085
	Pacific Islands	1.5025	0.042	–	–

P-values are rounded to three decimal places; trade data are rounded to four decimal places. A dash indicates an estimate not significant at the 10% level

Table VII
Relative economic risks of trade (*no trade lag*)

	Variable	Odds ratio	Change in odds	United Kingdom RER (lower) (million US$)	United Kingdom RER (upper) (million US$)
Importing from:	*Cattle*				
	North America	1.0006	0.0006	0.017	10.998
	Southern Asia	1.0003	0.0003	0.007	4.508
	Pigs				
	Western Asia	1.0180	0.0181	0.468	308.194
	Australia and New Zealand	0.9907	–0.0093	–0.241	–158.942
	Sheep				
	Southern Africa	0.9991	–0.0009	–0.024	–15.651
	Southern Europe	0.9996	–0.0004	–0.010	–6.477
Exporting to:	*Cattle*				
	Southern Africa	1.0006	0.0006	0.015	10.110
	Southeast Asia	0.9999	–0.0001	–0.002	–1.317
	Pigs				
	Eastern Africa	0.9979	–0.0021	–0.054	–35.652
	Western Asia	1.0011	0.0011	0.029	19.024
	Sheep				
	Central America	0.9859	–0.0141	–0.365	–240.477
	Eastern Asia	1.0004	0.0004	0.011	7.155
	UK value of exports (million US$)			25.918	
	UK agriculture value added (billion US$)			17.077	

RER: relative economic risk

UK: United Kingdom

US: United States

Relative economic risk is calculated as the product of the relative probability of foot and mouth disease outbreak (change in the odds) and the magnitude of potential damages (value at risk). Two measures of value at risk were tested: the value of all exports of cattle, pigs and sheep (lower bound), and the value of the agriculture sector (upper bound). Relative economic risk is from the perspective of the United Kingdom in 2011. The authors interpret the relative economic risk as, from a global perspective, the dollar value of risk associated with a one unit (1,000 head) increase in imports to/exports from a partner region. Positive values indicate the acquisition of additional risk; negative values indicate risk mitigation. Values at risk and relative economic risk are rounded to three decimal places; odds ratios and the change in the odds are rounded to four decimal places

Table VIII

Comparison of trade aggregations for imports

	Variable	Odds ratio	*P*-value		Variable	IRR	*P*-value
Importing from:	*Cattle*			Importing from:			
	Western Africa	0.9992	0.062		Disease-free, no vaccination	0.999999	0.054
	North America	1.0006	0.000		Disease-free, vaccination	1.000000	0.909
	Central America	0.9993	0.096		Disease-free zones, no vaccination	1.000004	0.706
	Eastern Asia	0.9999	0.002		Disease-free zones, vaccination	1.000003	0.075
	Southern Asia	1.0003	0.056		Not disease-free	1.000002	0.007
	Western Europe	0.9999	0.024				
	Pacific Islands	1.0294	0.002				
	Pigs						
	North America	0.9991	0.014				
	Western Asia	1.0180	0.000				
	Southern Europe	0.9996	0.022				
	Australia and New Zealand	0.9907	0.038				
	Sheep						
	Southern Africa	0.9991	0.061				
	Southeast Asia	0.9961	0.001				
	Southern Europe	0.9996	0.049				

IRR: incidence rate ratio

Note that odds ratios for the *no trade lag* model are presented for the regional trade aggregation

Table IX

Comparison of trade aggregations for exports

	Variable	Odds ratio	*P*-value		Variable	IRR	*P*-value
Exporting to:	*Cattle*						
	Southern Africa	1.0006	0.068	Exporting to:	Disease-free, no vaccination	0.999998	0.088
	North America	1.0214	0.000		Disease-free, vaccination	0.997832	0.014
	Central Asia	0.9989	0.000		Disease-free zones, no vaccination	0.999997	0.19
	Eastern Asia	1.0001	0.032		Disease-free zones, vaccination	1.000023	0.047
	Southeast Asia	0.9999	0.002		Not disease-free	1.000000	0.446
	Pigs						
	Eastern Africa	0.9979	0.005				
	Western Asia	1.0011	0.074				
	Sheep						
	Central America	0.9859	0.005				
	Eastern Asia	1.0004	0.013				
	Southern Asia	1.0006	0.000				
	Southeast Asia	0.9989	0.029				
	Pacific Islands	1.5025	0.042				

IRR: Incidence rate ratio

Note that the odds ratios for the *no trade lag* model are presented for the regional trade aggregation

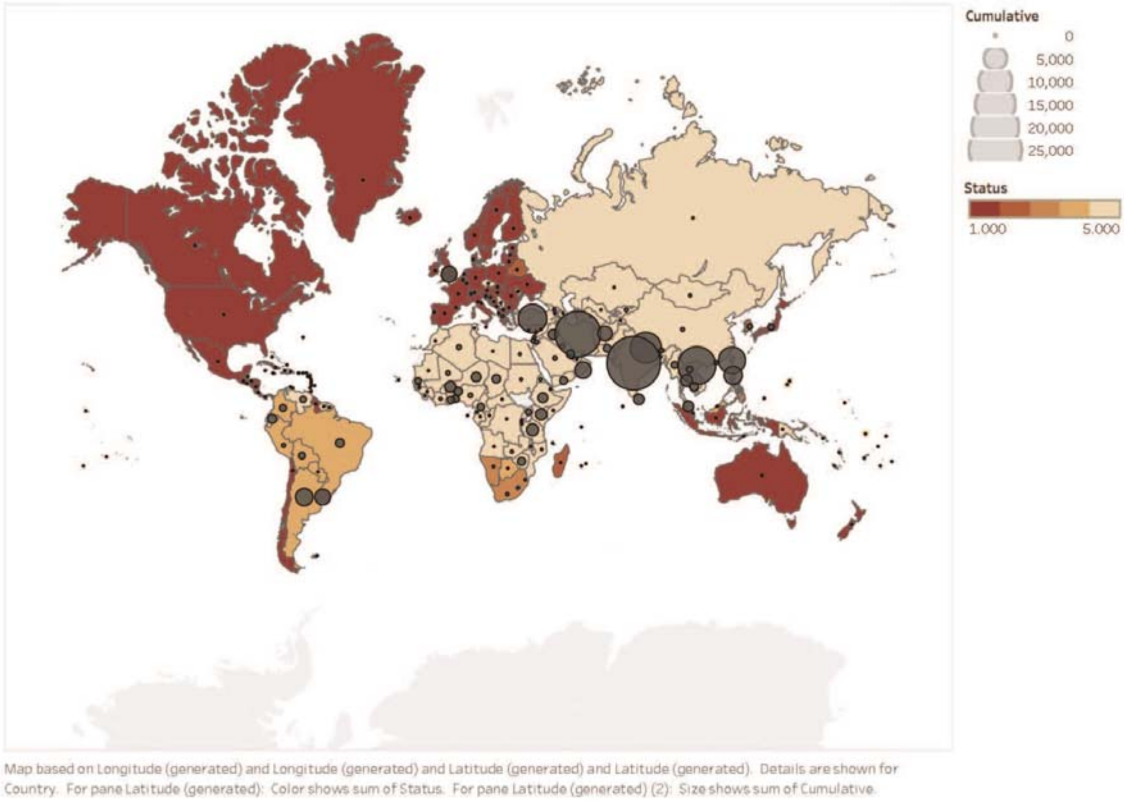
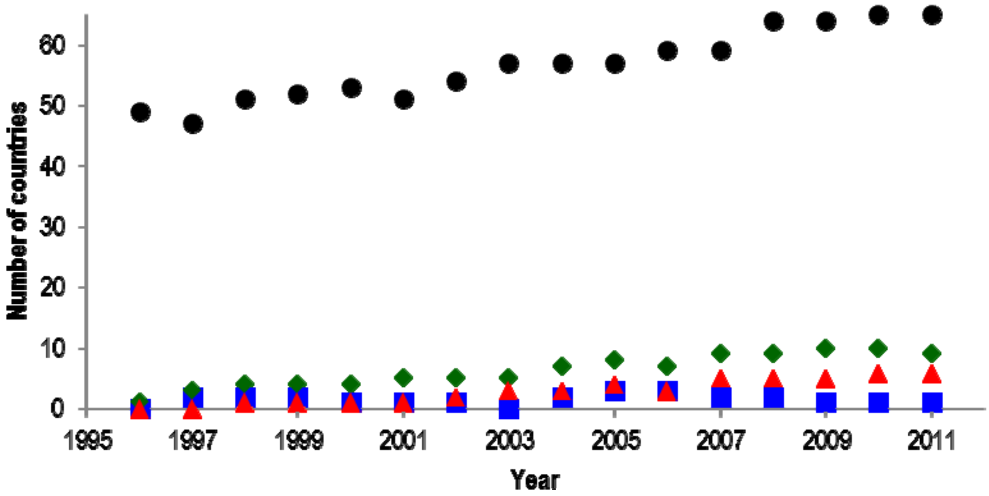


Fig. 1

Foot and mouth disease outbreaks by OIE disease-free designations as of 2011

Individual countries are coloured according to their disease-free designation: disease free, no vaccination; disease free, with vaccination; disease-free zones, no vaccination; disease-free zones, with vaccination; and not disease-free. Circle size indicates an increasing gradient in the number of *cumulative* foot and mouth disease outbreaks within a country during the study period. Data are from the World Organisation for Animal Health (www.oie.int/)

(a)



(b)

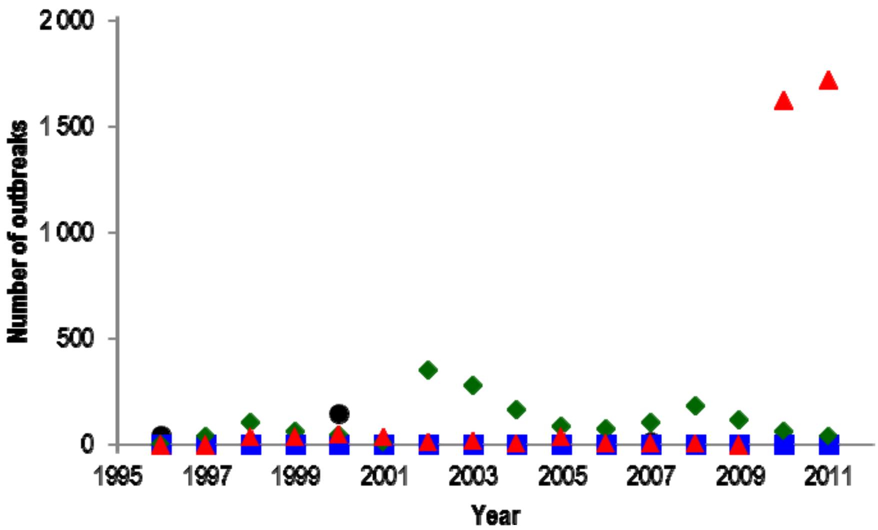


Fig. 2

Annual aggregate number of countries (a) and number of reported outbreaks (b) by disease-free category

Symbol and colour indicate the disease-free category: disease-free everywhere, no vaccination (black, circle); disease-free everywhere, vaccination (square, blue); disease-free zones, no vaccination (diamond, green); disease-free zones, vaccination (triangle, red). Total outbreaks by countries without a designation ('not disease-free') ranged between 2,164 and 24,321 outbreaks annually

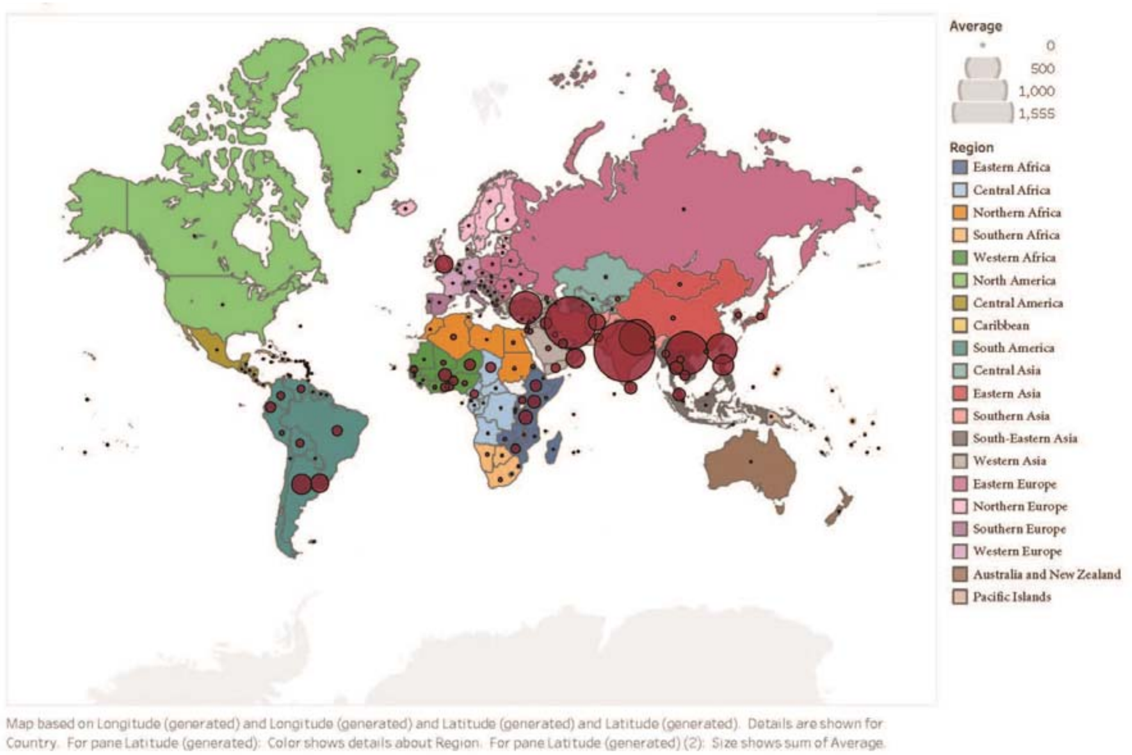
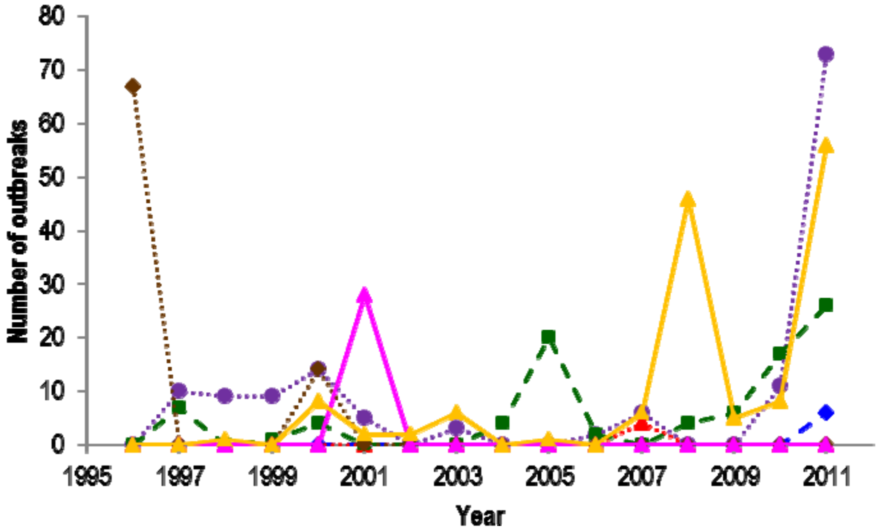


Fig. 3

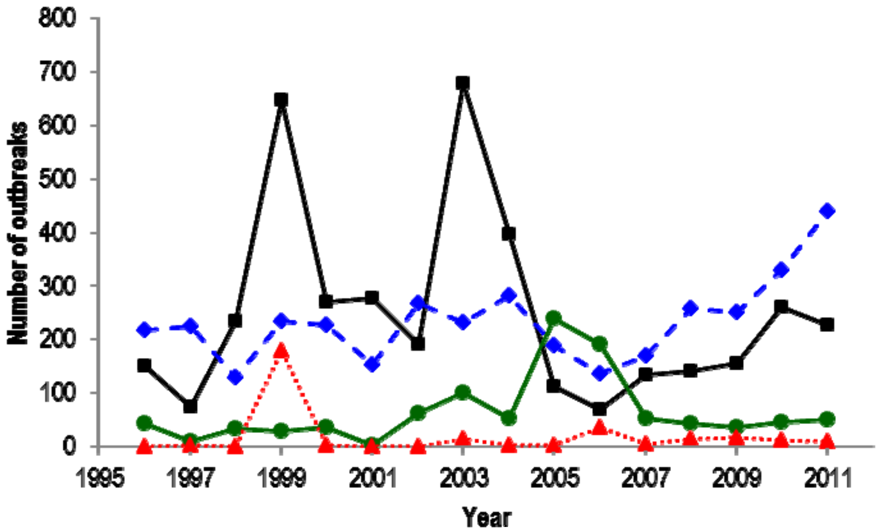
Foot and mouth disease outbreaks by Food and Agriculture Organization geographical regions as of 2011

Individual countries are coloured according to their FAO geographic group: Eastern Africa (■), Central Africa (■), Northern Africa (■), Southern Africa (■), Western Africa (■), North America (■), Central America (■), Caribbean (■), South America (■), Central Asia (■), Eastern Asia (■), Southern Asia (■), Southeast Asia (■), Western Asia (■), Eastern Europe (■), Northern Europe (■), Southern Europe (■), Western Europe (■), Australia and New Zealand (■), Pacific Islands (■). Melanesia, Polynesia and Micronesia are lumped into a single 'Pacific Islands' region. Circle size indicates an increasing gradient in the *average* number of foot and mouth disease outbreaks within a country during the study period. Information on the regional grouping of countries may be found at the FAO Trade Statistics Division (http://faostat3.fao.org/home/E). Outbreak data are from the World Organisation for Animal Health (www.oie.int/)

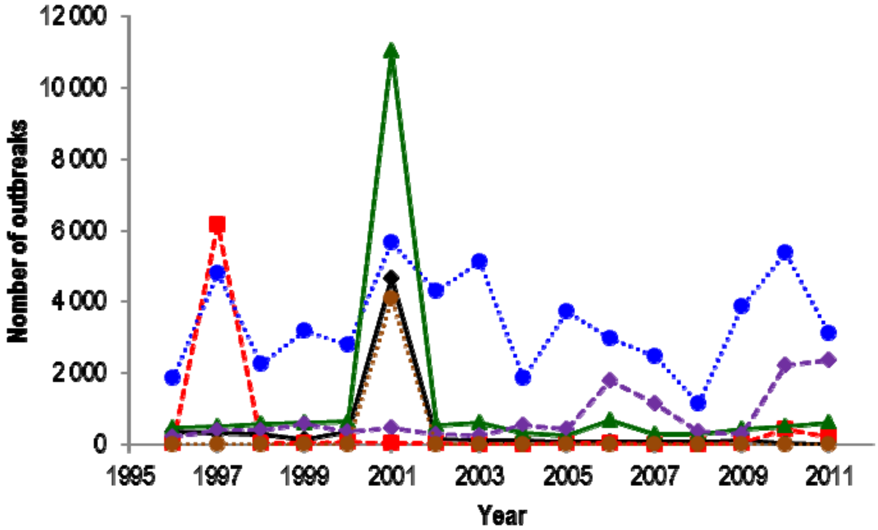
(a)


80
70
60
50
40
30
20
10
0
Number of outbreaks
1995
1997
1999
2001
2003
2005
2007
2009
2011
Year

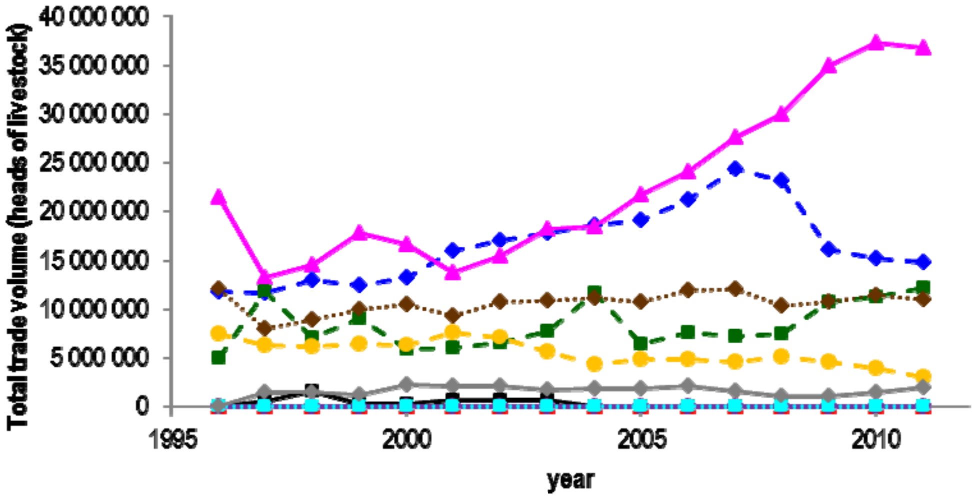
(b)


800
700
600
500
400
300
200
100
0
Number of outbreaks
1995
1997
1999
2001
2003
2005
2007
2009
2011
Year

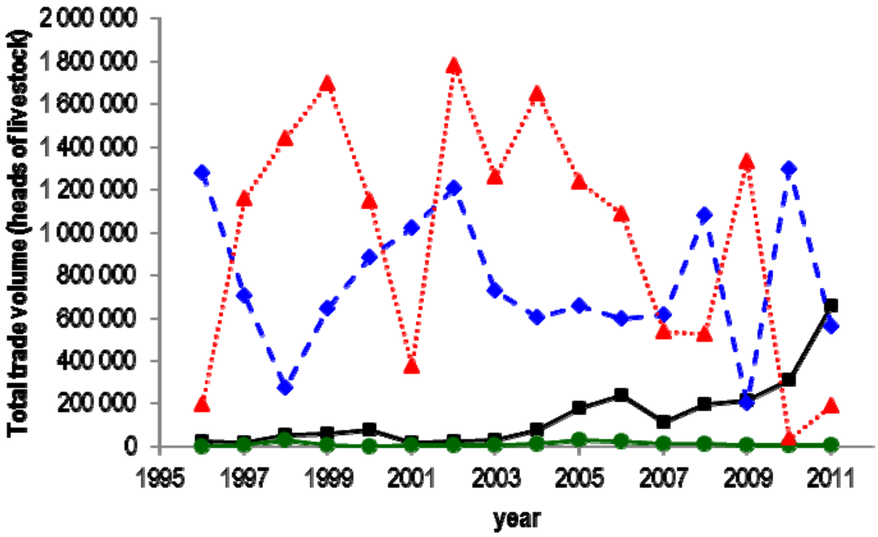
(c)


12 000
10 000
8 000
6 000
4 000
2 000
0
Nomber of outbreaks
1995
1997
1999
2001
2003
2005
2007
2009
2011
Year

(d)


40 000 000
35 000 000
30 000 000
25 000 000
20 000 000
15 000 000
10 000 000
5 000 000
0
Total trade volume (heads of livestock)
1995
2000
2005
2010
year

(e)



(f)

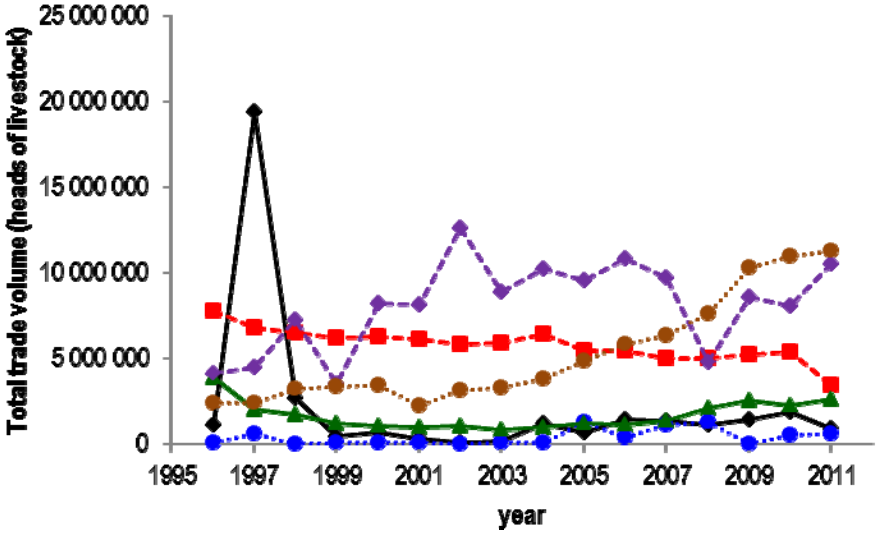


Fig. 4

Regional number of reported outbreaks (a–c) and total trade volume (d–f) over time

Regions are sorted into three categories based on the maximum number of outbreaks in a single year: (a, d) low risk (<100 outbreaks), (b, e) intermediate risk (<1,000 outbreaks) and (c, f) high risk (>1,000 outbreaks). The following regions reported no outbreaks during the study period: Central America, Australia and New Zealand, and the Pacific Islands. Total trade volume (d–f) is the regional sum of import and export quantity (heads) of cattle, sheep and pigs

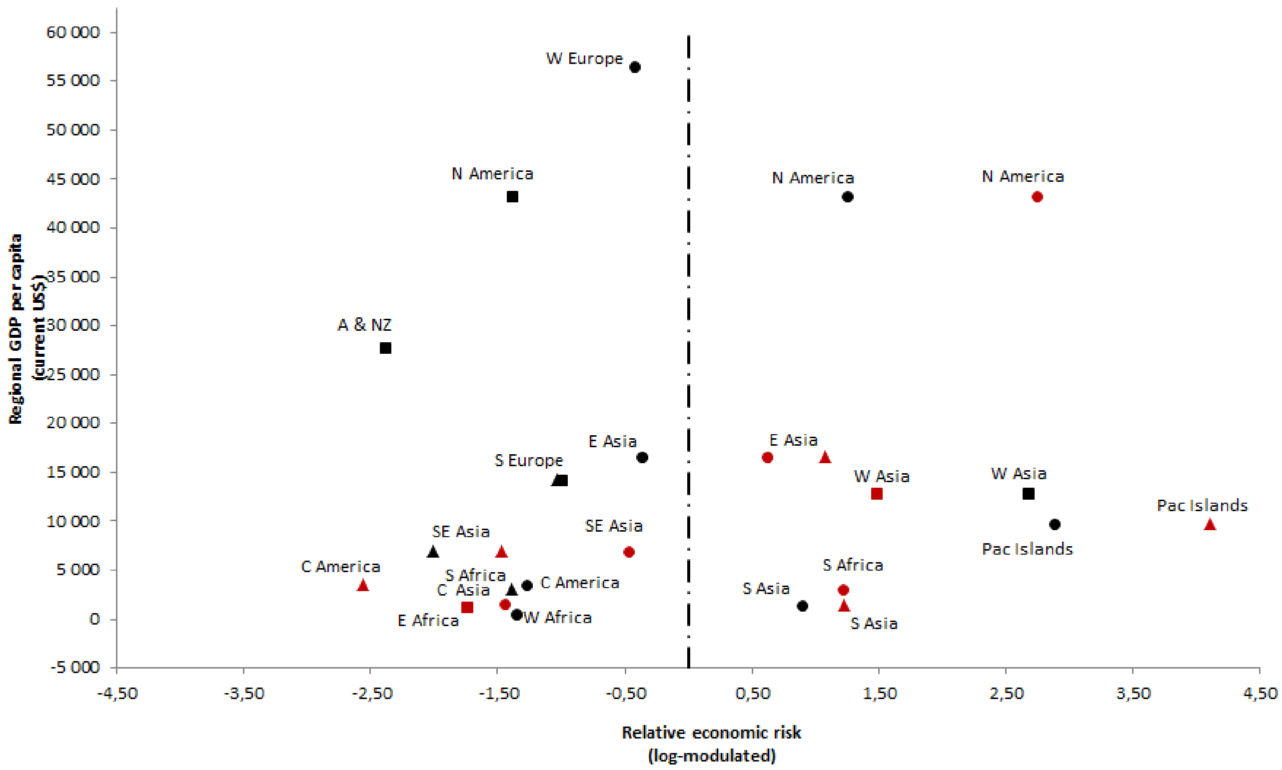


Fig. 5

Regional gross domestic product per capita versus relative economic risk calculated from the *no trade lag* model

Regional gross domestic product is the average gross domestic product per capita of all nations within a region, averaged over the study period (1996–2011). Relative economic risks have been log-modulated. Marker colour indicates imports (black) or exports (red), while the species is given by the marker shape (square, cattle; diamond, pigs; triangle, sheep). Regions are labelled next to their corresponding marker. Zero relative economic risk of trade is plotted as the dot-dashed reference line

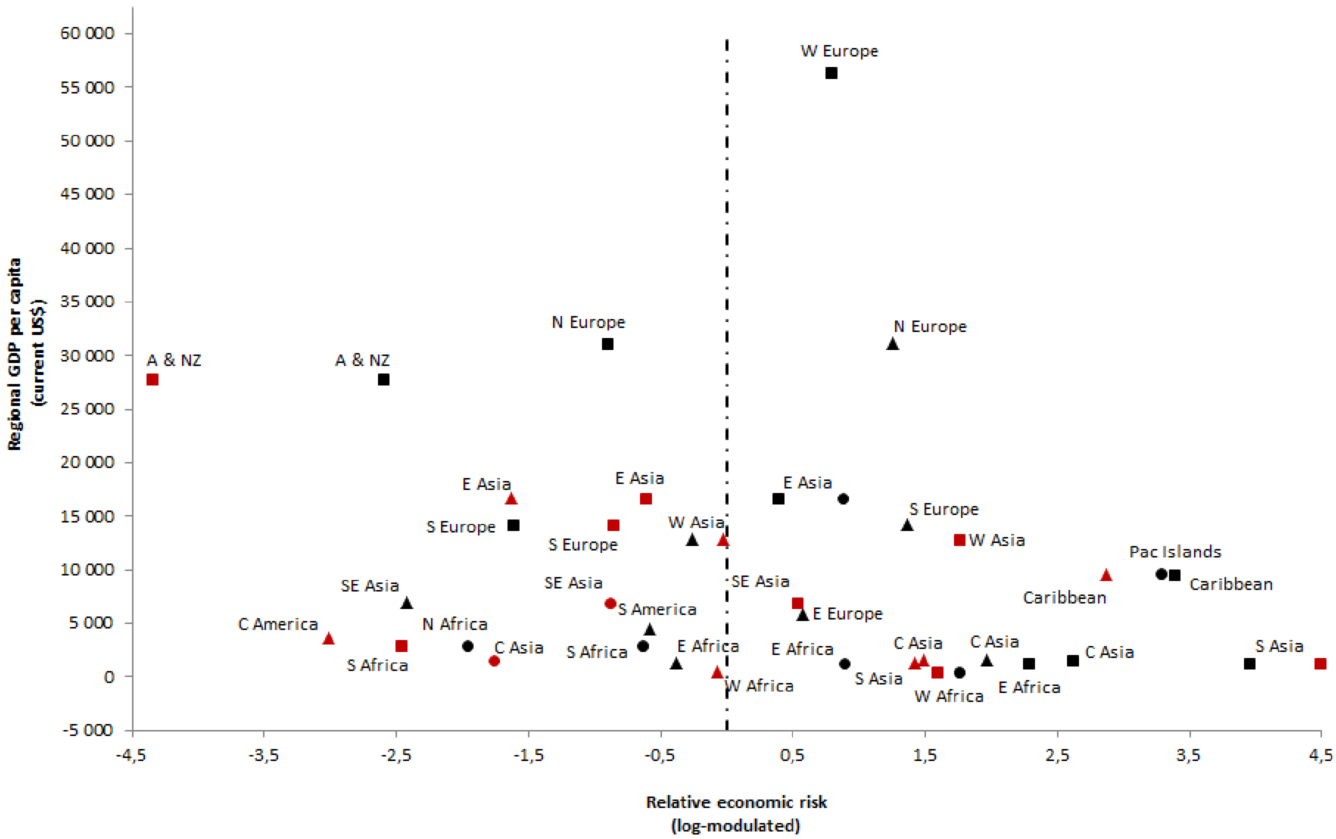


Fig. 6

Regional gross domestic product per capita versus relative economic risk calculated from the *one-year trade lag* model

Regional gross domestic product is the average gross domestic product per capita of all nations within a region, averaged over the study period (1996–2011). Relative economic risks have been log-modulated. Marker colour indicates imports (black) or exports (red), while the species is given by the marker shape (circle, cattle; square, pigs; triangle, sheep). Regions are labelled next to their corresponding marker. Zero relative economic risk of trade is plotted as the dot-dashed reference line

Appendix A
Full logistic trade regression

Table AI

Full logistic regression trade estimates from imports of cattle

	Variable	No trade lag		One-year trade lag	
		Odds ratio	*P*-value	Odds ratio	*P*-value
Importing from:	Eastern Africa	1.0001	0.372	1.0003*	0.055
	Central Africa	1.0002	0.472	0.9999	0.738
	Northern Africa	0.9993	0.524	0.9965*	0.033
	Southern Africa	1.0000	0.874	0.9999*	0.048
	Western Africa	0.9992*	0.062	1.0022*	0.005
	North America	1.0006*	0.000	1.0001	0.596
	Central America	0.9993*	0.096	0.9991	0.420
	Caribbean	0.9947	0.370	1.0014	0.430
	South America	1.0000*	0.034	1.0000	0.414
	Central Asia	0.9749	0.523	0.9890	0.646
	Eastern Asia	0.9999*	0.002	1.0003*	0.001
	Southern Asia	1.0003*	0.057	1.0007	0.107
	Southeast Asia	1.0000	0.499	1.0000	0.469
	Western Asia	1.0001	0.875	0.9983	0.124
	Eastern Europe	1.0000	0.733	0.9999	0.232
	Northern Europe	0.9997	0.503	1.0000	0.983
	Southern Europe	1.0002	0.164	0.9996	0.276
	Western Europe	0.9999*	0.024	1.0000	0.823
	Australia and New Zealand	1.0000*	0.007	1.0000	0.740
	Pacific Islands	1.0295*	0.002	1.0734*	0.005

P-values are rounded to three decimal places; trade data are rounded to four decimal places.

A single asterisk indicates significance at the 10% level

Table AII

Full logistic regression trade estimates from imports of pigs

	Variable	No trade lag		One-year trade lag	
		Odds ratio	*P*-value	Odds ratio	*P*-value
Importing from:	Eastern Africa	0.9969	0.183	1.0074*	0.062
	Central Africa	1.0062	0.253	0.9915	0.260
	Northern Africa	1.0000	(omitted)	0.7972	0.210
	Southern Africa	1.0001	0.692	1.0003	0.135
	Western Africa	0.9938	0.258	1.0008	0.902
	North America	0.9991*	0.014	1.0002	0.702
	Central America	1.0074	0.919	0.8342	0.175
	Caribbean	1.0604	0.330	1.0934*	0.047
	South America	1.0003	0.476	0.9997	0.482
	Central Asia	1.0010	0.787	1.0160*	0.015
	Eastern Asia	1.0000	0.352	1.0001*	0.000
	Southern Asia	1.1146	0.278	1.3422*	0.035
	Southeast Asia	1.0000	0.187	1.0000	0.339
	Western Asia	1.0181*	0.000	1.0285	0.126
	Eastern Europe	1.0000	0.512	1.0000	0.885
	Northern Europe	1.0000	0.253	0.9997*	0.054
	Southern Europe	0.9996*	0.022	0.9984*	0.095
	Western Europe	1.0000	0.170	1.0002*	0.024
	Australia and New Zealand	0.9907*	0.039	0.9846*	0.005
	Pacific Islands	1.0000	(omitted)	1.0000	(omitted)

P-values are rounded to three decimal places; trade data are rounded to four decimal places.

A single asterisk indicates significance at the 10% level

Table AIII
Full logistic regression trade estimates from imports of sheep

	Variable	No trade lag Odds ratio	 *P*-value	One-year trade lag Odds ratio	 *P*-value
Importing from:	Eastern Africa	1.0000	0.473	0.9999*	0.019
	Central Africa	0.9999	0.307	1.0001	0.217
	Northern Africa	1.0000	0.830	1.0000	0.127
	Southern Africa	0.9991*	0.060	1.0001	0.160
	Western Africa	1.0000	0.789	1.0000	0.456
	North America	1.0002	0.416	1.0001	0.527
	Central America	0.9986	0.842	0.9992	0.913
	Caribbean	0.9671	0.232	0.9324	0.105
	South America	1.0000	0.347	0.9999*	0.060
	Central Asia	1.0024	0.323	1.0035*	0.053
	Eastern Asia	1.0001	0.673	1.0001	0.539
	Southern Asia	1.0001	0.861	1.0002	0.532
	Southeast Asia	0.9961*	0.001	0.9898*	0.005
	Western Asia	1.0000	0.998	1.0000*	0.068
	Eastern Europe	1.0000	0.565	1.0001*	0.042
	Northern Europe	1.0001	0.268	1.0007*	0.033
	Southern Europe	0.9996*	0.049	1.0009*	0.079
	Western Europe	0.9998	0.339	0.9999	0.571
	Australia and New Zealand	1.0000	0.758	1.0000	0.764
	Pacific Islands	1.0000	(omitted)	1.0000	(omitted)

P-values are rounded to three decimal places; trade data are rounded to four decimal places.

A single asterisk indicates significance at the 10% level

Table AIV

Full logistic regression trade estimates from exports of cattle

	Variable	No trade lag		One-year trade lag	
		Odds ratio	*P*-value	Odds ratio	*P*-value
Exporting to:	Eastern Africa	1.0000*	0.032	1.0000	0.660
	Central Africa	1.0000	0.938	1.0005	0.251
	Northern Africa	1.0000	0.482	1.0000	0.707
	Southern Africa	1.0006*	0.068	1.0000	0.782
	Western Africa	1.0000	0.254	1.0000	0.551
	North America	1.0214*	0.000	0.9955	0.709
	Central America	1.0003	0.644	1.0001	0.927
	Caribbean	0.9780	0.107	1.0644	0.139
	South America	1.0000	0.117	1.0000	0.743
	Central Asia	0.9989*	0.000	0.9978*	0.004
	Eastern Asia	1.0001*	0.032	0.9998	0.110
	Southern Asia	0.9984	0.677	0.9835	0.403
	Southeast Asia	0.9999*	0.002	0.9997*	0.007
	Western Asia	1.0000*	0.024	1.0000	0.272
	Eastern Europe	1.0002	0.368	1.0006	0.556
	Northern Europe	0.9994	0.280	0.9996	0.574
	Southern Europe	1.0000	0.414	1.0000	0.876
	Western Europe	0.9999	0.337	1.0002	0.256
	Australia and New Zealand	0.9447	0.190	1.1043	0.197
	Pacific Islands	0.8777	0.289	1.2464	0.123

P-values are rounded to three decimal places; trade data are rounded to four decimal places.

A single asterisk indicates significance at the 10% level

Table AV
Full logistic regression trade estimates from exports of pigs

	Variable	No trade lag		One-year trade lag	
		Odds ratio	*P*-value	Odds ratio	*P*-value
Exporting to:	Eastern Africa	0.9979*	0.005	1.0013	0.329
	Central Africa	1.0055	0.444	0.9972	0.754
	Northern Africa	0.9993	0.916	0.9899	0.234
	Southern Africa	1.0002	0.897	0.9888*	0.010
	Western Africa	0.9997	0.620	1.0014*	0.069
	North America	0.9743	0.126	0.9748	0.119
	Central America	1.0000	(omitted)	0.1473	0.108
	Caribbean	0.5562	0.264	0.5055	0.158
	South America	1.0004	0.430	1.0007	0.227
	Central Asia	0.9956	0.418	0.9939	0.511
	Eastern Asia	1.0000	0.404	0.9999*	0.000
	Southern Asia	1.0567	0.396	2.1892*	0.041
	Southeast Asia	1.0000*	0.030	1.0001*	0.026
	Western Asia	1.0011*	0.075	1.0021*	0.059
	Eastern Europe	0.9999	0.219	0.9998	0.153
	Northern Europe	1.0000	0.525	1.0007	0.132
	Southern Europe	1.0000	0.741	0.9998*	0.009
	Western Europe	1.0000	0.311	0.9999	0.448
	Australia and New Zealand	1.0127	0.973	0.1329*	0.015
	Pacific Islands	0.9708	0.671	1.0000	(omitted)

P-values are rounded to three decimal places; trade data are rounded to four decimal places.

A single asterisk indicates significance at the 10% level

Table AVI
Full logistic regression trade estimates from exports of sheep

	Variable	No trade lag		One-year trade lag	
		Odds ratio	*P*-value	Odds ratio	*P*-value
Exporting to:	Eastern Africa	1.0001	0.526	0.9999	0.628
	Central Africa	1.0001	0.622	1.0000	0.984
	Northern Africa	0.9999	0.145	1.0001	0.245
	Southern Africa	1.0000*	0.064	1.0000	0.793
	Western Africa	1.0000	0.424	1.0000*	0.069
	North America	1.0003	0.894	1.0011	0.760
	Central America	0.9859*	0.005	0.9604*	0.037
	Caribbean	1.0082	0.493	1.0288*	0.035
	South America	1.0000	0.860	1.0000	0.488
	Central Asia	1.0003	0.168	1.0011*	0.079
	Eastern Asia	1.0004*	0.012	0.9984*	0.018
	Southern Asia	1.0006*	0.000	1.0010*	0.002
	Southeast Asia	0.9989*	0.029	0.9999	0.826
	Western Asia	1.0000	0.807	1.0000*	0.085
	Eastern Europe	1.0001	0.191	1.0000	0.659
	Northern Europe	0.9995	0.455	0.9993	0.196
	Southern Europe	1.0000	0.317	1.0000	0.126
	Western Europe	1.0001	0.132	0.9999	0.785
	Australia and New Zealand	0.9988	0.704	1.0030	0.374
	Pacific Islands	1.5025*	0.042	1.0081	0.878

P-values are rounded to three decimal places; trade data are rounded to four decimal places.

A single asterisk indicates significance at the 10% level

Appendix B
Alternative models and causality

As with other parametric studies, the authors assumed a particular function form for their models. However, neither the logistic nor the negative binomial regression explicitly accounts for the ‘tailed’ nature of foot and mouth disease (FMD) outbreaks. Non-parametric methods exist to estimate the probability density function of continuous data (including zero-inflated data), though they are less used in conventional statistics (1). See Bean & Tsokos (2), Cleveland & Devlin (3), Izenman (4), Racine & Li (5) and Wolter (6) for reviews and recent applications of this literature. Alternatively, a spatial model could capture the direct and indirect sources of risk. The authors used trade variables to establish the risks of imports and exports. A gravity model, in contrast, would incorporate all possible linkages between spatial locations into a single summary measure of disease exposure (7, 8). These are left for future work.

The models used are also correlative – that is, they are unable to establish causality. In economics, difference-in-differences, instrumental variables and regression discontinuity design (RDD) experiments have been shown to be viable methods for establishing causation outside randomised experiments (9). Each method has its strengths and weaknesses. Difference-in-differences requires countries to experience the same trend in disease in the absence of a treatment (10, 11). It then measures the differences between the countries, e.g. the treatment effect. Given the nature of the data used in this study, this assumption is not likely to be met. Instrumenting for all potentially endogenous variables is also not feasible given the large number of trade variables.

Regression discontinuity design (RDD) experiments are gaining popularity as a viable alternative to randomised experiments (9). The basic idea behind an RDD experiment is to exploit a discontinuity in the data (‘threshold effect’) due to a particular treatment (12, 13). The discontinuity arises as a break in the dependent variable at an exogenously determined threshold of an indicator or 'assignment' variable. By measuring the change in the dependent variable on either side of the discontinuity one may measure the effect of the treatment. Imbens & Lemieux (14), Lee & Lemieux (9) and Jacob *et al.* (15) provide comprehensive reviews of this literature.

Though they are mild compared to those of difference-in-differences and instrumental variable approaches, an RDD experiment makes several key assumptions that are of particular concern (9, 15). First, there must exist a clear structural break in the data, specifically in the assignment variable. Discontinuities in other covariates lead to problems in the identification of the treatment effect. Second, participants in the experiment (countries) have an equal chance of being on either side of the discontinuity. That is, they have no control in their placement around the discontinuity and (all else being equal) the treatment is the driving factor in determining the value of their assignment variable. Given the zero-inflated nature of the data and the degree of control that countries have over their biosecurity and sanitary measures, it is unlikely that both assumptions will be satisfied.

References

1. Higgins J.J. (2004). – An introduction to modern nonparametric statistics, Thomson Learning, Inc., Pacific Grove, California, 366 pp.

2. Bean S.J. & Tsokos C.P. (1980). – Developments in nonparametric density estimation. *Int. Stat. Rev.*, **48** (3), 267–287. doi:10.2307/1402941.

3. Cleveland W.S. & Devlin S.J. (1988). – Locally weighted regression: An approach to regression analysis by local fitting. *J. Am. Stat. Assoc.*, **83** (403), 596–610. doi:10.2307/2289282.

4. Izenman A.J. (1991). – Recent developments in nonparametric density estimation. *J. Am. Stat. Assoc.*, **86** (413), 205–224. doi:10.2307/2289732.

5. Racine J. & Li Q. (2004). – Nonparametric estimation of regression functions with both categorical and continuous data. *J. Econometrics*, **119** (1), 99–130. doi:10.1016/S0304-4076(03)00157-X.

6. Wolter J.L. (2016). – Kernel estimation of hazard functions when observations have dependent and common covariates. *J. Econometrics*, **193** (1), 1–16. doi:10.1016/j.jeconom.2016.01.002.

7. Thomas R.W. & Huggett R.J. (1980). – Modelling in geography: A mathematical approach. Barnes and Noble Books, Totowa, New Jersey, 338 pp.

8. Anderson J.E. (2011). – The gravity model. *Ann. Rev. Econ.*, **3**, 133–160. doi:10.1146/annurev-economics-111809-125114.

9. Lee D.S. & Lemieux T. (2010). – Regression discontinuity designs in economics. *J. Econ. Lit.*, **48** (2), 281–355. doi:10.1257/jel.48.2.281.

10. Card D. & Krueger A.B. (2000). – Minimum wages and employment: A case study of the fast-food industry in New Jersey and Pennsylvania: Reply. *Am. Econ. Rev.*, **90** (5), 1397–1420. doi:10.1257/aer.90.5.1397.

11. Angrist J.D. & Pischke J.-S. (2009). – Mostly harmless econometrics: An empiricist's companion. Princeton University Press, Princeton, New Jersey, 392 pp.

12. Anderson M. & Magruder J. (2012). – Learning from the crowd: Regression discontinuity estimates of the effects of an online review database. *Econ. J.*, **122** (563), 957–989. doi:10.1111/j.1468-0297.2012.02512.x.

13. Hahn J., Todd P. & Van der Klaauw W. (2001). – Identification and estimation of treatment effects with a regression-discontinuity design. *Econometrica*, **69** (1), 201–209. doi:10.1111/1468-0262.00183.

14. Imbens G.W. & Lemieux T. (2008). – Regression discontinuity designs: A guide to practice. *J. Econometrics*, **142**, 615–635. doi:10.3386/w13039.

15. Jacob R., Zhu P., Somers M. & Bloom H. (2012). – A practical guide to regression discontinuity. MDRC, 92 pp. Available at: www.mdrc.org/publication/practical-guide-regression-discontinuity (accessed on 15 May 2016).