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The potential spread of highly pathogenic avian influenza virus via dynamic contacts between poultry premises in Great Britain

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Abstract

Background: Highly pathogenic avian influenza (HPAI) viruses have had devastating effects on poultry industries worldwide, and there is concern about the potential for HPAI outbreaks in the poultry industry in Great Britain (GB). Critical to the potential for HPAI to spread between poultry premises are the connections made between farms by movements related to human activity. Movement records of catching teams and slaughterhouse vehicles were obtained from a large catching company, and these data were used in a simulation model of HPAI spread between farms serviced by the catching company, and surrounding (geographic) areas. The spread of HPAI through real-time movements was modelled, with the addition of spread via company personnel and local transmission.

Results: The model predicted that although large outbreaks are rare, they may occur, with long distances between infected premises. Final outbreak size was most sensitive to the probability of spread via slaughterhouse-linked movements whereas the probability of onward spread beyond an index premises was most sensitive to the frequency of company personnel movements.

Conclusions: Results obtained from this study show that, whilst there is the possibility that HPAI virus will jump from one cluster of farms to another, movements made by catching teams connected fewer poultry premises in an outbreak situation than slaughterhouses and company personnel. The potential connection of a large number of infected farms, however, highlights the importance of retaining up-to-date data on poultry premises so that control measures can be effectively prioritised in an outbreak situation.

Background

For a wide range of epidemic infections, contact structures can be used to describe the potential transmission of infection in a population [1-4]. The validity of such models, however, depends on the parameterisation of the contact structures analysed. The existence of the animal movement licensing scheme and cattle tracing system in Great Britain (GB), for which the identification and movements of cattle, sheep, goats, pigs, deer and horses, must be recorded [5], allows for the reconstruction and analysis of the network of contacts in order to predict the spread of infectious disease across these industries. This is not the case for the poultry industry where, before 2005, there was no national register of poultry farms. Motivated by numerous outbreaks of H5N1 highly pathogenic avian influenza (HPAI) across the world and the occurrence of several incursions of avian influenza viruses (AIV) in GB [6,7], information was collected by the British government on poultry farm locations, and on the frequency and types of movements between farms.

In GB, the poultry industry can be divided into the primary breeding sector and the production sector. The biosecurity levels in the primary breeding sector are considered to be consistently high, making the probability of introduction of pathogens into this sector extremely low. In the production sector, birds are purchased from a primary breeding company when they are one day old. Birds then remain on specialist rearing farms until approximately eighteen weeks of age before they

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are moved to production farms or to hatcheries. Before meat birds enter the food chain, a catching company may be brought in to assist in the catching of birds to be sent to slaughter. Some catching companies may operate on multiple independently owned farms, and some farms may not use a catching company at all, choosing to send birds directly to the slaughterhouse. Vehicles used to transport birds between farms and slaughterhouses are often owned by the slaughterhouse and therefore may act as a link between different production farms. Partly due to the increase in the number and types of movements made on to and off production farms and partly due to increased exposure of birds to the environment in the production sector, it is here where diseases such as AIV have the opportunity to enter a farm, rendering the production sector the focus of this study.

It has already been shown that AIVs have the potential to be spread to a large number of poultry premises via movement of humans and fomites [8,9]. Company personnel, feed lorries, egg collectors, slaughterhouse and catching company personnel (and equipment) have been identified as contact mechanisms between farms, over which disease may transmit [10]. It has also been shown [10] that up to 97%, 42% and 11% of premises associated with slaughterhouses, catching companies and multi-site companies, respectively, are connected. However, this result was reached on the assumption that all premises using the same slaughterhouse, catching company or belonging to the same multi-site company are all potentially connected, with all links being undirected. While most models assume that all potentially infectious connections are always "active" (though see also [1]), in practice there are other factors that will limit the dissemination of disease across the commercial poultry industry. First, over the time that a premises might be expected to be able to transfer infection to other premises, the number of actual connections will depend on the frequency at which the contacts are made. Furthermore, there are likely to be important distance constraints on how far people, vehicles and livestock will travel between premises. Therefore the range over which infection is likely to travel via these means will be limited (although there is currently no maximum journey time for poultry [11]). Also, for catching companies and company personnel, it is possible that there are regional divisions within the company, e.g. geographical sub-divisions within multi-site companies and area-based teams for catching companies, and this has not previously been considered in models of HPAI transmission in GB. Therefore, obtaining detailed data on catching company and slaughterhouse movements for simulation modelling of HPAI in GB has been highlighted as necessary for realistic modelling of HPAI

transmission [10]. The objective of this study was to collect detailed movement data from a large catching company and to further explore the potential for HPAI to spread via the routes highlighted.

Based on these new data, an individual farm-based transmission model was developed where nodes are poultry premises with links representing potential transmission routes between premises. Although the static approach (assuming all links between farms are potentially active) that we have previously adopted [10] was appropriate in the absence of detailed link data, the nature of these newly collated data enables us to use a dynamic network model, as is standard practice in disease modelling [2,12], to determine if the frequency and size (distance travelled) of movements between farms is of such a nature as to reduce the concern for a large HPAI epidemic in GB. In this updated model, the presence of links between premises is drawn from the collected movement data. This model also incorporates link directionality allowing for a more realistic and accurate model. Here, the potential for an HPAI epidemic is determined by considering the results of the individual-based transmission model.

Methods
Data sources
Movement data from a major catching company were obtained for all movements made over the 32 month period between 02/01/2005 and 11/08/2007. These data contain the times, dates and premises details for approximately 55,500 movements associated with 68 catching teams (within the company) over 415 poultry premises in GB. The premises associated with this catching company are distributed across GB, as shown in Figure 1. Given that if a premises is visited by a catching team, then there must be a movement on the same day between the premises and a slaughterhouse, these movement data also include movements of birds from premises to slaughter.

Population data on all commercial poultry premises housing 50 or more birds, and within 15 km of farms visited by teams belonging to the catching company, were taken in November 2007 from an extract of the GB Poultry Register (GBPR), provided by the Department for environment, food and rural affairs (Defra). The addition of these premises allowed us to consider disease transmission that can occur between premises that are in close spatial proximity, enabling us to consider how likely infection is to jump from the network of premises for which we have movement data to another network of premises for which no movement data were available for analysis. The addition of these premises brought the number of premises studied up to 10,692. The total number of premises recorded in the

Figure 1 Distribution of catching company farms in GB. Map to show the distribution of poultry premises associated with the catching company studied. Each point represents a poultry farm.
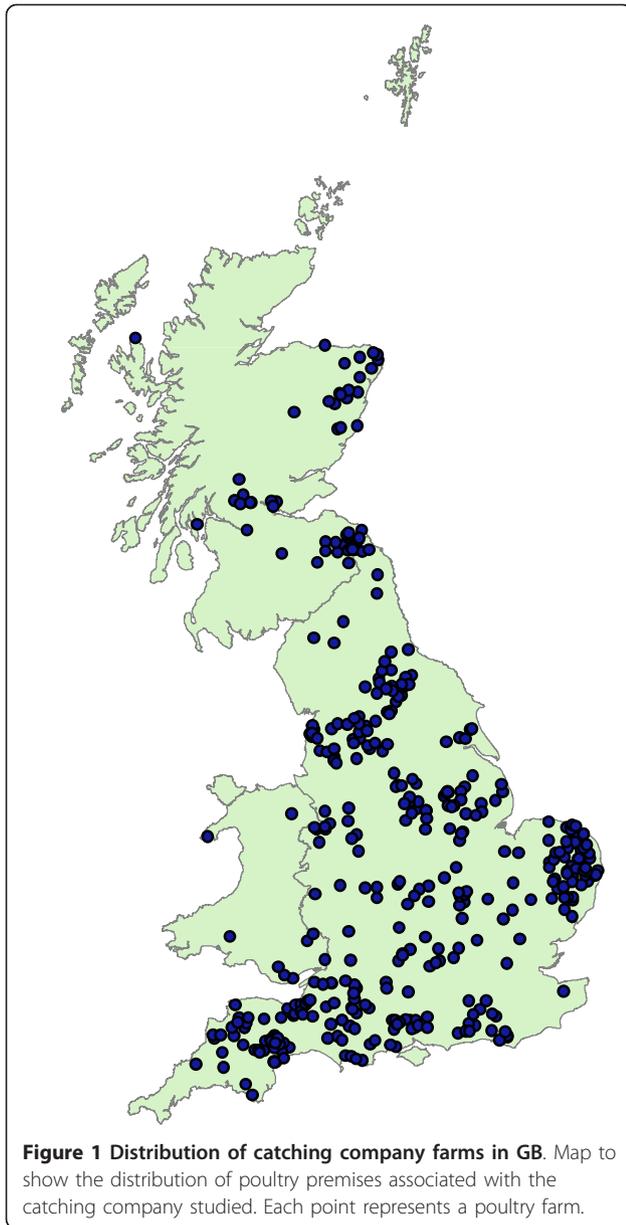
GBPR extract studied was 24,075. Although the total number of premises serviced by the catching company is small (approximately 2% of all premises in the GBPR), by comparing the number of premises serviced by the catching company with the number of premises known to be associated with the largest catching companies in England and Wales, we estimate that between 30% and 50% of premises serviced by a major contracted catching company are accounted for in this dataset [13 and unpublished data]. No data were available for small, independent catching companies.

Premises in the catching company database were matched to premises in the GBPR so that the model could be parameterised using location, premises

population size and species data. Temporal aspects were accounted for by preserving the order in which poultry premises were visited by individual catching teams on a daily basis. Additional information on which premises belong to integrated companies was obtained from a sample survey of integrated companies.

In the absence of quantitative movement data of company personnel for the farms studied, we sought expert opinion [P. Mcmullin, Poultry Health Services, *pers. comm.*] to inform the model of the likely frequency of movements of personnel between farms, based on species type, farm size and distance between farms belonging to the same company. The probability of companies using staff on multiple farms was estimated as well as the estimated frequency of visits of veterinary officials and area managers to poultry premises (Table 1).

Descriptive analysis

A descriptive analysis of the collected data is given in Additional File 1. This analysis was used to identify any trends in the data that could have important implications for disease transmission. In particular we considered how far catching teams and slaughterhouse vehicles travelled between premises, as it was shown in [10] that this had a large impact on the potential size of an HPAI outbreak. The frequency of catching team movements to premises, dependent on farm size, was also considered in order to determine if premises size should be recorded as an output of the simulation model.

Simulation model (see also Additional File 2)

A stochastic simulation model at the farm level was developed where farms were classed as susceptible, infected, detected or culled. HPAI could be transmitted between premises in close spatial proximity or through contact via catching teams, slaughterhouse vehicles or personnel movements within an integrated (multi-site) company. A random number generator chooses a premises in the network to infect and a random date of infection (within the 886 days covered by the catching company data set). If the seed farm was not visited within 15 days of this time point, assumed to be the maximum time that HPAI would survive in the farm environment, then transmission will be limited to local spread, often resulting in little or no onward transmission from the seed premises. When transmission beyond the seed premises did occur, outbreaks were allowed to run their course.

We assumed a time step of one day in the model, so that for each day of the simulation, once a premises had become infected, we assumed silent spread up to the time of detection. Detection and culling dates were set within the model at time of infection and were

Table 1 Model parameters

Parameter	Value	Source
Incubation period	Up to 1 day (shedding after 8 hours, death after one day)	I. Brown (*pers. comm*); [14,15]
Survival of virus on seed premises	Up to15 days	[16]
Probability of staff working on multiple premises (Farm size)	0.45 (< 50,000 birds) 0.1 (50,000 to 200,000 birds) 0 (> 200,000 birds)	P. McMullin (*pers. comm*)
Distance travelled by staff between premises	Up to 35 km	P McMullin (*pers. comm.*)
Frequency of vet visits	Every 50 days	P. McMullin (*pers. comm*)
Frequency of manager visits	Every 10 days (non-layer farms) Every 50 days (layer farms)	P. McMullin (*pers. comm*)
Probability catching team catches species (multi species farms only)	0.7 Chicken 0.12 Turkey 0.16 Duck/goose 0.01 Other	Calculated from catching company data, where species type available
Probability of catching team, slaughterhouse and owner transmission	0 to 0.2, in steps of 0.01, with additional parameter at 0.001 added.	N/A
Time to detection	2 to 6 days (15 days later for ducks/geese)	Extrapolation from [15-17]

Parameter values for the network simulation model of avian influenza transmission in Great Britain

dependent on whether the infected premises was in a protection zone (PZ), a surveillance zone (SZ), or neither, as described below.

On detection of notifiable HPAI in poultry, 10 km SZs and 3 km PZs are typically set up around infected premises. In the model, we assumed no transmission within the PZ/SZ via the normal movement of catching companies or slaughterhouse equipment since all movements in those zones would be monitored. Therefore, spread would only continue within the PZ/SZ via local spread. Time to detection within an infected flock was assumed to occur between 2 and 6 days (mean at 4 days) after infection [14-18], with the mean reduced to 3 days for flocks within a PZ or SZ. Culling occurs at the end of an epidemic day. Using the time taken to cull birds in the most recent outbreak of HPAI H5N1 in GB [19], we assumed that culling was completed on infected farms within 3 days of detection. One hundred simulations were run for a range of parameter values (Table 1). Up to 1,000 simulations were run for a subset of parameter combinations with no qualitative change in the results. For each simulation, the times at which each farm had become infected and the times at which their state changed from infected to detected and from detected to culled was recorded.

Catching team and slaughterhouse movements

When a movement occurred between infected and susceptible farms, infection was spread between farms with probability relating to the type of movement made. Where multiple species were held on one farm, we assumed that catching teams catch, on average, one species per visit with probability defined in Table 1. This species became infected with probability of transmission via catching team. If a susceptible farm had multiple links from an infected premises, then each link was treated independently, and the probability of infection therefore increased. We assumed that catching team and slaughterhouse vehicles do not remain infectious overnight, as we assume that effective decontamination procedures were in place. A premises was designated as infected if one or more species on the premises was infected.

Company (personnel) movements

We assume that spread of infection between farms belonging to the same multi-site, integrated company could occur either via the movements of area managers or veterinary officials between premises, or via staff working on multiple farms. Movements of veterinary officials, of area managers and of company personnel were simulated on a per day basis by using farm size and distance between farms belonging to the same multi-site company to identify using parameters in Table 1 if a) two premises are to be visited on the same day by the same person and, b) if the link made between premises will result in transmission of disease. The model assumes independence between days so that the last time a premises was visited is not accounted for.

Local (spatial) spread (see Additional Files 2 and 3)

Based on expert opinion, we assume spatial (primarily airborne) spread in GB is likely to occur with small probability ($p \leq 0.01$) and only for distances up to a maximum 0.5 km [D. Alexander, R. Irvine *pers. comm*.], according to the density kernel that is given in Equation 1.

For dist < 0.5 km:

$$p(trans|dist) = 0.01 \left[\left(1 - {dist}/{0.5}\right)^2 \right]^2 \qquad (1)$$

Else p(trans|dist) = 0

A sensitivity analysis of the model to the assumption that airborne spread could occur is given in Additional File 3.

Analysis of simulation output

We first consider the proportion of outbreaks that resulted in onward spread beyond the seed case. Here, the results follow a linear trend and, as the outcome is a binary variable (essentially secondary spread, or no secondary spread) dependent on explanatory variables that can be categorised into multiple levels, the analysis lends itself to a logistic regression. Thus a binary logistic regression was done (using Minitab v16) on the proportion of outbreaks that resulted in onward spread beyond the seed case. We next consider final epidemic size. In order to determine how the different types of transmission affect the epidemic size, two logistic regression models were fitted (Minitab v16). In the first, the binary response variable describes whether a small (< 25 premises) epidemic occurs or not. In the second, the binary response variable describes whether a large (> 65 premises) epidemic occurs or not. In both cases, the explanatory variables are the simulated transmission probabilities for AIV transmission via catching company, slaughterhouse- and owner-related movements.

Results

Additional File 1 gives a data summary and descriptive analysis of the catching company data. The key points of this analysis are given below:

1. When the frequency of movements is not accounted for, slaughterhouse related movements connected 94% of premises, catching team movements connected 76% of premises and owner movements 11% of premises that are associated with the catching company. However, when time is considered, catching teams connect only 2 premises per day and slaughterhouses an average of 3 premises per day.

2. Contrary to expectations, the data presented show that premises do use multiple slaughterhouses and are associated with multiple catching teams within the same company (consecutively over the time period studied). There is no overlap between poultry companies (i.e. poultry premises are associated with only one poultry company).

3. There is an increase in frequency of visits to larger premises, implying that these premises will be at a higher risk of infection should infection be transmitted by catching team or slaughterhouse vehicles/equipment.

4. Slaughterhouse vehicles and catching teams travel long distances between premises, with 72% of movements between premises exceeding 10 km in length.

Simulation modelling

One hundred simulations were run for a total of 10,648 scenarios. Each scenario represents a different combination of transmission values for each of the transmission routes studied. In particular, each scenario was created by ranging parameters from 0 to 0.2, in a step-wise fashion, such that each parameter took on one of 22 possible values within this range, giving rise to $22^3 = 10,648$ scenarios.

Proportion of positive epidemics spread beyond the index case

The aims of the simulation model are to determine if a large outbreak of AIV is possible in the poultry industry in GB and, if so, what might cause a large outbreak to occur. One way of answering the first question is to consider how often infection spreads beyond the seed premises. That is to ask "how many simulated outbreaks result in secondary spread?"

When all scenarios and all simulation results are considered together, infection spread beyond the seed premises in approximately 15% of the simulations run (mean value over all simulations and all scenarios). Figure 2 shows how the distribution of infections that result in secondary spread varies as the probability of AIV transmission is increased. For this, the probability of transmission was calculated by combining the probability of transmission via catching team, slaughterhouse and company personnel, as shown in Equation 2.

$$P(i\ Infected) = 1 - (\prod_{j-1}^{3}(1 - p_j)) \tag{2}$$

for p_j probability of infection for via link type *j*.

Infection resulted in secondary spread (beyond the seed premises) in up to 35% of scenarios. The simulation that gave the maximum number of cases that spread beyond the seed premises was from the following scenario: catching team (cc) = 0.04, company personnel (owner) = 0.19 and slaughterhouse (sh) = 0.13. This suggests that high probabilities of transmission are not necessary in all three potential transmission routes for infection to (relatively) frequently spread beyond the index case.

Results from a logistic regression analysis are shown in Tables 2, 3 and 4. Consider the odds ratios in Tables 2, 3 and 4. The results show that transmission via the movement of catching teams does not have a significant effect on the probability that an outbreak will result in
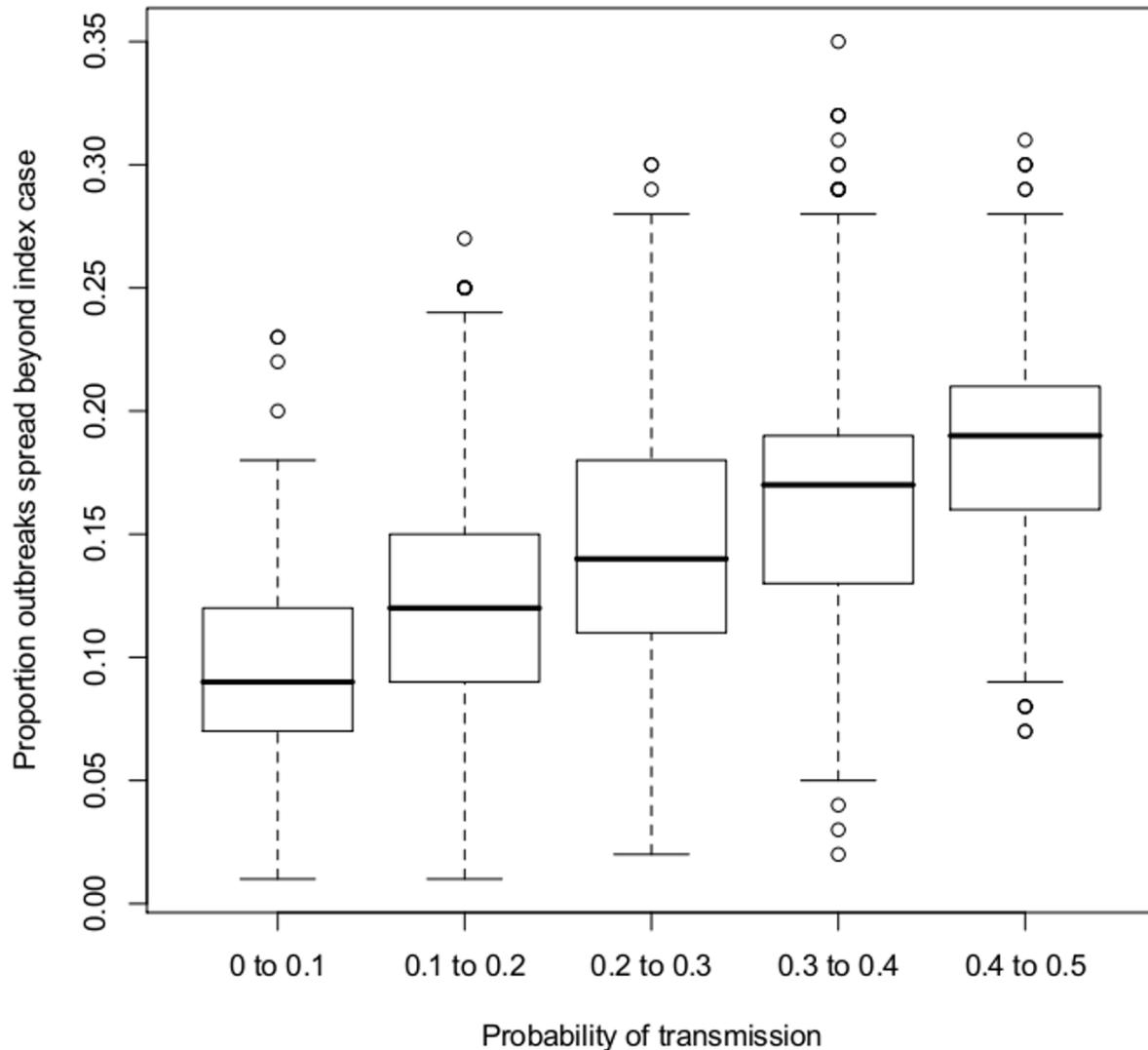
Figure 2 The proportion of outbreaks that spread beyond the seed premises for all simulation results. Boxplots to show the median, quartiles and outer points of the proportion of outbreaks (over 100 simulations) that spread beyond the seed premises, for increasing rates of transmission. Here, transmission is recorded as the combined risk of AIV transmission over all routes, according to Equation 2.

secondary spread. However, movements related to company personal appear to be significant at all levels, with the exception of transmission set to $p = 0.001$. Movements related to slaughterhouse vehicles are significant in the probability that an outbreak will result in onward spread only when the probability of transmission is high enough (here, the model predicts a rate of > 0.06 for a significant effect to be seen). Further, the odds ratios also tell us that, under the assumptions made, as the

rate of transmission increases for owner movements in particular, the effect on the probability of secondary spread is increasingly large, with the odds ratio rising to 2.11 (2.03, 2.19 (95% CIs)) for a transmission rate of 0.14 compared to zero. This suggests that the probability of secondary spread beyond the seed premises is not uniformly affected by transmission rates across the different link types. This is driven by the characteristics of the networks over which disease can spread.

Table 2 Binary logistic regression, with odds ratios calculated for the probability of secondary spread versus catching company transmission rates

Transmission rate	Odds Ratio	Lower 95% CI	Upper 95% CI	p-value
0.001	0.97	0.93	1	0.064
0.01	1	0.97	1.04	0.813
0.02	0.95	0.92	0.98	0.005
0.03	0.97	0.94	1.01	0.14
0.04	1.02	0.98	1.06	0.303
0.05	0.96	0.93	0.99	0.024
0.06	0.96	0.93	1	0.043
0.07	0.99	0.95	1.02	0.451
0.08	0.96	0.93	1	0.038
0.09	0.95	0.92	0.99	0.011
0.1	0.97	0.94	1.01	0.124
0.11	0.98	0.94	1.01	0.23
0.12	0.99	0.96	1.03	0.677
0.13	1	0.97	1.04	0.906
0.14	0.98	0.94	1.01	0.187
0.15	0.98	0.95	1.02	0.267
0.16	0.96	0.92	0.99	0.018
0.17	1	0.96	1.03	0.871
0.18	0.98	0.95	1.02	0.313
0.19	0.96	0.93	1	0.047
0.2	0.98	0.95	1.02	0.359

Table 3 Binary logistic regression, with odds ratios calculated for the probability of secondary spread versus owner transmission rates

Transmission rate	Odds Ratio	Lower 95% CI	Upper 95% CI	p-value
0.001	0.98	0.94	1.03	0.488
0.01	1.09	1.04	1.14	0
0.02	1.19	1.14	1.24	0
0.03	1.27	1.22	1.33	0
0.04	1.38	1.33	1.44	0
0.05	1.42	1.37	1.48	0
0.06	1.47	1.41	1.53	0
0.07	1.53	1.47	1.59	0
0.08	1.66	1.59	1.72	0
0.09	1.74	1.67	1.81	0
0.1	1.75	1.69	1.83	0
0.11	1.86	1.79	1.94	0
0.12	1.97	1.89	2.04	0
0.13	1.94	1.87	2.02	0
0.14	2.11	2.03	2.19	0
0.15	2.09	2.01	2.17	0
0.16	2.19	2.11	2.27	0
0.17	2.24	2.16	2.33	0
0.18	2.33	2.24	2.42	0
0.19	2.38	2.29	2.47	0
0.2	2.38	2.29	2.47	0

In order to visualise the effect that the interaction of different transmission routes can have on the results, each potential transmission route was considered on its own as well as in combination with one or more other potential routes of transmission. Figure 3 shows boxplots that describe the proportion of outbreaks that result in onward spread for different scenarios. The figure shows that a higher proportion of outbreaks occur for transmission via owner-related (gp2) movements than for catching company (gp1) or slaughterhouse-related (gp3) movements. It appears that adding catching company transmission to either transmission via slaughterhouse- or owner-related movements (gp5 and gp6, respectively) has little impact on the proportion of outbreaks that would result in secondary spread if the main effects were considered alone. However, the combination of slaughterhouse- and owner-related movements (gp4) suggests that this combination can result in a large proportion of outbreaks resulting in secondary spread. Finally, it is interesting to note that Figure 3 also shows that when all three transmission routes (cc, sh and owner) are greater than zero, a large proportion of outbreaks can result in onward spread (gp7).

The statistical significance of interaction terms can be determined by refitting the logistic regression model, with interaction terms included. As the model did not converge when all tested transmission rates were considered as a single level, in order to consider the potential interaction between different networks the data were categorised into "high", "medium" and "low" probabilities of transmission and the model refitted (see Additional File 4 Table S1). Although the results (Additional File 4 Table S1) show that only medium and high levels of owner transmission have a significant effect on the results, for all levels of owner/slaughterhouse interaction, there was a significant difference between the results from this interaction, compared to zero. This implies that whilst slaughterhouse transmission alone is not enough for an outbreak to result in secondary spread, the combination of owner and slaughterhouse related movements has a significant effect on the probability that an outbreak results in secondary spread, even for low levels of transmission of disease. The results from Additional File 4 Table S1 also show that there is no significant interaction effect from the catching company - owner interaction or from the catching company - slaughterhouse interaction (the confidence

Table 4 Binary logistic regression, with odds ratios calculated for the probability of secondary spread versus slaughterhouse transmission rates

Transmission rate	Odds Ratio	Lower 95% CI	Upper 95% CI	p-value
0.001	0.97	0.93	1.01	0.093
0.01	0.99	0.95	1.02	0.435
0.02	0.99	0.95	1.03	0.597
0.03	1	0.96	1.03	0.861
0.04	1	0.96	1.03	0.824
0.05	1	0.96	1.04	0.927
0.06	1.04	1	1.08	0.036
0.07	1.03	1	1.07	0.068
0.08	1.04	1.01	1.08	0.019
0.09	1.04	1.01	1.08	0.019
0.1	1.05	1.01	1.09	0.012
0.11	1.07	1.03	1.11	0
0.12	1.05	1.01	1.09	0.008
0.13	1.09	1.05	1.13	0
0.14	1.08	1.04	1.12	0
0.15	1.09	1.06	1.13	0
0.16	1.08	1.04	1.12	0
0.17	1.08	1.04	1.12	0
0.18	1.09	1.06	1.13	0
0.19	1.1	1.06	1.14	0
0.2	1.1	1.06	1.14	0

intervals on all odds ratio include zero). This means that, in theory, catching company transmission can be dropped from the model. With catching company removed from the results and the regression rerun, the final logistic regression results are given in Table 5.

Epidemic size

In this part of the analysis, only epidemics that result in spread beyond the seed premises are considered. This accounts for approximately 15% of all simulation results.

For all results, there were no epidemics of size between 23 and 66 premises (see Figure 4). The number of large epidemics, which we consider here to involve more than 65 infected premises (those epidemics in Figure 4b), is small, representing 0.2% of all results. However, these are the epidemics that are likely to cause the most strain on resources in an outbreak situation, so it is important to determine from the data if the rate of transmission via different routes, or the index premises in these epidemics, have any notable characteristics.

There were a total of 330 individual premises that were included in the set of outbreaks that resulted in onward spread (~80% of population for which movement data were available). Of these, 95 individual

premises were seed premises in the (249) "large" epidemics recorded. All 95 of these premises were also seed premises in the list of (130939) "small" epidemics. Premises size (number of birds) was available for 78% of seed premises for large epidemics, and for 94% of seed premises for small epidemics. The results (Table 6) suggest that a large epidemic is more likely to occur when infection is seeded in large premises (37 of 74 "large" epidemics began in large premises). However, infection into large premises does not imply a large epidemic will occur. Interestingly, the mean epidemic size when infection is seeded in small premises (3.8) is larger than that of both medium (2.8) and large premises (3.1). This may be connected to the probability of an outbreak resulting in spread beyond the seed premises, as owner links have been shown to be important and owner movements are more likely to occur in small premises (an immediate effect of the model assumptions).

In order to determine how the different types of transmission affect the epidemic size, two logistic regression models were fitted. In the first, the binary response variable describes whether a small (< 25 premises) epidemic occurs or not. In the second, the binary response variable describes whether a large (> 65 premises) epidemic occurs or not. In both cases, the explanatory variables are the simulated transmission probabilities for AIV transmission via catching company, slaughterhouse- and owner-related movements. The results are shown in Additional File 4 Table S2 to S7.

For small epidemics, Additional File 4 Tables S2 to S4 show that catching company movements have a significant influence on the results for a range of probability values between 0.02 and 0.16. Interestingly, when these results are significant (the odds ratio confidence intervals do not contain zero), the odds ratios show that the probability of a small epidemic decreases (the odds ratios are less than 1) with an increase in catching company transmission rates, when compared to zero. This suggests that an increase in catching company transmission might result in a higher proportion of epidemics being larger. Additional File 4 Table S3 shows that transmission via owner movements is significant at all levels above $p = 0.001$. Above this value, the odds ratios are all larger than one, implying that increasing the rate of transmission results in the likelihood of a small epidemic occurring to increase. For slaughterhouses (Additional File 4 Table S4), significant results are obtained for transmission rates > 0.05. The strength of the significance does not increase in proportion with the increase in transmission, with all transmission rates > 0.12 having an odds ratio value of between 1.07 and 1.10. These results therefore suggest that the most influential parameter for the probability of a small epidemic to occur is transmission via owner movements.
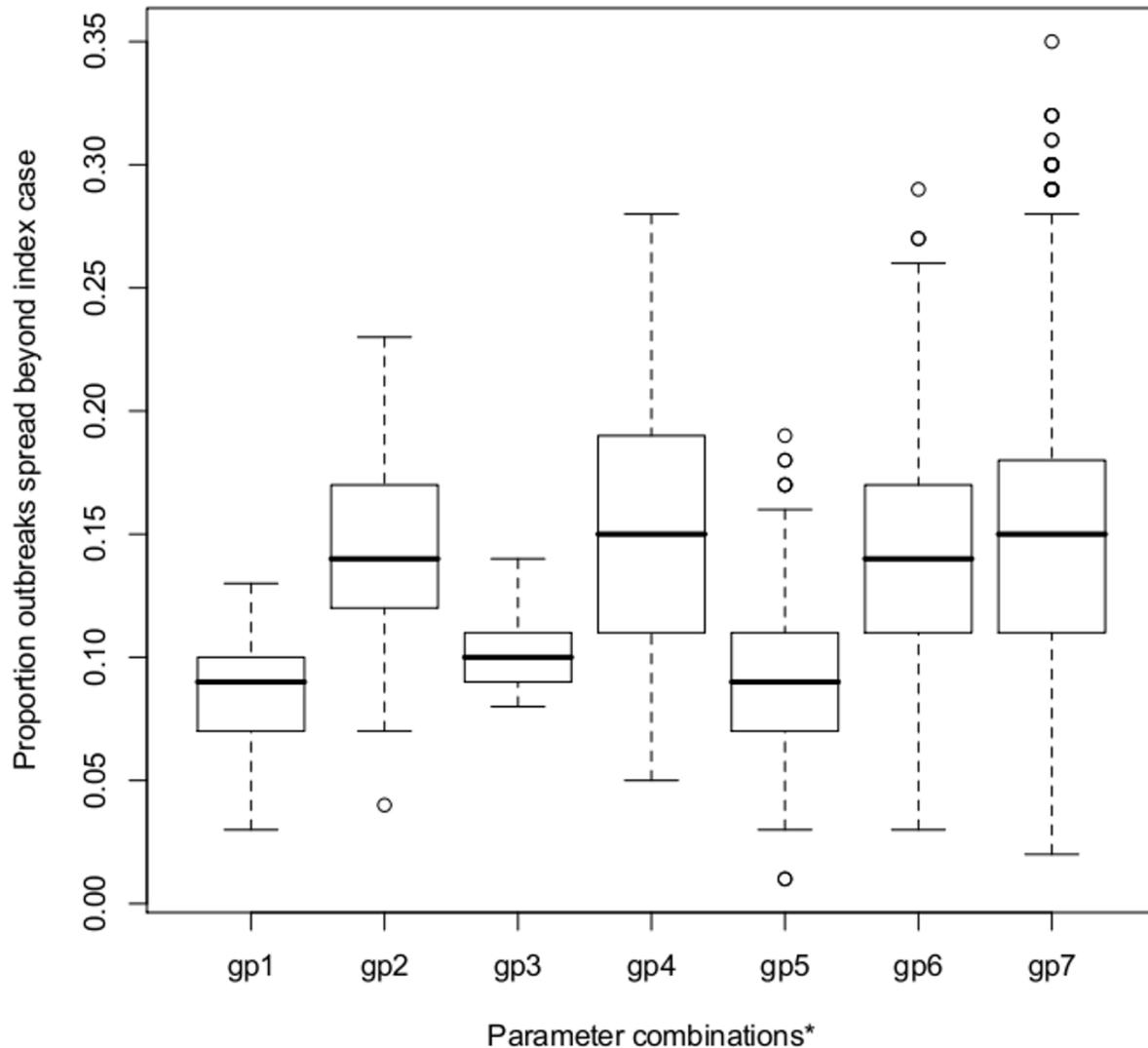
Figure 3 The proportion of outbreaks that spread beyond the seed premises for different parameter combinations. Boxplots of the proportion of outbreaks that result in spread beyond the seed premises, for different parameter combinations. gp1 = sh, gp2 = owner, gp3 = cc, gp4 = owner and sh, gp5 = cc and sh, gp6 = cc and owner, gp7 = cc, owner and sh. Within each group, parameters are varied from 0 to 0.2.

Additional File 4 Table S5 and S6 show that, contrary to expectations, neither catching company nor owner movements play a significant role in the probability that an outbreak will result in a large epidemic. For large epidemics, the most influential predictor is the transmission rate via slaughterhouse linked movemernts (Additional File 4 Table S7). Analysis of the odds ratios for slaughterhouse transmission versus large epidemics shows that this transmission route is only influential if it is high enough (above 0.12). However, when it is high enough, the upper 95% limits (for the odds ratios) show that an increase from zero transmission to a higher transmission rate will result in a large epidemic being up to 28 times more likely. This is a very striking result with heavy implications on resources, for example, in the event of an outbreak. It is therefore essential to

Table 5 Binary Logistic regression: secondary spread versus transmission rates for interaction between transmission routes at different levels of transmission

Predictor	Coefficient	SE	Odds Ratio	Lower 95% CI	Upper 95% CI	p-value
Constant	-2.16587	0.071836				0
owncat						
1	0.004215	0.076562	1	0.86	1.17	0.956
2	0.415397	0.075335	1.51	1.31	1.76	0
3	0.631829	0.074869	1.88	1.62	2.18	0
shcat						
1	-0.22299	0.077486	0.8	0.69	0.93	0.004
2	-0.12265	0.077053	0.88	0.76	1.03	0.111
3	-0.0784	0.076875	0.92	0.8	1.07	0.308
owncat*shcat						
1*1	0.248773	0.082484	1.28	1.09	1.51	0.003
1*2	0.227419	0.082041	1.26	1.07	1.47	0.006
1*3	0.229411	0.081855	1.26	1.07	1.48	0.005
2*1	0.207304	0.0812	1.23	1.05	1.44	0.011
2*2	0.154659	0.080772	1.17	1	1.37	0.056
2*3	0.140458	0.080593	1.15	0.98	1.35	0.081
3*1	0.228509	0.0807	1.26	1.07	1.47	0.005
3*2	0.174293	0.080272	1.19	1.02	1.39	0.03
3*3	0.15525	0.080095	1.17	1	1.37	0.053

Final model.
Level 1 = low transmission rate 0 - 0.06, level 2 = medium transmission rate 0.07 - 0.13, level 3 = high transmission rate 0.14 - 0.2. sh = slaughterhouse, own = company personnel. SE = standard error.

determine the true probability of transmission via this route.

Spatial spread

While the majority of outbreaks did not result in further onward transmission from the index premises, outbreaks could potentially cover up to 20% of the population (for a range of parameter values < 0.2) for which network data were available, covering distances of up to 730 km between premises (see Additional File 5, Figure S1). Although for the largest distances to be covered (> 700 km), at least one transmission parameter must be as high as 0.12, occasionally, distances over 600 km between premises are reached for transmission parameters between zero and 0.07. This has important implications for the availability of control resources as the number of premises in the SZs will be greater if dissemination of virus is geographically widespread and therefore potentially involving a larger number of local disease control centres. Large epidemics invariably resulted in widespread geographical dissemination of virus.

In this model, infection can only be spread into premises that are not serviced by the catching company, by spatial transmission of disease, to premises within 500 m of infected premises. This results in infection of premises that are potentially connected to different sub-networks (via other catching companies, slaughterhouses or poultry companies for example) in less than 1% of the simulations run. However, we have seen that transmission via sh-linked movements is an important factor in determining final epidemic size, and slaughterhouses that are included in the network studied may also be used by poultry premises not included here. This implies that if this route is important, infection may leak into other sub-networks of the industry much more frequently.

Discussion

Despite the extent of data previously available on the British poultry industry, the detailed contact structures within the poultry industry in GB have only been poorly understood. Previous studies have been able to identify potential contact structures but assumptions have had to be made on the frequency and patterns of movements between farms [10,15,20]. Whilst it is important to acknowledge that the models presented here rely heavily on expert opinion (which is arguably a drawback of such a modelling approach), in the absence of outbreak data for AIV in GB, this cannot be avoided. For this reason, we have considered many scenarios by varying parameter values and by combining expert opinion
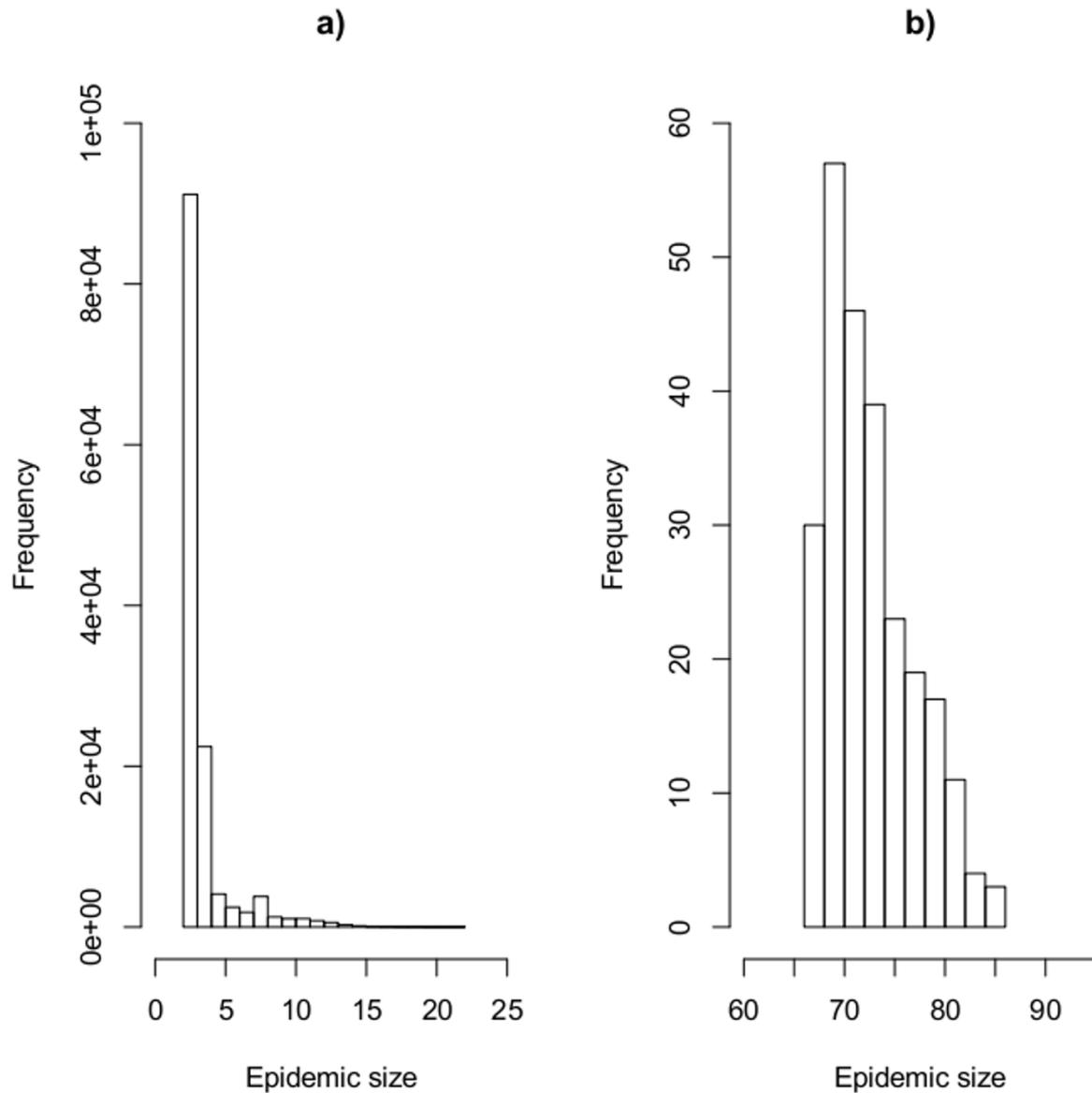
Figure 4 Epidemic size. Histogram of epidemic size for infections resulting in onward spread beyond the seed premises. a) epidemics including fewer than 25 infected premises and b) epidemics including more than 65 infected premises.

Table 6 Effect of seed premises on outbreak size

Seed premises size	Number unique premises in small epidemics (seed)	Number unique premises in large epidemics (seed)	Proportion outbreaks resulting in large epidemics
Small (≤ 100,000 birds)	35	20	0.57
Medium (100,000 - 200,000 birds)	59	17	0.29
Large (> 200,000 birds)	141	37	0.26

The proportion of outbreaks that result in large/small epidemics for different size categories of seed premises.

with real time movement data from a large catching company, we have been able to adopt a similar approach to that used in [1] to investigate the potential spread of AIV in the GB poultry industry.

The results presented here show that restrictions on the frequency of movements can have an important role in determining disease spread risk. In particular, connections via slaughterhouses can connect a large number of premises over a large geographical area, important in the potential for virus dissemination. Spread via slaughterhouse-linked movements is most prominent when partial flock depopulation is being undertaken at a farm, as this action results in more premises being visited in one day and potential infection of birds that remain on the farm. This is also an important output for the control of diseases other than HPAI, such as *Salmonella* or Campylobacter spp., where the slaughterhouse is a more likely reservoir for pathogens [21]. We note here that, whilst slaughterhouses and catching teams are separated in this study, in some cases one might group the two transmission routes together under the assumption that any movement that arises due to a catching team visiting a farm is considered a 'catching company' movement. The results are likely to be sensitive to such an assumption and thus it is important not to misinterpret them. However, the principles used in this study remain valid for the potential transmission of diseases spread by the faeco-oral route, such as Campylobacter spp. and *Salmonella*, as well as different strains of HPAI. The model is well-suited to investigating diseases where expert opinion does not have to be so heavily relied upon for model parameterisation (as expert opinion adds uncertainty to results, resulting in one only being able to answer 'what-if' scenarios, in a situation the model assumptions may affect interpretation of results). In Campylobacter research, for example, one would expect the model results to be quite different due to difference in epidemiological characteristics of Campylobacter spp. compared to HPAI. With a perceived higher prevalence of the pathogen, we would expect the results of the model presented here, applied to Campylobacter spp. to show that catching company movements are likely to have a bigger effect on the spread of disease between farms.

Despite the relatively heavy use of expert opinion to estimate model parameters in this study - in particular for the frequency of movements made by company personnel, we can use the model presented here to hypothesise about the importance of different types of potentially infectious links between poultry premises and we can conclude from these results that, where slaughterhouses can act as a reservoir for pathogens, the spread via this route should be minimized. This can be achieved through additional bio-security measures, such

as thorough cleaning of the crates and vehicles that carry the birds, for example.

The results that catching team movements have little effect both on the probability of an outbreak resulting in onward spread beyond the seed premises and on the probability of a large epidemic occurring are important results, as they suggest that the number of farms that a catching team visits during the infectious period of the virus is too low to link a high number of farms, in GB, during an epidemic. For pathogens that can survive for longer periods in the environment or that are more prevalent than HPAI (such as Campylobacter spp.), the number of farms that can be linked by catching team movements will be (potentially significantly) higher. However, while extensive and therefore of value, the data used here correspond to only one (large) catching company that is made up of a 68 distinct catching teams. As each farm may be visited by one or more of the catching teams, there are no distinct regional divisions apparent within this company as was initially expected. Further, these data do not consider further spread once other networks (e.g. connected by slaughterhouses and catching companies) contain infected premises.

Although all three transmission routes were positive when a large proportion of (simulated) outbreaks resulted in spread beyond the seed premises, the fitting of a regression models suggests that only company personnel movements significantly influence the probability that infection will spread beyond the seed premises. This highlights the importance of obtaining more accurate estimates on the frequency of movements of company personnel and the probability of transmission via this route.

There was a significant interaction effect for the owner*slaughterhouse interaction on the proportion of outbreaks that result in onward spread. However, the combinations of potential transmission of disease via catching company and company personnel movements, or slaughterhouse-linked and catching company movements have little effect on the proportion of outbreaks that result in onward spread, particularly compared to the individual owner effect. This can be explained by the frequency of movements relative to premises size (Additional File 1 Figures S6 to S9), such that the increased frequency of catching company movements in particular (and also, but less so for slaughterhouse-linked movements), to larger premises is not high enough to force these potential transmission routes to have a large effect on the proportion of outbreaks that result in spread beyond the seed premises, compared to transmission via owner movements. Having highlighted owner movements as important in previous studies [10] and given that they can have a large effect on the

number of outbreaks resulting in an epidemic, it is recommended that data collection is expanded to include movement data from an integrated company, furthering our ability to provide more robust estimates of epidemic size and likelihood.

The results show that there is a "jump" from epidemics of size lower than 23 infected farms (< 5% of premises), to epidemics containing more that 65 infected farms (~20% of premises). This is in line with results published by [22], who report that a predictor of the need to intensify control efforts in GB is whether an outbreak exceeds 20 infected premises. The results follow the pattern of epidemic outbreak sizes (at least qualitatively) as expected for any stochastic epidemic model, with epidemics either going extinct early, or growing to reach a substantial proportion of the population. Whilst this result, which represents a threshold for the basic reproduction number, R_0, will be affected by the structure of the networks, investigating network structure alone is not enough to fully investigate the effect of R_0. To do this, one would need to understand the effect of the individual transmission rates on the probability of a large outbreak.

When comparing the results for small epidemics against those for large epidemics, two factors that differ significantly between the two categories are worth noting: the effect of the probability of transmission via slaughterhouse movements and seed premises size. Large epidemics are up to 28 times more likely for higher levels of slaughterhouse transmission (compared to zero), implying that the characteristics of the network of slaughterhouse links are maintained even when a time component and control measures are added, resulting in connectivity between a higher proportion of premises via this route than via any other route. This result confirms that slaughterhouses are an important factor in this model. The size of seed premises plays a role here as there is an increase in frequency of catching team and slaughterhouse visits to larger premises (Additional File 1 Figure S10). This results in large outbreaks being more likely to occur, as a result of infection in a large seed premises. It is reiterated however that this does not imply that infection seeded in large premises will always result in a large outbreak. Nevertheless, this result does suggests that if premises are to be prioritised during contact tracing, there will be some benefit to targeting large premises ahead of smaller ones in a epidemic situation. Further investigation into all premises included in these epidemics to identify whether the same premises are included in the large epidemics is highlighted here as an area for further research. This will also identify premises that might be considered particularly high risk.

We note that all slaughterhouses that appear in the movement data analysed are recorded as slaughtering birds from farms that are not visited by the catching company studied. This implies that the network of premises studied is not closed; with up to 131 additional farms sending birds to the same slaughterhouse (unpublished data), the possibility of disease spreading into other sub-networks within the industry is potentially high. It is therefore very important to ensure the data held on slaughterhouses and their customers is both complete and up to date. This will enable better prioritisation of the potentially large number of premises that could undergo surveillance in an outbreak situation.

Our results show that the distribution of poultry premises in GB is not dense enough for airborne transmission of AIV contribute significantly to between premises spread amongst premises recorded in the GBPR, so long as the distance for airborne transmission is less than 500 m. This has not been the case in past outbreaks in other countries, such as the Netherlands and Italy, where local spread is likely to have played a role in the transmission of disease from one farm to another. Should a virus strain that can easily transmit via airborne transmission be modelled, then local spread may result in spread between premises that have no other direct connections. For other virus strains, this could have a large impact on the proportion of outbreaks resulting in spread beyond the seed premises and the maximum epidemic size. This implies that there is possible scope to reduce the size of the 10 km SZs, freeing resources for use elsewhere. This could be explored further by using network data currently available to explore how large a SZ should be, taking into account resource constraints and simulating over a range of assumptions regarding transmission rates. The mean number of premises affected by an epidemic may be dependent not only on the underlying epidemiological parameters, but also on the total resources available. Resource constraints were not included in this model but the model could be adapted to aid future work in this area, important for exploring optimal resource allocation in order to provide the most efficient detection of AIV and the curtailing of the outbreak.

Conclusions

Previous work has shown that large proportions of the poultry industry are potentially connected by catching companies and by slaughterhouse [10]. However, such analyses did not take into account the restriction in the number of interaction events that could occur over the course of a typical infectious period. Including these effects, such as via the explicit spatio-temporal simulations explored in this study, shows that such restrictions

can have an important role in determining disease spread risk.

In line with previous work [10], we have shown that slaughterhouses connect the highest number of premises in the poultry industry. Furthermore, the potentially high frequency of company personnel between farms renders this type of movement more important in the beginning of an outbreak. Contrary to expectations, however, the frequency of movements of catching teams between premises is not high enough to connect large numbers of premises, reducing the potential for a large outbreak spread via this route, in GB. The size of seed premises played a role in final epidemic size suggesting that there will be some benefit to targeting large premises ahead of smaller ones in an epidemic situation. The ability of the virus to jump from one sector of the industry to another highlights the importance of keeping data on movements on and off poultry farms both detailed and up to date.

Additional material

Additional file 1: Descriptive analysis of catching company data.

Additional file 2: Simulation modelling methods and outputs.

Additional file 3: Sensitivity to spatial spread.

Additional file 4: Results - supplementary tables.

Additional file 5: Maximum distance between infected premises.

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Authors' contributions
MA designed the study. JED collected the data. JED, RRK and IZK analysed the data. JED wrote the simulation model. JED wrote the manuscript with input from MA, RRK and IZK. All authors have read and approved the final manuscript.

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S1 Additional File 1 - Descriptive analyis of catching company data.

S1.1 Individual network characteristics

For these data, a connection was assumed between premises if the two premises were visited on the same day. Under this assumption, over the time period of 936 days, catching teams connected 317 of the 415 (76%) poultry premises visited. The remaining premises were visited either as a one off, or were never visited on the same day as other premises, by the same catching team. Using Tarjan's algortithm [Sedgewick, 2001] to identify clusters of premises that are connected by catching teams, a total of 12 disjoint clusters were found, 11 of these 12 clusters contain fewer than 5 poultry premises. This implies that, over the time period studied, almost 300 premises are connected in at least one direction. In fact, each poultry premises was connected, by catching teams, to an average of 3.98 other premises over the time period studied (this figure, which describes the mean degree per poultry premises, excludes self-loops and counts repeated links only once).

Over the same time period, slaughterhouses connected 391 of the 415 (94 %) poultry premises, immediately suggesting that this network is better-connected than that of premises linked by catching team. These data contained 4 clusters (excluding isolated nodes), one containing 383 premises and the remaining three with four or fewer premises. Each premises was connected, via slaughterhouses, to an average of 15.33 other premises during the time period studied.

The in- and out-degree distributions for premises linked by catching company are given in Additional File 1 Figure S1. In order to show that the network of premises connected by catching team is approximately scale free (i.e. is made up of a small number of highly connected nodes and high number of nodes with a small number of connections), a power-law distribution was fitted to both in- and out-degree to give the number of nodes, x_{in} and x_{out}, with degree, d, as shown in Equation (1) (corresponding R^2 values for in- and out-degree distributions were $R^2_{in} = 0.92$ and $R^2_{out} = 0.86$).

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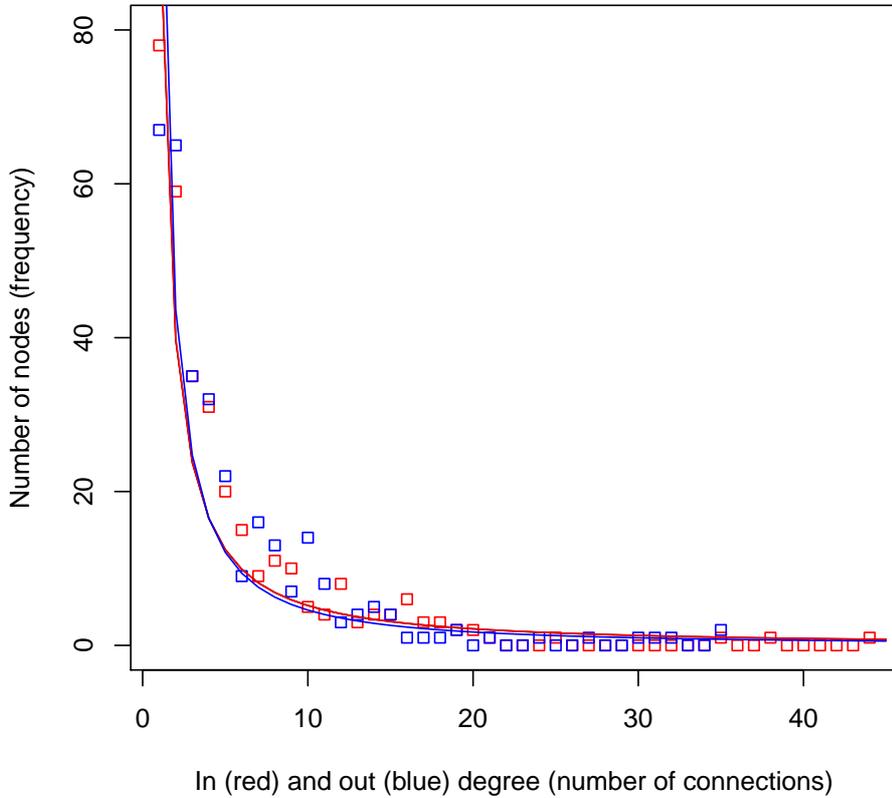
Figure S1. Degree distribution for premises linked by catching company. In-degree = red, out-degree = blue. Points represent true data, lines represent fitted power-law.

$$x_{in} = 95.73x^{-1.27}, x_{out} = 115.20x^{-1.4} \tag{1}$$

For slaughterhouse linked movements, the in- and out-degree distributions, shown in Additional File 1 Figure S2, could not be characterised by a power-law distribution (the R^2 values for a fitted power-law distribution were 0.49 and 0.43 for in- and out-degree, respectively). The slaughterhouse degree distribution showed a distribution that is closer to a Poisson distribution. However, as the mean and variance are not equal, a Poisson distribution could also not be fitted to the data. Despite displaying Poisson characteristics, implying the network is random, the
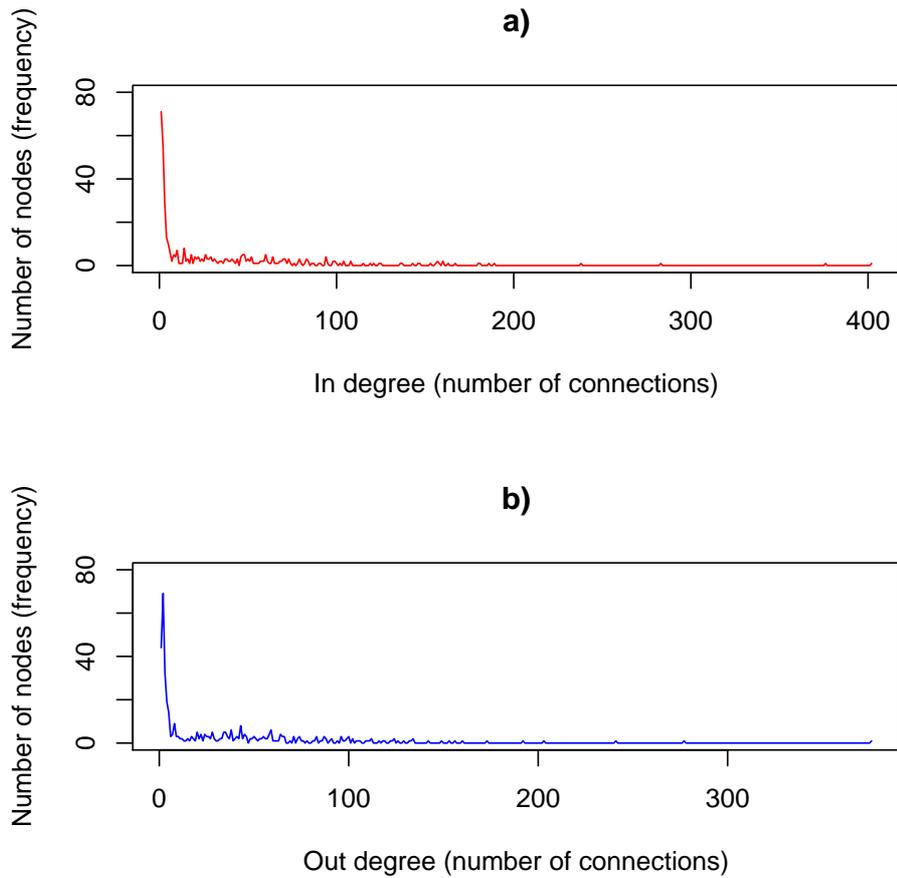
Figure S2. Degree distribution for premises linked by slaughterhouse. (a) In-degree (red) and (b) out (blue).

data showed some exponential decay, which implies that the network may be held together by only few 'hub' nodes, with high degree.

S1.2 Frequency of movements per day

If all links between premises associated with the Catching Company are considered at once (as previously assumed [Dent et al., 2008]) and a per link probability of transmission assumed between farms that are linked, then links between the same premises on different days become important as they can increase the probability of disease transmission between premises. However, in reality AIV is not likely to transmit over such an extended time period and so

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the frequency of movements on a daily basis may be more important to consider than that of connectivity over a longer time period.
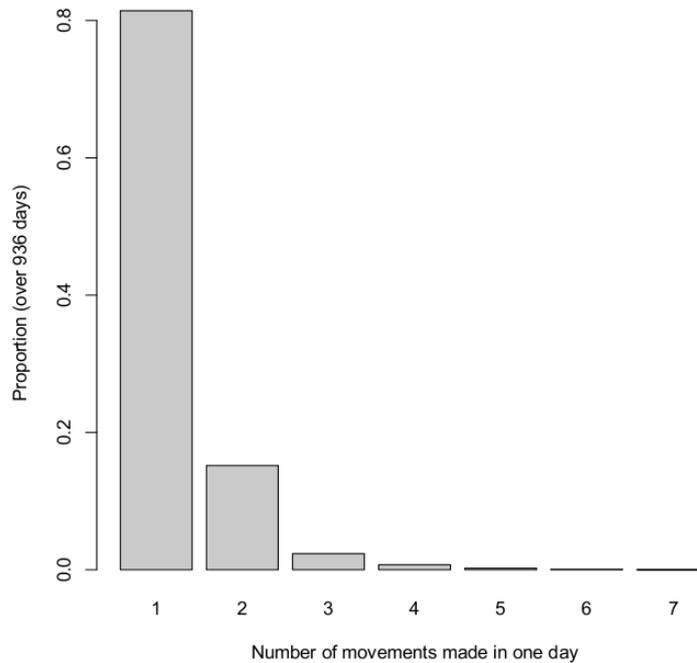

Figure S3. Number of poultry premises visited per catching team per day.

The average number of connections per node for premises connected on the same day is 0.19 for connections made by catching team movements and 2.53 for slaughterhouse linked movements (this figure assumes that self-loops -where the same premises is visited multiple times on one day by the same catching team or slaughterhouse vehicle- are not accounted for). There were a large number of visits to premises that did not result in onward movements. When an onward movement did occur, a mean of 1.22 (variance $= 0.39$) and 3.33 (variance $= 9.5$) premises were connected by catching team and slaughterhouse, respectively. Additional File 1 Figures S3 and S4 show the empirical distributions of data describing how many premises are visited per day by catching teams and slaughterhouse vehicles, over the full 936-day period.

Additional File 1 Figure S3 shows that in approximately 84% of cases, only one premises is
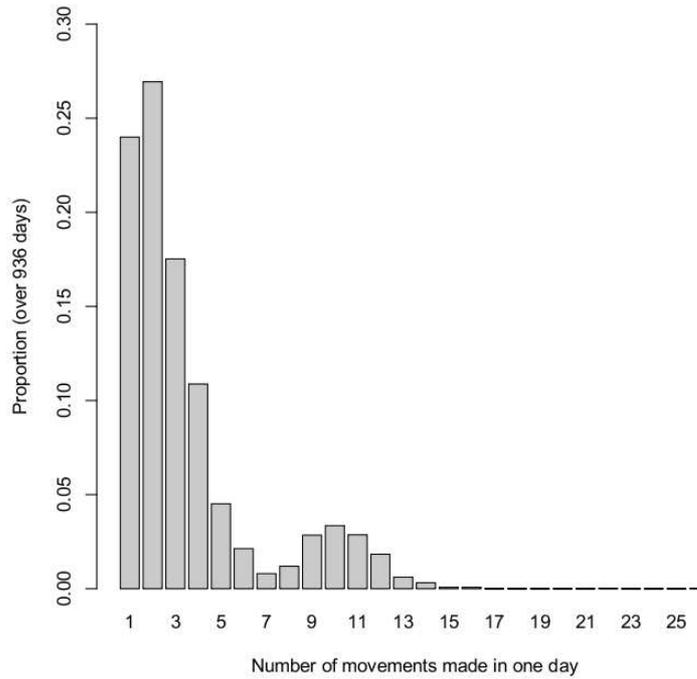
Figure S4. Number of poultry premises visited by slaughterhouse vehicles, per day.

visited by a catching team on a given day, implying that the event that catching teams visit more than one premises in a day is rare.

Despite the low probability that more than one premises was visited in a day by catching teams, the data show that up to seven premises were visited in one 24-hour period (see also Additional File 1 Figure S3), so it is not wise, at this stage, to eliminate this as an important transmission route between premises. In addition, the data show that only 24% of poultry premises are serviced by a single catching team, with some premises being visited by up to 30 different catching teams (Additional File 1 Figure S5) within the time period studied. Although no premises were visited on the same day by different teams, this results implies that there is mixing between teams and that catching teams can indeed connect multiple farms.

Conversely, for slaughterhouses, only 24% of visits were to single premises, implying that the event that a slaughterhouse vehicle visited more than one premises on a single day was much
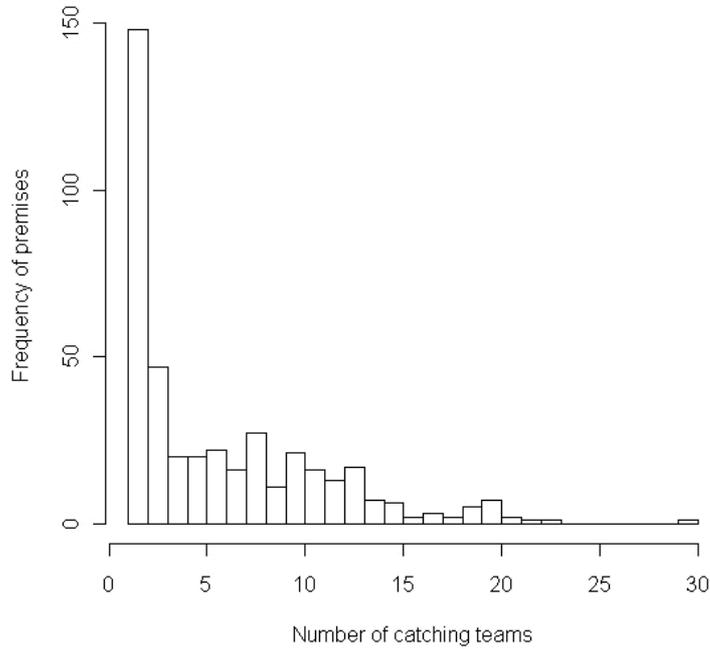
Figure S5. Number of catching company teams associated with poultry premises.

less rare. This occurs due to the lower number of slaughterhouses (compared to catching teams) associated with the Catching Company. Furthermore, when more than one poultry premises was visited by a slaughterhouse vehicle, Additional File 1 Figure S4 shows that up to 26 movements (to different premises) were made in one day. This implies that, even when frequency of movements are taken into account, slaughterhouse-related movements might be frequent enough to cause an outbreak to reach multiple premises. Interestingly, Additional File 1 Figure S4 also shows that there is a bi-modal pattern in these data. There is a large peak at 2 movements per day and another smaller peak at 10 movements per day. This could be related to the capacity of the slaughterhouses to handle birds. An explanation for this could be that it is possible that larger slaughterhouses have the capacity to visit an average of 9 - 12 farms per day, whereas the smaller ones (of which there may be more) can visit only two or three premises per day. Visitng over 13 or 14 farms a day appears to be only occur in exceptional

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cases. Investigating this further could provide an area of further research.

Consistent with the data in the PND, although just over half of premises send birds to just one slaughterhouse, some premises send birds to multiple slaughterhouses (up to six according to data from the Catching Company and up to eight according to the PND). This may be a result of slaughterhouses operating on a species-specific basis, so farms housing multiple species send birds to multiple slaughterhouses. According to the movement data from the Catching Company, premises using the Catching Company send birds to one or more of eight slaughter-houses. Data collected from 96 slaughterhouses however, suggests that up to 35 slaughterhouses are associated with the premises that use the Catching Company. This suggests that either premises use multiple catching companies, or premises catch birds themselves and send to multiple slaughterhouses. Due to the ability of slaughterhouses to connect a larger number of premises than catching companies, it is important to determine which case is most likely. Results from the static network analyses presented in [Dent et al., 2008] suggest that it is more likely that premises use multiple slaughterhouses than they do multiple catching companies.

S1.3   Movement dependent on farm size

There is evidence to suggest that the probability that more than one farm is visited by a catching team, in a day, is related to the size of the first farm visited.

Figures S6 and S7 show the empirical distributions of data describing whether or not an onward movement was made (by catching teams) for different farms sizes (measured by the number of houses (S6) and the number of birds (S7) on a farm).

The light grey peak in Additional File 1 Figure S6 shows that onward movements were most likely to have occured after a medium sized farm had been visited (farms with 10-11 houses). We would expect these farms to be operating in cycles, so that there are always birds on the farms and only a small number of houses are visited per catching team visit. The dark grey peak at farms of size 12-14 houses suggests that no onward movement was most likely to have occured after large farms had been visited (however, there is only a slight difference in the

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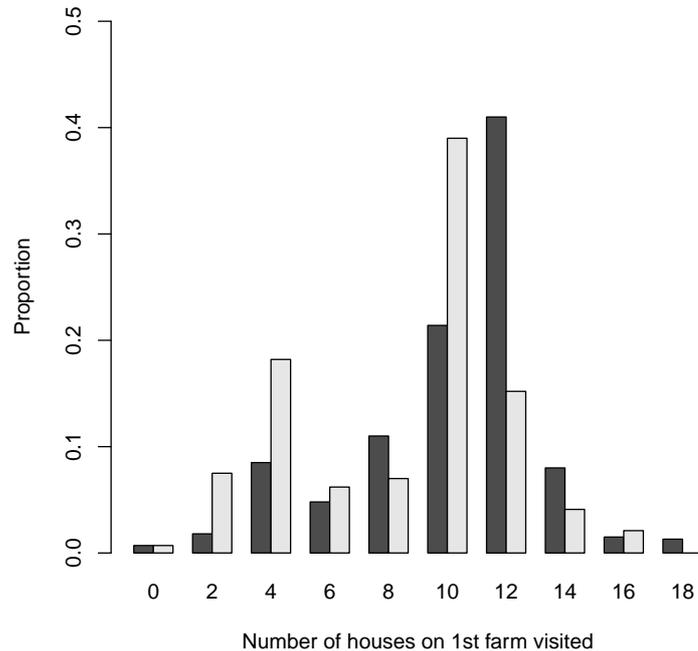
Figure S6. Distribution of whether or not onward movements (dark grey, no onward movement and light grey, onward movement) were made by a catching team, given the number of houses on the first farm visited.

location of the light and dark grey peaks). These farms may be operating an all-in-all-out procedure, where all birds are caught at once and sent to slaughter. There was another small peak of onward movement from small farms (with 4-5 houses), implying that catching team visits to small farms are likely to have resulted in the team visiting other premises on the same day. When number of birds was used to determine farm size (Additional File 1 Figure S7), then onward movement was still most likely to occur from medium to large farms (housing between 240,000 and 280,000) birds and no onward movement most likely from larger farms (housing 320,000 to 360,000 birds). The small-farm peak seen in Additional File 1 Figure S6 can also be seen for onward movements from farms housing 40,000 to 80,000 birds. These results imply that when catching teams visit more than one farm, they are most likely to have come from a small to medium sized farm first. However, if they visit only one farm in a day, it is most likely

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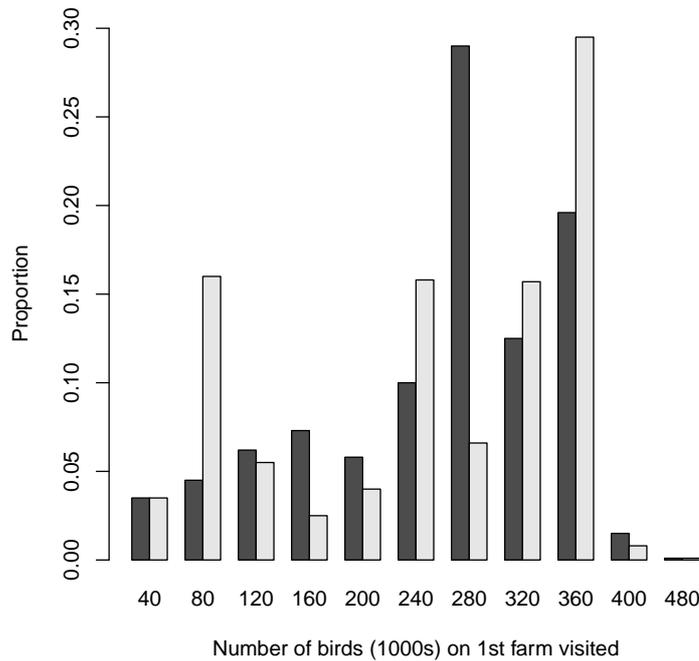
Figure S7. Distribution of whether or not onward movements (dark grey, no onward movement and light grey, onward movement) were made by a catching team, given the number of birds (in 1000s) on the first farm visited.

that this farm is a large farm.

Similar conclusions however, cannot be drawn from the empirical distributions of data describing whether or not an onward movement was made by slaughterhouse vehicles and personnel. Additional File 1 Figures S8 and S9 show the distribution of how often onward movements occurred according to farm size (houses and number of birds), for movements made by slaughterhouse vehicles and personnel. Additional File 1 Figure S8 shows that onward movements were least likely to have occurred after visiting large farms (more than 7 houses) and most likely to have occurred when the first farm visited has four or fewer houses. There is another peak at farms with 7 houses, which occurs because there are two farms with 7 houses that are frequently visited by vehicles from the same slaughterhouse. Although no onward movements were most likely to have occurred when a farm with four houses was visited by a slaughterhouse

9
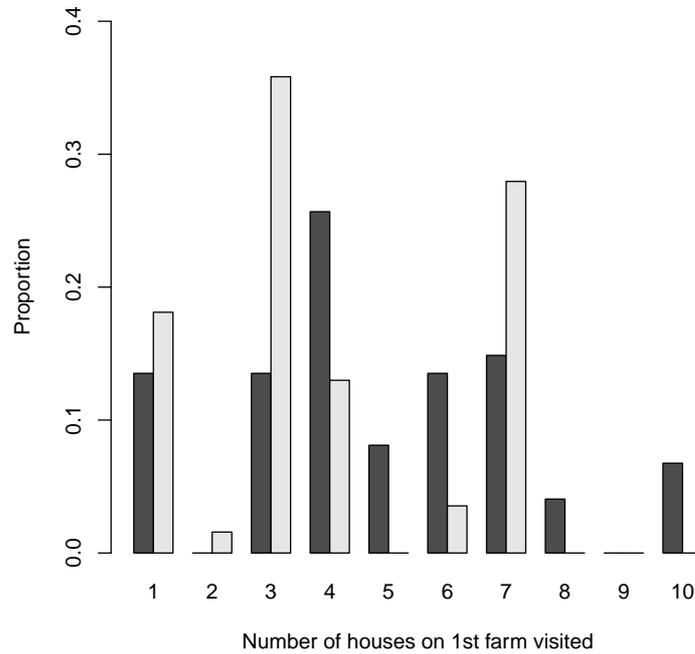
Figure S8. Distribution of whether or not onward movements (dark grey, no onward movement and light grey, onward movement) were made by a slaughterhouse vehicles, given the number of houses on the first farm visited.

vehicle (dark grey peak in Additional File 1 Figure S8), patterns in the data are not evident. When the distribution was replotted against the number of birds on a farm (Additional File 1 Figure S9), the data tell a different story. First of all, the data show that the first farm to be visited by a slaughterhouse vehicle was almost always a small to medium farm (fewer than 200,000 birds). For this reason, if only one farm is visited is is likely to be small, if more than one farm is visited, it is likely that a small farm was visited first. The data for farm size by number of birds supports that of farm size by number of houses in that onward movements did not occur in large farms. This could suggest that slaughterhouse vehicles require a long time to load and transport birds from large farms, leaving no time (and perhaps no free equipment) in the day for movement to other farms. Interestingly, no onward movement was most likely to occur from farms housing 40,000 or fewer birds. This implies that all birds on these farms are
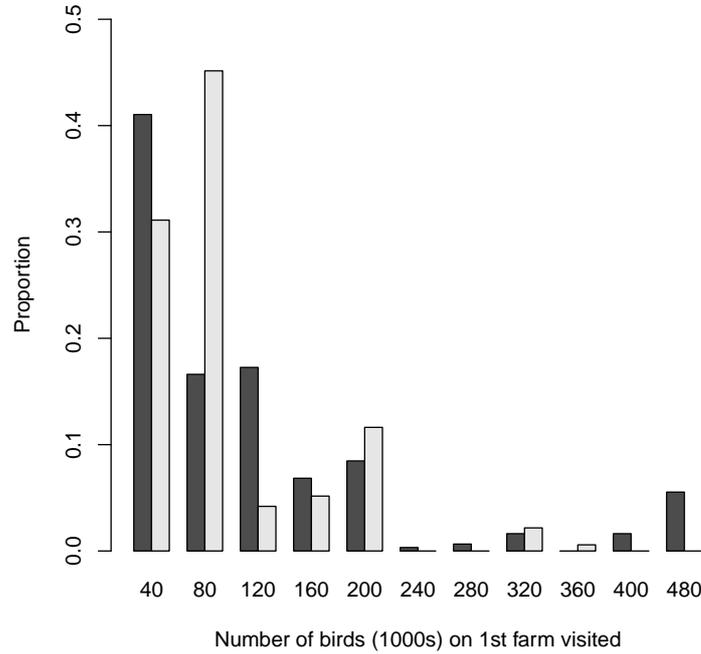
Figure S9. Distribution of whether or not onward movements (dark grey, no onward movement and light grey, onward movement) were made by slaughterhouse vehicles, given the number of birds (in 1000s) on the first farm visited.

taken to slaughter in one batch (i.e. they operate on an all-in-all-out basis and not in cycles). For slightly larger farms (40,000 to 80,000 birds), onward movements were more likely to have occurred, perhaps because these farms operate in cycles, so fewer birds are taken to slaughter in one batch, allowing vehicles to collect birds from other farms in order to fill the truck. In conclusion, the patterns of onward movements of slaughterhouse vehicles cannot easily be predicted from farm size, though the data do suggest that there is some prioritisation of the order of visits, in that small farms are more likely than large farms to be visited at the beginning of a day.

S1.4 Repeated movements

Under the assumption that risk of infection is related to the frequency of visits, large premises are at a higher risk of becoming infected via the movement of catching teams (and slaughterhouse vehicles).

According to the data, 51% of links between premises that are created by the movement of catching teams were repeated at least once over the time period studied. Seventeen percent of premises were only visited once in the data set. Approximately 1% of premises were visited over 200 times, with one premises being visited 370 times (one visit every 2 to 3 days). According to the GBPR, this premises consists of seven houses of 36,000 broiler chicks per house, so if the cycle in each house is one week apart and each house is visited separately, thinned (once birds reach a certain size, a small proportion are removed, freeing up space for remaining birds to grow bigger) and has part depopulation (not all houses are emptied of birds at the same time, so that there are always birds present on the farm, and depopulation takes place over a prolonged period of time), at different times, it is possible that the site is visited every few days. Generally speaking, larger premises are visited more frequently than smaller premises.

Additional File 1 Figure S10 shows the distribution of the number of visits made by catching teams, according to premises size. The Figure shows that large premises (>200,000 birds or more than 10 houses) were visited more frequently, perhaps as a result of 'thinning' (over 100 visits in the time period (936 days), corresponding to visits made every 10 days or more frequently). Interestingly, small and medium premises are less frequently visited (the majority receiving fewer than 100 visits over the 936 day period). There could be several explanations for this: such premises may be using multiple catching companies (or catching birds themselves) or they may operate an all-in-all-out procedure as there are not enough birds on the farm to justify a stratified production procedure. It is noted that other factors, such as biosecurity measures employed by farm staff for example, may vary according to farm size. This is less relevant here as the biosecurity measures employed by personnel associated with catching company are set by the catching company rather than by the farm being visited.
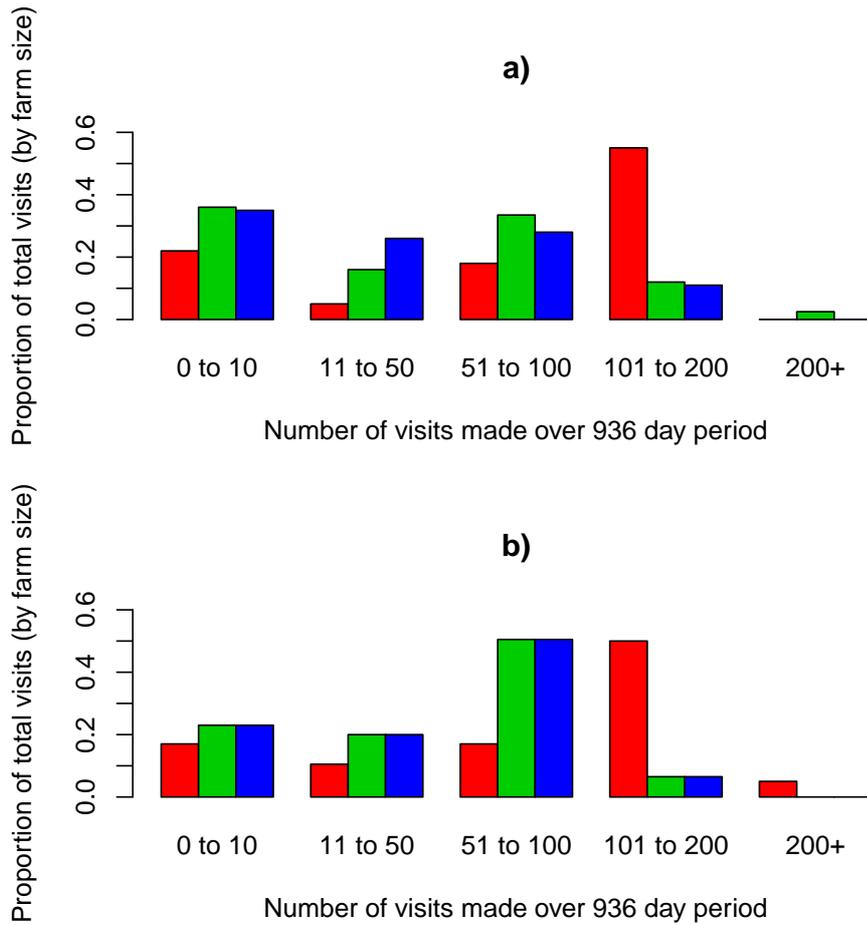
Figure S10. Distribution of number of catching team visits per premises for (a) premises size defined by number of houses (red = 10 or more houses, green = 5 to 10 houses, blue = 0 - 5 houses) and (b) premises size defined by number of birds (red = more than 200,000 birds, green = 100,000 - 200,000 birds, blue = 0 - 100,000 birds).

S1.5   Distance between associated premises

In an outbreak situation, surveillance and protection zones are set up at 10km and 3km, respectively, around infected premises. If these zones are to be effective in controlling disease, then movements between premises should be restricted to occurring within these zones. For these data, the majority of premises are situated more than 3km (the current PZ put around infected premises) from each other.

Additional File 1 Figure S11 shows the distribution of the number of premises located within
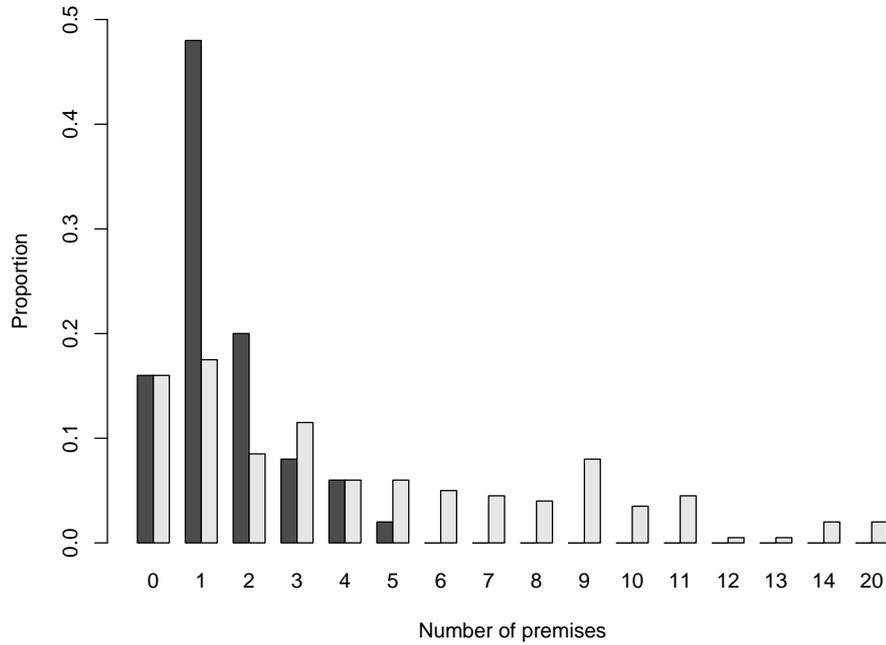
Figure S11. Distribution of the number of premises located within 3km (dark grey) and 10km (light grey) of each premises associated with the catching company.

3km (dark grey) and 10km (light grey) of each premises associated with the Catching Company. The figure shows that almost 50% of premises have only one other premises located within 3km, with no more than 5 premises located within 3km of each other. The figure also shows that there are up to 20 premises (corresponding to approximately 5% of premises) located within 10km of each other. As only a maximum of 5% of premises are located within 10km of each other, this implies that there may be many premises that are associated with the Catching Company that would not be located within the surveillance zone of a (potentially) infected poultry farm. In fact, for these data, approximately 16% of premises are located more than 10km away from all other premises. However, when GBPR premises are added to the data, a total of 1987 additional premises are located within 3km of the studied premises and 9298 premises within 10km. We further note that a total of 504 GBPR premises are located within 500m of a premises associated with the catching company, suggesting that a limit of 500m for

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spatial spread (that is assumed in the simulation model) could still result in transmission via this route.

When we consider the distance between premises that are linked by catching teams and the distances travelled between premises and slaughterhouses, we see that the majority of linked premises are further than 10km apart.
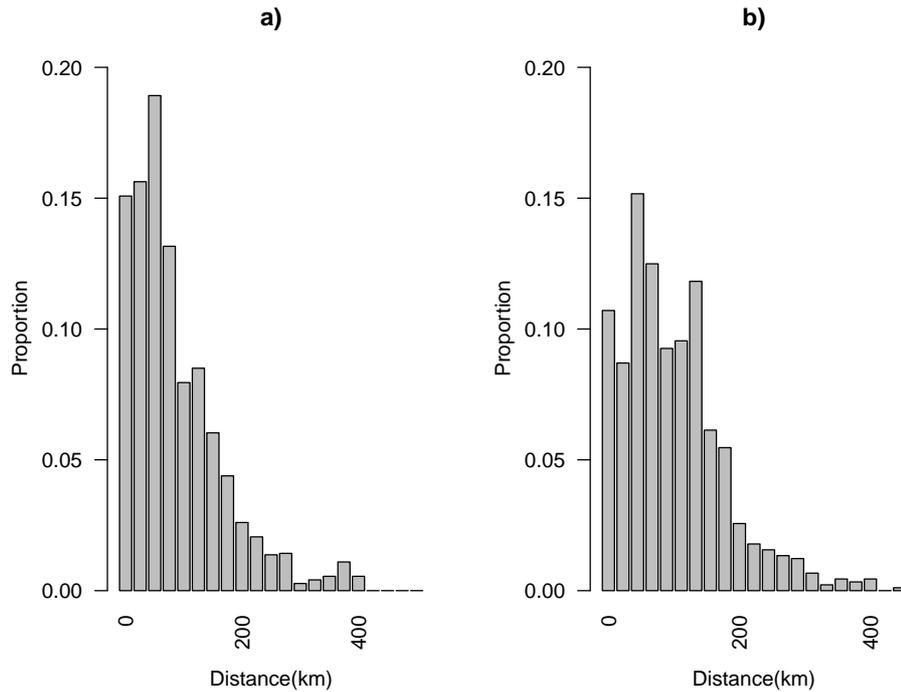
Figure S12. Distribution of distances travelled for (a) catching teams between premises and (b) from premises to slaughterhouse.

The movements of catching teams between premises and the movements made from premises to slaughterhouse could cover long distances (Additional File 1 Figure S12), resulting in the potential for geographically widespread dissemination of virus. Only 28% of catching team movements were made between premises less than 10km apart (within the current SZ), with some catching teams travelling very long distances between premises on the same day. The increase in the proportion of movements that are greater 300km apart is caused by catching teams visiting a single premises located in a more remote area of GB. The Euclidean distance

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travelled by slaughterhouse vehicles, from premises to slaughterhouse was also relatively long, with a mean distance of 106.2km (with a large standard deviation of 73.15, implying diversity in the data).

When road distance is considered as a measure for distance, there is little difference in the results obtained.
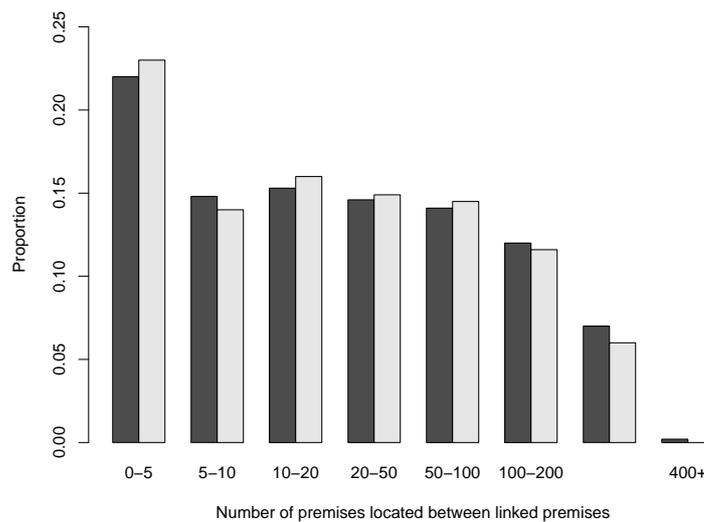
Figure S13. Comparison of road and Euclidean distances. Distribution of the number of premises located between premises that are linked, according to Euclidean distance (dark grey) and road distance (light grey).

Additional File 1 Figure S13 shows the distribution of the number of premises located between two linked premises, counted using Euclidean distance and road distance to measure the distance between linked premises. The figure shows that there is little difference between using road and Euclidean distance to measure distance between linked premises, for these data. Road density is high in the South and East of GB, compared to the North and West and, given that a high proportion of premises associated with the Catching Company are located in the East of GB, this might explain why there is little difference between road and Euclidean distance for these data. Furthermore, the figure shows that most movements are made between premises that are close to one another, with over 20% of links occurring from one premises to one of the five

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closest neighbouring premises. These results thus suggest that the use of Euclidean distance as a distance measure for these data is acceptable.

S1.6   Owner movements

In addition to these data, it was assumed that links could occur because of premises being linked by poultry company i.e. poultry premises with the same owner. Owner movement data were not available for analysis and were therefore simulated, based on expert opinion. However, information about which poultry premises belong to which company was obtained from a combination of the Catching Company data and the PND. Similar data were not available for farms that were added to the dataset from the GBPR. This is highlighted as an area for further study.

Of the 415 farms in the data set, 114 were associated with a multi-site poultry company. There were 10 multi-site companies associated with the Catching Company, the largest of which contains 43 of the poultry premises associated with the Catching Company. The number of links per node via owner (representing the mean degree) for these data is 24 premises. The owner network clearly represents only a small proportion of the 415 farms that use the Catching Company and so we might expect that transmission via this route is not likely to be the most influential to the model results. It is also noted that there is no overlap between companies, so each poultry farm can only be associated with one poultry company.

Bibliography

[Dent et al., 2008] Dent, J., Kao, R., Kiss, I., Hyder, K., and Arnold, M. (2008). Contact structures in the poultry industry in Great Britain: Exploring transmission routes for a potential avian influenza virus epidemic. *BMC Veterinary Research*, 4(1):27.

[Sedgewick, 2001] Sedgewick, R. (2001). *Algorithms in C, Part 5: graph algorithms*. Addison-Wesley Professional.

S2 Additional File 2 - Simulation modelling: methods.

The simulation model, written in C language, is designed to simulate the spread of avian influenza virus between a sample of premises in Great Britain (GB). Virus is spread via the movements of catching teams, slaughterhouse vehicles or personnel, company personnel or by limited airborne spread.

The simulation can be broken down into a number of steps as shown in Additional File 2 Figure S1, summarised by Additional File 2 Algorithms S1 to S5.
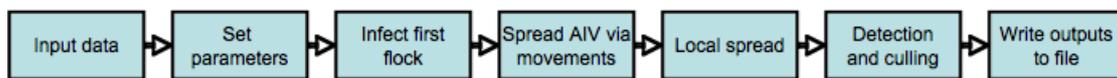
Figure S1. Programme design for AIV simulation.

S2.1 Simulation model: input data

Input data are read in to the programme as a series of text files as described in Additional File 2 Table S1. Movement data of catching teams (CC) and slaughterhouse vehicles (SH) were obtained for a period of 936 days, for a sample of 415 farms in GB. These farms will be referred to as 'network' farms. Movements of farm personnel between premises and local spread are simulated based on expert opinion. Data for poultry farms located within 15km of network farms are collected from the GB poultry register and included in the simulation in order to allow for virus to spread outside the network of farms for which we have movement data.

Table S1. Input data for AIV simulation (GB)

File name	Size (cols x rows)	Description
Link_index	Number link types x Number farms in network*	Number of farms connected to each farm by each link type.
Continued on next page		

Table S1 – continued from previous page

File name	Size (cols x rows)	Description
GBPRlocal15	5 x Number farms in study region (within 15km of network farms)	Farm input data: farm number, farm ID (from Defra database - not required), easting, northing, size (birds).
GBPR_local15_flocks	6 x Number flocks** in region studied	Flock input data: farm number, flock number, easting, northing, size (birds), species type.
Nwork_SZ10	19 x Number Farms in network	Vector of network farms within 10km of each network farm.
Nwork_SZ10index	1 x Number Farms in network	Number of network farms within 10km of each network farm.
flockprem_GBPR_Nwork	1 x Number flocks	Which farm each flock is in.
flocksinprem_GBPR_Nwork	1 x Number farms	Number flocks on each farm.
Premtoflock_GBPR_Nwork	23 x Number Farms	Vector of flocks that are on each farm.
own_links	2 x Number of links	One link per row: Farm A, Farm B.
Events_CC	7 x Number catching company events	List of farms visited by each catching team per day. One team per day per row.
Width_CC	1 x Number catching company events	Number farms visited per day per team. Row number corresponds to row in Events_CC.
Date_CC	1 x Number catching company events	Day of catching team event. Day 1 = starting date. Row number corresponds to row in Events_CC.
Continued on next page		

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Table S1 – continued from previous page

File name	Size (cols x rows)	Description
Time_CC	4 x Number days	Day number; number CC events for that day; 1st CC event, last CC event. CC event = row number from Events_CC.
Events_SH	7 x Number catching company events	List of farms visited by each catching team per day. One team per day per row.
Width_SH	1 x Number catching company events	Number farms visited per day per team. Row number corresponds to row in Events_CC.
Date_SH	1 x Number catching company events	Day of catching team event. Day 1 = starting date. Row number corresponds to row in Events_CC.
Time_SH	4 x Number days	Day number; number CC events for that day; 1st CC event, last CC event. CC event = row number from Events_CC.
Non_Nwork_SZ10	5 x Number non-network farms within 10km of network farms	Row ID, Farm number, farm ID, easting, northing.

*Network farms refer to farms in the study region for which movement data are available, or simulated. **Flocks: we assume that all birds of the same species and purpose (eg layer chickens or meat chickens) are kept together on a farm and we therefore refer to them as a single flock, so a farm that houses ducks, broiler chickens and layer chickens will be recorded as a farm of three flocks.

The movement data are then transformed into an array with dimensions as shown below. The array describes the exact order of events per flock per day, these data are combined with

information about the potential links that may occur due to premises belonging to the same integrated company and the distance between the premises. Each entry in $array[0]$, $array[1]$ and $array[2]$ is a flock ID number, the entries in $array[3]$ are distances (m) corresponding to links in $array[2]$:

$array[0][][]$ =(Number network premises)$*$(Number days in data)$*$(number CC visits per premises per day)

$array[1][][]$ =(Number network premises)$*$(Number days in data)$*$(number SH visits per premises per day)

$array[2][]$ =(Number network premises)$*$(Number premises in same integrated company)

$array[3][]$ =(Number network premises)$*$(Distance between premises linked by integrated company)

S2.2   Simulation model: set parameters

Parameters are set in the programme as shown in Additional File 2 Table S2.

Table S2. Parameters (inc. matrices) used in simulation model

Parameter	Description/comments
Number iterations	100
Run time	Number of days to run model for = 50 days
Random number	Pseudo random number generator, using real time as seed
Random farm	Farm chosen at random, on which to seed infection
Random time	Day, chosen at random, on which to seed infection
Max Dist	Maximum distance between infected farms
Species type	Type of species in flock
Species prob	Probability of a given species being visited varies according to species, based on the number of each flock type visited, where data were available chicken = 0.71, ducks/geese = 0.16, Turkeys = 0.12, other = 0.01 (2dp).
Continued on next page	

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Table S2 – continued from previous page

Parameter	Description/comments
Probability of transmission via local (airborne) transmission given by distance kernel	Probability of transmission between two farms within a certain distance of each other is based on a distance kernel described by Boender (2007) in analysis of geographical spread of infectious diseases (see section A-1.5, equation 1). Maximum transmission set to 0.01 at zero meters (ie. between flocks on same farm). Maximum distance over which airborne spread can occur = 500m.
Probability of transmission (via farm personnel, catching team, slaughterhouse vehicle)	Transmission rates between premises are currently unknown so they are varied between 0 and 0.2 in a stepwise fashion, with an extra parameter value added at 0.001. This results in 22 parameter values per potential transmission route.
Time to detection	Number of days between infection and detection (at farm level). It is assumed that detection occurs within 6 days of infection, with a 2-day latent period, described by a triangular distribution based on mean time to detection of 4 days to estimate time to detection for premises outside a PZ/SZ and mean time to detection of 3 days inside these zones. Time to detection is the same for all species apart from ducks, where we add 15 days on the estimated time to detection.
Time to culling	3 days after detection outside PZ/SZ, 2 days after detection in SZ and 1 day after detection in PZ. Based on Defra report from outbreak in GB 2007.
Probability of staff working on multiple farms	Expert opinion. Dependent on farm size and species as described previously. We assume small premises are more likely to share staff. Assume premises only share staff within 35km radius.
Probability of area manager visit	Expert opinion (discussed below). Fewer visits expected to layer farms.
Probability of vet visit	Expert opinion (discussed below).
Infected Farm List	List of premises infected during outbreak
Infection Time	Day premises becomes infected
Detection Time	Day infected premises are detected
Culling Dates	Day infected premises are culled
Farm Inf	Infectious state of a premises (susceptible (0) infected (1), detected (2), culled (-1))
Proportion positive	Proportion outbreaks that result in spread beyond the seed premises, for each parameter set.
Continued on next page	

Table S2 – continued from previous page

Parameter	Description/comments
SZ Matrix	Premises in surveillance and protection zones

S2.3 Simulation model: infect 1st flock

For 100 simulations of each combination of transmission parameters, the random number generator chooses a premises in the network to infect and a time to infect the premises from day zero to day 886 (total number of days minus number of days epidemic is left to run for). If the premises is visited within 15 days of infection, then the programme chooses a flock on the seed premises to infect, based on the species type, where known, such that chickens are the most likely to be infected (as they are the most likely to be visited by the catching company). If the premises is visited within 15 days of infection, transmission can occur via movement of catching teams and slaughterhouse vehicles. Otherwise, transmission is restricted to local spread or spread via company personnel movements (see Additional File 2 Algorithm S1). The infectious state of the first premises is set to 1 and the model enters the 'transmit disease' stage, where it first transmits infection via movements and then via local spread.

```
Algorithm S1: AIV MAIN FUNCTION(pseudocode)

for transmission probabilities (CC, SH, own) ← 0 to 0.2
do {
    do {
        for iterations ← 1 to 100
        do {
            choose a random farm to visit
            choose a random time to start infection
            for time ← t to t+50
              do if farm visited within 15 days of start time
                 then {
                     choose a flock to infect based on species type
                     set detection dates for 1st infected farm
                     set culling dates for 1st infected farm
                     Transmit AIV as in Alg. A-5
                 }
            Transmit AIV via local spread as below

            comment: Update SZ and PZ

            for number farms ← 1 to Number newly infected farms
              do {
                  find all farms within 10km and label as in SZ
                  find all farms within 3km and label in PZ
              }

            comment: Do detection and culling of infected farms

            for infected farms ← 1 to total number infected farms
              do {
                  if Detection Time of Infected Farm = t
                     then update status to detected
                  if Culling Dates of Infected Farm = t
                     then update status to culled
              }
        }
        output data
    }
}
```

S2.4 Simulation model: spread AIV via movements

Movements of catching teams and slaughterhouse vehicles are determined entirely by the real-time movement data, this means that infection via these transmission routes is independent of farm type and dependent only on the movement between an infected and susceptible premises taking place. Catching team movements always precede slaughterhouse vehicle movements. Spread of infection between premises belonging to the same integrated company, or via spatial transmission are determined stochastically, based on species type and farm size and simulated after infectious movements via catching team and slaughterhouse have occurred. Additional File 2 Algorithm S2 gives pseudocode for the spread of AIV via movements.

```
┌─────────────────────────────────────────────────────────────────────┐
│ Algorithm S2: AIV VIA MOVEMENTS(pseudocode)                         │
│                                                                     │
│  for time(days) ← 1 to 50                                          │
│        ⎧ for Farms ← 1 to Number of infected farms                │
│        ⎪       ⎧ for farm visited by CC ← 1 to No. visits in 1 day │
│        ⎪       ⎪ do if farm is already detected/frozen/culled      │
│   do  ⎨   do ⎨ then break                                         │
│        ⎪       ⎪ else if infected farm is not yet detected         │
│        ⎪       ⎩ then Infect via movements (Alg. A-3 to A-5)       │
│        ⎩                                                           │
└─────────────────────────────────────────────────────────────────────┘
```

S2.5   Catching company and slaughterhouse movements

Once a poultry farm has been infected at random, the programme runs for 50 days (this time was chosen as in test runs of the programme, no epidemic exceeded 50 days under the assumptions made), infecting, detecting and culling premises as follows (shown in Additional File 2 Algorithm S3).

Assuming the seed premises (premises i) is visited by a catching team (and hence a slaughterhouse vehicle) within 15 days of seed infection (day j), then the programme accesses the appropriate place in the links array (see above). For the ith premises, on the jth day, the links array gives a list of all premises that are visited after the ith premises. Given that AIV has an incubation period of only several hours, it is assumed that birds are able to spread disease from the point that they become infected, so that all premises visited after the seed premises becomes infected and on the same day, are susceptible to transmission of disease. Before transmitting disease to susceptible premises, the programme checks that the susceptible premises is in fact susceptible (by checking infectious state of the premises $= 0$). The programme then checks that the premises does not have any restrictions placed on it (ie is not in a PZ or SZ) and, assuming there are no movement restrictions, proceeds by infecting a flock on the susceptible premises with a probability equal to the probability of transmission via catching company movements (varied between 0 and 0.2). Where the number of flocks on the premises is greater than one, one or more flocks are chosen to be infected according to the probabilities highlighted in Additional File 2 Table S2. A premises is infected when one or more flocks on the premises is infected. If

a premises is visited multiple times in one day, then it is potentially connected to more than one infected premises and the probability of infection is given by Equation (1).

$$P\left(i \text{ gets infected}\right) = 1 - \left(\prod_j \left(1 - p_j\right)\right),$$

for j infected premises and p probability of infection for each contact.

(1)

As soon as a premises is infected, the infectious status of the premises is updated and the premises ID added to the list of infected premises. Detection and culling dates are set (though detection and culling occur at the end of each time step) for each newly infected farm. This process is then repeated for slaughterhouse-linked movements.

Algorithm S3: TRANSMIT AIV VIA CC/SH(*pseudocode*)

for *susceptible farm ← 1st farm visited* **to** *last farm visited*

do {
   count number of flocks and number of duck flocks
   if *susceptible farm has not been frozen*
   then {
      choose a flock to be visited by CC
      for *susceptible flock ← 1* **to** *number flocks on farm*
      do {
         infect using random number generator
         if *random num < transmisison probability*
         then {
            infect flock
            note change in flock status
            update farm status to infected
            if *flock is ducks*
               then *make special note*

note number of new infections, and date of new infection
comment: set detection time of newly infected farms

comment: if not in PZ or SZ, time to detect is slower

if *farm is neither in SZ or PZ*

then {
   use time to detection function: expected = 4days
   if *only ducks are infected*
      then *add 5 days to detection time*
   Set culling date to detection date + 3days

else if *farm is in SZ/PZ*

then {
   expected time to detection reduced to 4 days
   if *only ducks are infected*
      then *add 5 days to detection time*
   Set culling date to detection date + 2/1 days (SZ/PZ)

S2.6 Company personnel movement

The programme then moves on to transmission of disease via company-related movements (referred to as owner movements), as shown in the pseudocode in Additional File 2 Algorithm S4. These movements are simulated in the programme, based on expert opinion from P. Mcmullin (Poultry Health Services, UK). For each infectious premises, the programme determines if the premises is, on each day, sharing staff, according to the probability of staff working on multiple premises as shown in Additional File 2 Table S3

Table S3. Probability of premises share staff, according to premises size (number birds on premises)

Probability of staff working on multiple premises (dependent on farm size)	0.45 (<50,000 birds)
	0.1 (50,000 to 200,000 birds)
	0 (>200,000 birds)
Frequency of vet visits	Every 50 days
Frequency of manager visits	Every 10 days (non-layer farms)
	Every 50 days (layer farms)

If staff shares are found to occur on an infected premises, the programme uses the links array to search for other premises in the same company, within a 35km radius, which can also have a staff share and determines, with the probabilities given in Additional File 2 Table S3, if these premises are also sharing staff on each day of the simulation. If there exists two premises within the same company that are within this region and both 'sharing staff', then we assume that there is a link between the premises and the second premises is classed as susceptible. We also assume that there is a small probability, based on whether or not a premises houses laying hens (Additional File 2 Table S3), that a vet or an area manager will visit an infected premises on each day of the simulation. If this occurs, susceptible farms within the same company are searched for and also visited by the vet or area manager with the same small probability, creating a link between infected and susceptible farms. The programme then infects susceptible farms in a similar way as with catching team and slaughterhouse-related movements; first confirming the infectious status of susceptible premises and then infecting a flock according to species type

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and setting detection and culling dates for all newly infected premises.

Once infection has occurred via movements, the programme uses the input file, 'Nwork_SZ10' (Additional File 2 Table S1), to create 10km surveillance zones (SZ) and 3km protection zones (PZ) around infected premises (refer to Additional File 2 Algorithm S1) and writes these premises to the 'SZmatrix' array (Additional File 2 Table S2). The date at which susceptible premises enter and leave these zones is set so that movement can be frozen within these zones if desired. The programme then adds GBPR premises to the SZ and PZ in preparation for local spread.

Algorithm S4: TRANSMIT AIV VIA OWNER(*pseudocode*)

for *infected flock* ← 1 **to** *total number infected flocks*
  do
    assign staffshare probability, based on farm size
    determine if layer flock or not
    assign probability of manager visit
    for susceptible farms ← 1 **to** *Number farms in company*
        if *manager visit occurs on infected and susceptible farms*
            then *assume link between infected and susceptible farms*
            if *random num < transmisison proability for owner*
                then *infect a flock according to species*
                note change in flock status
                update farm status to infected
                if *flock is ducks*
                    then *make special note*
  do
        repeat for vet visits
        if *staff sharing on both farms and distance close enough*
            then *assume link between infected and susceptible farms*
            if *random num < transmisison proability for owner*
                then *infect a flock according to species*
                note change in flock status
                update farm status to infected
                if *flock is ducks*
                    then *make special note*
  note number of new infections, and date of new infection
  set detection time of newly infected farms as in Alg. A-3
  set culling dates as in Alg. A-3

S2.7 Local spread

Irrespective of infectious status, local (airborne) spread can occur between all premises within a predefined distance, as shown in Additional File 2 Algorithm S5.

Algorithm S5: AIV LOCAL TRANSMISSION(*pseudocode*)

for *flocks* ← 1 **to** *number infected flocks*

do $\begin{cases} \textit{find all susceptible flocks within 0.5km} \\ \textbf{if } \textit{random num} < \textit{transmission probability} * \left(\left(1 - \frac{dist}{0.5}\right)^2 \right)^2 \\ \qquad \textbf{then } \begin{cases} \textit{infect susceptible flock} \\ \textit{note change in flock status} \\ \textit{update farm status to infected} \\ \textit{note date and number of new infections} \\ \textit{set detection time of newly infected farms as above} \\ \textit{set culling dates as above} \end{cases} \end{cases}$

As a result of particulate (though not necessarily still infectious) material being detected 500m from poultry houses in the H7N7 outbreak in the Netherlands [D. Alexander, pers. comm.], expert opinion was that spatial (primarily airborne) spread in GB is likely to occur with small probability and only for distances up to a maximum 0.5km [D. Alexander and R. Irvine, pers. comm.]. By assuming that the distance between flocks on the same farm is zero, this allows for between-species spread on multi-species farms and some spatial spread between separate farms. Between-species transmission is important on multi-species sites as it may allow for disease to spread into different industry sectors, which may otherwise not be connected. Based on expert opinion and a density kernel described in [Boender et al., 2007], it is assumed that spatial transmission could occur at a maximum probability of 0.01, up to 0.5km from the infected premises, before detection of disease. This resulted in the probability distribution described in Equation (2) and shown in Additional File 2 Figure S2. The use of this kernel means that the probability of infection via local spread between flocks on the same premises is greater than transmission between flocks on neighbouring premises, as would be likely if, for example, same premises implies greater proximity, or if local spread is actually mediated by human activity,

such as movement of workers on the same premises and poor biosecurity.

$$p\left(transmission|dist\left(km\right)\right) = \begin{cases} 0.01\left(\left(1 - \frac{dist}{0.5}\right)^2\right)^2 & dist\left(km\right) < 0.5km \\ 0 & otherwise \end{cases} \quad (2)$$
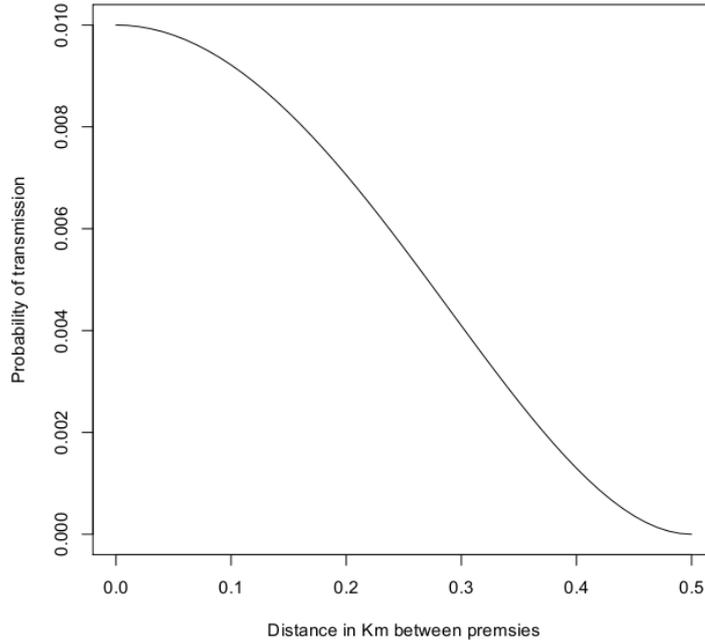
Figure S2. Transmission kernel corresponding to Equation (2), for distances ranging from 0 to 0.5km. The kernel equates to zero for distances larger than 0.5km.

For the list of infected premises, susceptible (ie in this case not culled) premises are found using the 'GBPR_local15_flocks' file (Additional File 2 Table S1). We assume that local spread can occur between flocks on the same premises as well as between premises. There is no within flock spread in the model. Detection and culling dates are set for newly infected premises.

S2.8 Detection and culling

The probability of detection on a daily basis, following infection, will vary according to species, housing type, virus dose and virus strain [Yoon et al., 2005]. Detection (and culling) dates

are set at the same time that a premises becomes infected, dependent on the species infected. The time to detection is given by a triangular distribution, based on mean latent period from the literature [Savill et al., 2008, Sharkey et al., 2008, Stegeman et al., 2004] (Additional File 2 Table S2). For all infected premises, if the infected flock is known to be a duck or goose flock, then the time to detection is increased by 15 days. If multiple flocks are infected, then the time to detection of a premises is equal to the shortest time to detection of all infected flocks on the premises. Premises that are within the PZ or SZ are detected more quickly than those outside these zones (see Table S2). Using the time taken to cull birds in the most recent outbreak of HPAI H5N1 in GB, it is assumed that culling occurs 3 days after detection of an infected premises, reduced to 2 days if the premises is in a SZ and 1 day if it is in a PZ. Once infection has been spread via different routes, detection and culling begins such that for all infected premises, if the detection or culling dates are the same as the current date, the status of the farm is updated (to 2 (detected) or -1 (culled) in 'Farm Inf'). The number of new infections is noted at the end of each day (Additional File 2 Algorithm S1). It is assumed throughout that premises that have been culled are no longer involved in the outbreak. There is no re-housing of culled premises in this model.

The time step is increased by one day and the above processes are repeated on the list of infected premises, up to day 50 and for all transmission parameter combinations.

S2.9 Outputs

Once infection has ceased, the programme records a list of all premises involved in the outbreak. This includes premises that have been infected, detected and culled, as well as premises in the SZ and PZ. The maximum distance between infected premises is calculated as well as mean number of infected premises over all iterations for each combination of transmission probabilities. Four output files are created.

(i) inf_prems_step.txt: a list of premises infected, the dates that they have been infected, detected and culled, for each simulation.

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(ii) PSZSstep.txt: a list of premises included in the PZ and SZ, the dates that they entered the zones for the first time and the date they expect to be removed, for each simulation.

(iii) results_step.txt: the seed farm, the transmission probabilities used, the total epidemic size and the maximum distance between infected premises for each simulation and for each parameter set.

(iv) Output_step.txt: for each parameter set the mean epidemic size, the proportion of seed infections resulting in secondary spread, the largest epidemic simulated (number of premises infected), longest distance between infected premises within largest epidemic, the longest distance between infected premises over all simulations and the number of premises included in the epidemic that is the most widespread are recorded.

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S3 Additional File 3 - Sensitivity to spatial spread

As there is no evidence of airborne spread in any outbreak in GB to inform the model [D. Alexander, pers. comm.], the sensitivity of the simulation model to the assumption that local spread can occur up to 500m was investigated and the results compared for all transmission parameters set to 0.2 (Additional File 3 Table S1). When HPAI was able to spread up to 3km, as seen in parts of the Netherlands in 2002 [Boender et al., 2007], the number of times infection left the network for which movement data were available was more than three times larger for 3km (7.4%) than for 500m (2.4%). There seems to be no significant difference in the number of times infection went beyond the seed premises, for all scenarios. This implies that the probability of infection beyond the seed premises is more heavily dependent on other transmission routes than local spread. An increase of local spread from 500m to 3km was also sufficient to increase both the mean and maximum epidemic size. This highlights the importance of being able to accurately predict the probability of local spread between premises.

Table S1. The impact of assumptions regarding the maximum distance for local spread on the simulated outbreak size for an avian influenza virus in Great Britain.

Local spread limit	Epidemic size		Percentage outbreaks resulting in		Mean number premises	
	Mean	Max	Onward spread	Spread outside system	In PZ	In SZ
0km	2.12	12	21%	0%	124	18
0.5km	1.54	10	20%	2%	78	10
3km	2.53	22	25%	7%	107	15

Bibliography

[Boender et al., 2007] Boender, G., Hagenaars, T., Bouma, A., Nodelijk, G., Elbers, A., de Jong, M., and van Boven, M. (2007). Risk maps for the spread of highly pathogenic avian influenza in poultry. *PLoS Comput Biol*, 3(4):e71.

S4 Additional File 4 - Results - supplementary tables

Table S1. Binary logistic regression: secondary spread versus transmission rates for interaction between transmission routes at different levels of transmission.

Category	Level	odds ratio	Lower 95%	Upper 95%	p-value
cc	1	1.06	0.86	1.31	0.556
	2	1.04	0.85	1.29	0.699
	3	1.11	0.90	1.37	0.325
own	1	1.06	0.85	1.32	0.625
	2	1.65	1.32	2.05	0.00
	3	2.06	1.66	2.56	0.00
sh	1	0.82	0.67	1.00	0.05
	2	0.89	0.73	1.08	0.243
	3	0.96	0.79	1.17	0.694
cc*own	1*1	0.95	0.80	1.12	0.526
	1*2	0.93	0.79	1.10	0.423
	1*3	0.93	0.79	1.10	0.393
	2*1	0.98	0.83	1.16	0.808
	2*2	0.95	0.80	1.13	0.573
	2*3	0.94	0.80	1.11	0.490
	3*1	0.93	0.78	1.10	0.396
	3*2	0.88	0.74	1.04	0.126
	3*3	0.87	0.74	1.03	0.100
cc*sh	1*1	0.97	0.85	1.12	0.688
	1*2	0.99	0.86	1.14	0.916
	1*3	0.97	0.84	1.11	0.651
	2*1	0.99	0.86	1.14	0.870
	2*2	1.00	0.87	1.15	0.967
	2*3	0.96	0.83	1.10	0.534
	3*1	0.98	0.86	1.13	0.831
	3*2	1.01	0.88	1.16	0.871
	3*3	0.97	0.84	1.11	0.635
own*sh	1*1	1.28	1.09	1.50	0.003
	1*2	1.25	1.07	1.47	0.006
	1*3	1.25	1.07	1.47	0.006
	2*1	1.23	1.05	1.44	0.012
	2*2	1.16	0.99	1.36	0.061
	2*3	1.15	0.98	1.34	0.089
	3*1	1.25	1.07	1.47	0.005
	3*2	1.19	1.01	1.39	0.033
	3*3	1.16	0.99	1.36	0.058

Level 1 = low transmission rate 0 - 0.06, level 2 = medium transmission rate 0.07 - 0.13, level 3 = high transmission rate 0.14 - 0.2. cc= catching company, sh = slaughterhouse, own = company personnel.

Table S2. Binary logistic regression: small outbreaks versus catching company transmission rates.

Transmission rate	Odds ratio	Lower 95%	Upper 95%	p-value
0.001	0.97	0.93	1.00	0.064
0.01	1.00	0.97	1.04	0.820
0.02	0.95	0.92	0.98	0.005
0.03	0.97	0.94	1.01	0.153
0.04	1.02	0.98	1.06	0.303
0.05	0.96	0.93	0.99	0.024
0.06	0.96	0.93	1.00	0.044
0.07	0.99	0.95	1.02	0.451
0.08	0.96	0.93	1.00	0.037
0.09	0.95	0.92	0.99	0.011
0.10	0.97	0.94	1.01	0.109
0.11	0.98	0.94	1.01	0.230
0.12	0.99	0.96	1.03	0.697
0.13	1.00	0.97	1.04	0.971
0.14	0.98	0.94	1.01	0.172
0.15	0.98	0.94	1.01	0.241
0.16	0.96	0.92	0.99	0.016
0.17	1.00	0.96	1.03	0.807
0.18	0.98	0.95	1.02	0.313
0.19	0.96	0.93	1.00	0.045
0.20	0.98	0.95	1.02	0.373

Table S3. Binary logistic regression: small outbreaks versus owner transmission rates.

Transmission rate	Odds ratio	Lower 95%	Upper 95%	p-value
0.001	0.98	0.94	1.03	0.488
0.01	1.09	1.04	1.14	0.000
0.02	1.19	1.14	1.25	0.000
0.03	1.27	1.22	1.33	0.000
0.04	1.38	1.33	1.44	0.000
0.05	1.42	1.37	1.48	0.000
0.06	1.47	1.41	1.54	0.000
0.07	1.53	1.47	1.59	0.000
0.08	1.66	1.59	1.73	0.000
0.09	1.74	1.67	1.81	0.000
0.10	1.76	1.69	1.83	0.000
0.11	1.86	1.79	1.94	0.000
0.12	1.97	1.89	2.05	0.000
0.13	1.94	1.87	2.02	0.000
0.14	2.11	2.03	2.19	0.000
0.15	2.09	2.01	2.17	0.000
0.16	2.19	2.11	2.28	0.000
0.17	2.24	2.16	2.33	0.000
0.18	2.34	2.25	2.43	0.000
0.19	2.38	2.29	2.48	0.000
0.20	2.38	2.29	2.48	0.000

Table S4. Binary logistic regression: small outbreaks versus slaughterhouse transmission rates.

Transmission rate	Odds ratio	Lower 95%	Upper 95%	p-value
0.001	0.97	0.94	1.01	0.101
0.01	0.99	0.95	1.02	0.446
0.02	0.99	0.96	1.03	0.623
0.03	1.00	0.96	1.03	0.883
0.04	1.00	0.96	1.03	0.846
0.05	1.00	0.96	1.03	0.897
0.06	1.04	1.00	1.08	0.037
0.07	1.03	1.00	1.07	0.068
0.08	1.04	1.01	1.08	0.022
0.09	1.04	1.01	1.08	0.021
0.10	1.05	1.01	1.08	0.014
0.11	1.07	1.03	1.11	0.000
0.12	1.05	1.01	1.09	0.010
0.13	1.09	1.05	1.13	0.000
0.14	1.08	1.04	1.12	0.000
0.15	1.09	1.05	1.13	0.000
0.16	1.07	1.04	1.11	0.000
0.17	1.08	1.04	1.12	0.000
0.18	1.09	1.05	1.13	0.000
0.19	1.09	1.05	1.13	0.000
0.20	1.10	1.06	1.14	0.000

Table S5. Binary logistic regression: large outbreaks versus catching company transmission rates.

Transmission rate	Odds ratio	Lower 95%	Upper 95%	p-value
0.001	1.00	0.43	2.31	0.999
0.01	1.09	0.48	2.47	0.836
0.02	1.09	0.48	2.47	0.836
0.03	0.54	0.20	1.47	0.232
0.04	1.00	0.43	2.31	0.999
0.05	0.91	0.39	2.14	0.826
0.06	0.91	0.39	2.14	0.826
0.07	1.00	0.43	2.31	0.999
0.08	1.09	0.48	2.47	0.836
0.09	1.00	0.43	2.31	0.999
0.10	1.64	0.77	3.46	0.199
0.11	1.00	0.43	2.31	0.999
0.12	0.73	0.29	1.81	0.492
0.13	1.82	0.87	3.79	0.112
0.14	1.45	0.67	3.13	0.339
0.15	1.64	0.77	3.46	0.199
0.16	1.36	0.63	2.97	0.435
0.17	1.82	0.87	3.79	0.112
0.18	1.00	0.43	2.31	0.999
0.19	1.18	0.53	2.64	0.685
0.20	0.73	0.29	1.81	0.492

Table S6. Binary logistic regression: large outbreaks versus owner transmission rates.

Transmission rate	Odds ratio	Lower 95%	Upper 95%	p-value
0.001	1.00	0.45	2.23	0.999
0.01	0.58	0.23	1.48	0.256
0.02	0.58	0.23	1.48	0.256
0.03	0.67	0.27	1.63	0.374
0.04	1.08	0.49	2.37	0.843
0.05	0.92	0.40	2.08	0.834
0.06	0.92	0.40	2.08	0.834
0.07	0.83	0.36	1.93	0.669
0.08	1.00	0.45	2.23	0.999
0.09	1.33	0.63	2.82	0.452
0.10	1.25	0.58	2.67	0.565
0.11	1.00	0.45	2.23	0.999
0.12	1.58	0.77	3.26	0.213
0.13	1.17	0.54	2.52	0.696
0.14	0.83	0.36	1.93	0.669
0.15	1.83	0.91	3.70	0.091
0.16	0.92	0.40	2.08	0.834
0.17	0.92	0.40	2.08	0.834
0.18	1.08	0.49	2.37	0.843
0.19	1.08	0.49	2.37	0.843
0.20	1.33	0.63	2.82	0.452

Table S7. Binary logistic regression: large outbreaks versus slaughterhouse transmission rates.

Transmission rate	Odds ratio	Lower 95%	Upper 95%	p-value
0.001	0.00	0.00	na	0.996
0.01	0.50	0.09	2.73	0.422
0.02	0.00	0.00	na	0.996
0.03	0.25	0.03	2.23	0.214
0.04	0.25	0.03	2.23	0.214
0.05	2.00	0.60	6.63	0.259
0.06	1.25	0.34	4.65	0.741
0.07	1.00	0.25	3.99	0.998
0.08	2.50	0.78	7.96	0.122
0.09	2.25	0.69	7.29	0.178
0.10	2.25	0.69	7.29	0.178
0.11	3.00	0.97	9.29	0.057
0.12	3.49	1.15	10.62	0.027
0.13	3.00	0.97	9.29	0.057
0.14	3.25	1.06	9.95	0.04
0.15	5.49	1.89	15.94	0.002
0.16	6.49	2.27	18.60	0.000
0.17	6.99	2.45	19.94	0.000
0.18	6.24	2.17	17.94	0.001
0.19	10.24	3.67	28.59	0.000
0.20	7.24	2.55	20.60	0.000

S5 Additional File 5 - Maximum distance between infected premises.

The results of the maximum distance between infected premises are displayed in Additional File 5 Figure S1
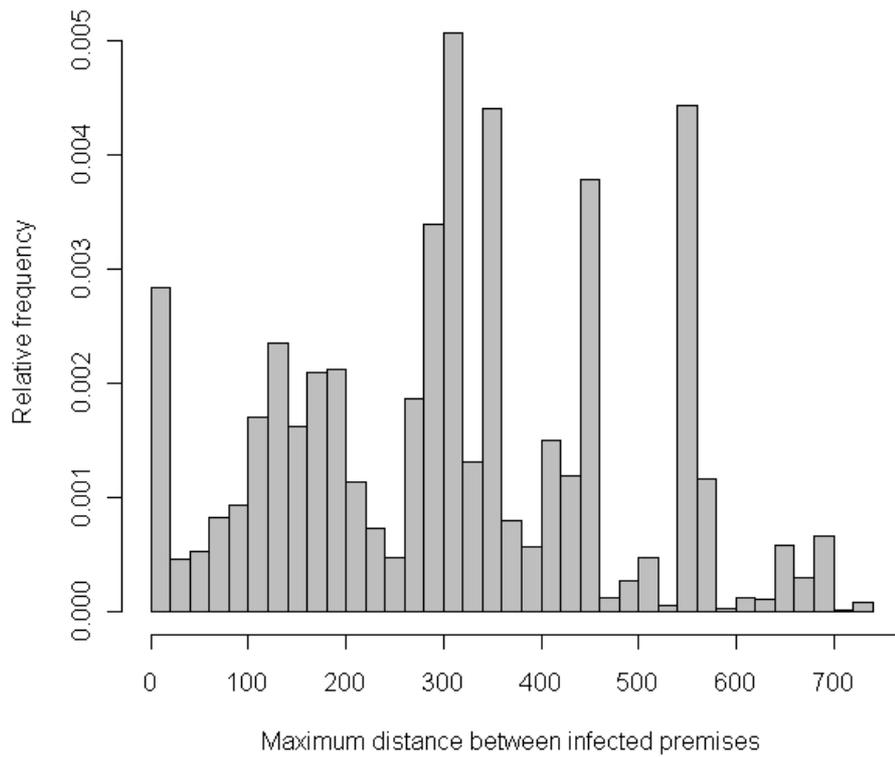

Figure S1. Histogram of maximum distance between infected premises for all outbreaks that spread beyond the seed premises