Transboundary and Emerging Diseases

ORIGINAL ARTICLE

Quantifying the Risk of Introduction of West Nile Virus into Great Britain by Migrating Passerine Birds

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Keywords:
arboviruses; bird migration; Europe; mosquitoes; risk analysis; West Nile virus

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Received for publication August 8, 2014

doi:10.1111/tbed.12310

Summary

West Nile virus (WNV) is a mosquito borne arbovirus that circulates within avian reservoirs. WNV can spill over into humans and Equidae that are dead-end hosts for WNV but suffer fever, acute morbidity and sometimes death. Outbreaks of WNV are common across Africa and Eastern Europe, and there have also been sporadic outbreaks in Spain and the Camargue Regional Park in France, but never in Great Britain (GB). These areas all fall along a major bird migration route. In this study, we analyse a scenario in which WNV is circulating in the Camargue or in other wetland areas in France and we estimate the risk of northward migrating passerine birds stopping in a WNV hotspot, becoming infected and carrying active infection to GB. If the disease were circulating in the Camargue during a single migratory season, the probability that one or more migrating birds becomes infected and lands in GB whilst still infected is 0.881 with 0.384 birds arriving in areas of suitable vector habitat. However, if WNV became established in the Grand Brière National Park or La Brenne Regional Park wetland areas further to the north, the model predicts that at least one infected bird will continue to GB. Thus, GB is at risk of WNV introduction from the Camargue, but the risk is considerably greater if WNV were to circulate further north than its previous focus in France, but this is highly sensitive to the force of infection in the infected area. However, the risk of establishment and infection of humans in GB is dependent upon a number of additional factors, in particular the vector and epidemiological situation in GB.

Introduction

West Nile virus (WNV) is an arbovirus of the family Flaviviridae that is transmitted by mosquitoes (*Diptera: Culicidae*) to avian reservoir hosts, Equidae and humans. Equidae and humans are dead-end hosts, but humans develop WNV fever with symptoms including meningitis, encephalitis and polyradiculoneuritis (Del Giudice et al., 2004). WNV lineage I is common throughout Africa, Asia and Southern Europe and was introduced to North America where it spread widely (Pradier et al., 2012). WNV lineage II has been restricted to sub-Saharan Africa. (Zeller and Schuffenecker, 2004; Pradier et al., 2012). In the Old World, the main avian reservoir of WNV is passerine species (order: Passeriformes) and a wide range of mosquito vectors circulate the virus (Medlock et al., 2005). In Western Europe, birds infected with WNV lineage I remain largely asymptomatic (Hubálek and Halouzka, 1999), but

the clade of WNV in North America is commonly fatal in birds, particularly corvids (Komar et al., 2003).

In recent years, there have been a number of outbreaks of WNV lineage I in Western Europe (Murgue et al., 2001a; Balenghien et al., 2006; Balança et al., 2009; Pradel et al., 2009; López et al., 2011; Monaco et al., 2011). In particular, there have been outbreaks in the Camargue Regional Park in France (Murgue et al., 2001b; Balenghien et al., 2006; Leblond et al., 2007; Jourdain et al., 2008). This is a particularly high risk area for WNV introduction and spread due to the presence of migratory birds and WNV bridging vectors, in particular *Culex modestus* but also *Culex pipiens, Aedes caspius, Aedes vexans and Anopheles hyrcanu* (Balenghien et al., 2006, 2008) and migratory birds from West Africa as modelled by Durand et al. (2010). The local horse population in the Camargue region inadvertently act as sentinels to indicate virus circulation (Balenghien et al., 2006; Leblond et al., 2007). At the time of writing, WNV had only ever been identified in the Camargue. Accordingly, vector and avian sampling has been restricted to the Camargue and nearby Dombes (Pradel et al., 2009).

To date, there have been no reports of WNV among either Equidae or humans in Great Britain (GB), although there is some evidence that the virus may have circulated in UK birds (Buckley et al., 2003, 2006). However, during 2010, the WNV bridging vector *Culex modestus* was found to be established in nature reserves in south-east England (Golding et al., 2012). This discovery was the first time this vector had been found in natural habitats in GB since 1945 (Golding et al., 2012), and it has subsequently been found in several other locations in the south of England (Medlock and Vaux, 2012). *Cx. modestus* is of particular importance because it is one of the principal vectors for WNV in Western Europe (Pradier et al., 2012) and is an extremely efficient vector that can become infected when exposed to relatively low viraemia (Balenghien et al., 2006, 2007, 2008).

Culex spp. mosquitoes typically only fly relatively short distances (<2 km) (Tsuda et al., 2008) so are unlikely to introduce WNV directly to GB, unless carried by trans-Atlantic aircraft (Brown et al., 2012). Another route of introduction is migrating birds (Jourdain et al., 2007; Calistri et al., 2010; Randolph and Rogers, 2010), specifically passerines (order Passeriformes) that have been identified as the most competent order of birds for WNV infection in terms of susceptibility and virus amplification (Komar et al., 2003; Jourdain et al., 2008). One of the most common flyways for birds migrating north during the spring is the East Atlantic Flyway, by which birds travel from West or North Africa, over the Iberian peninsula then over France and on to GB, Ireland or further north (Moreau, 1961; Wernham et al., 2002; Figuerola et al., 2008; Jourdain et al., 2008; Bächler et al., 2010; Tøttrup et al., 2012). We do not consider direct introduction into GB by birds migrating from WNV hot spots in West Africa because the distances involved prevent birds reaching GB whilst still infected (Pradier et al., 2012). Instead, we consider stopping in an outbreak area in France, becoming infected and carrying WNV infection to GB.

In this study, we use a stochastic model framework to model a scenario in which WNV is circulating in wild birds in the Camargue. Specifically, we address the following questions:

1 What is the risk that WNV will be introduced into GB by infected northward migrating passerines?
2 How many WNV infected birds would arrive in GB?
3 What is the risk that WNV will be introduced into areas of GB that have been shown to have some potential to be habitats for both enzootic and bridging vectors for WNV?

Materials and Methods

This analysis fits a stochastic model to data on the population of passerines in GB that migrates north along the East Atlantic Flyway to GB during the spring. We assume that one or more stop(s) during migration will be in France and calculate the number of birds that stop in the Camargue by fitting a spatial model to recoveries of ringed birds (details in the Figs S1 and S2). Based upon the force of infection, a number of birds become infected. Given the flight speed of the bird and the duration of infection of the bird, we calculate the number of birds that reach GB whilst infected. The model pathway is illustrated by Fig. 1, and the model and uncertainty are outlined below.

Data

We process and combine the data in the following steps:

1 The numbers of passerine species in GB that migrate along the East Atlantic flyway in GB are identified from published bird population data (Musgrove et al., 2013) (Table 1). These numbers are typically recorded as territories or breeding pairs, so numbers are multiplied by 2.
2 Data on bird habitats in GB are taken from the land cover map (LCM) 2007 data set of dominant land cover types in 1-km grid cells (Morton et al., 2011). This is classified into 10 aggregate land cover types as well as the land cover subclass that represents 'fen, marsh and swamp' which is important vector habitat (Morton et al., 2011) (land cover types are listed in Table 2).
3 Bird habitat data used here are the modelled likelihoods of bird species being found in different habitat types (Fuller et al., 2007). These likelihoods are combined

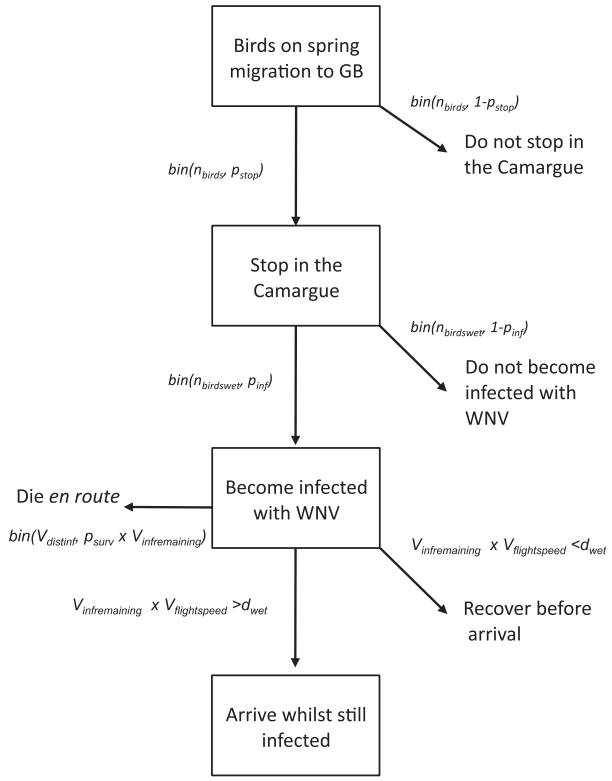

Fig. 1. Schematic representation of the model used in these analyses.

with the species abundance data to calculate the number of migratory birds of each species in each habitat class.

4 Polygons representing the boundaries of the Camargue, Grande Brière and La Brenne are taken from the World Database on Protected Areas (2014). To allow for the flight of the vector, these polygons are buffered by 1 km, to allow for the maximum flight distance of WNV vectors (Tsuda et al., 2008).

5 The probability of an individual bird stopping off in an outbreak area during migration is calculated using the British Trust for Ornithology (BTO) ringing recoveries database (Robinson and Clark, 2012). The data are smoothed to calculate the probability of stop off in the Camargue of 0.0008 and for the sensitivity analysis for the Grand Brière 0.0012 and La Brenne 0.0037 (Fig. 2) (details in Figs S1 and S2). This is inflated by a factor of 2.82 as there is a greater likelihood of stopping in a wetland (details in Figs S1 and S2).

6 Data on suitable vector habitat in the UK are taken from a predictive map showing the probability of the presence of a potential WNV vector community (Golding, 2013). This is a conservative estimate of risk as data were not available for all potential WNV vector species in the UK. Specifically, insufficient data were available to separately model *Culex pipiens molestus* and *Cx. pipiens pipiens*, so these were modelled together as *Cx. pipiens* s.l. Similarly, *Cx. modestus* has only been reported from a handful of locations in the UK, and so, a distribution map for this species could not be produced. Similarly, *Cx. torrentium* and *An. plumbeus* could not be mapped on account of there being a small number of occurrence records. A potential WNV vector community is defined as one where either (i) a species is present which could fulfil both bridge and enzootic vector roles (*Culiseta morsitans*) or (ii) a potential enzootic vector (*Culex pipiens* s.l.) and potential bridge vectors (of *Aedes cinereus*, *Coquillettidia richiardii*, *Cs. annulata*, *Ochlerotatus cantans/annulipes*, *Oc. detritus* and *Oc. punctor*) are present. Medlock et al. (2005) indicate that *Culiseta morsitans* should be considered a potential bridge vectors, with their potential to feed on humans evidenced by precipitin tests identifying human blood in females, as reported in Service (1994). Predictive maps of the probability of the presence of each of these vectors are used to estimate the probability that a WNV vector community is present which could both maintain virus circulation in birds and transmit it to humans and Equidae.

Model parameters

The data were combined in the model following the steps described below with a generalized representation in Fig. 1, and parameters are listed in Table 2.

1 Of the birds that migrate to GB, only a proportion stop in the Camargue. This number of birds is sampled from a binomial distribution $bin(n_{\text{bird}}, p_{\text{stop}} \times w_{\text{inf}})$, where p_{stop} is the probability that a bird will stop in that particular wetland, w_{inf} is an inflation factor for preferentially stopping in wetland and n_{bird} is the number of migrating birds.

2 The median force of infection per bird is 0.00029 day^{-1}. This is based upon the seroprevalence in WNV areas with a median of value of 0.048, described by a beta distribution beta(19 374)/166. This allows for the seroprevalence representing infection on any day of life to that day (details in the supplementary material). Given a 5-day duration of infection, this gives a proportion of viraemic birds at any given point of 0.00145. This is somewhat higher than viraemic rates estimated from modelling studies by Durand et al. (2010) that peak at around 0.001 for resident and migratory birds during the main transmission season in France. To allow for this, we conducted sensitivity analysis using a range of smaller values of force of infection.

3 The duration of viraemia is from Komar et al. (2003) with a median 5 days, minimum of 4 days and maximum of 7 days, so we used a triangle distribution (triangle(4,7,5)).

Table 1. Breakdown of passerine species considered in these analyses. Note that the UK population figures are for territories, so are multiplied by 2 to give the full migratory population

Common name	Latin name	UK population	Birds ringed	Recoveries in France
Blackcap	*Sylvia atricapilla*	1 100 000	856 552	31
Chiffchaff	*Phylloscopus collybita*	1 100 000	680 006	5
Garden Warbler	*Sylvia borin*	170 000	176 563	9
Grasshopper Warbler	*Locustella naevia*	13 000	37 161	0
House Martin	*Delichon urbicum*	510 000	382 071	8
Lesser Whitethroat	*Sylvia curruca*	74 000	123 883	0
Linnet	*Carduelis cannabina*	410 000	455 730	12
Meadow Pipit	*Anthus pratensis*	1 900 000	329 566	15
Nightingale	*Luscinia megarhynchos*	6700	12 526	0
Pied Flycatcher	*Ficedula hypoleuca*	18 500	634 504	5
Redstart	*Phoenicurus phoenicurus*	100 000	106 636	0
Reed Warbler	*Acrocephalus scirpaceus*	130 000	897 320	13
Sand Martin	*Riparia riparia*	105 000	1 013 156	59
Sedge Warbler	*Acrocephalus schoenobaenus*	260 000	971 240	11
Spotted Flycatcher	*Muscicapa striata*	33 000	101 559	0
Swallow	*Hirundo rustica*	760 000	1 952 168	23
Tree Pipit	*Anthus trivialis*	88 000	21 849	0
Wheatear	*Oenanthe oenanthe*	230 000	91 675	0
Whinchat	*Saxicola rubetra*	47 000	43 365	2
Whitethroat	*Sylvia communis*	1 100 000	431 818	0
Willow Warbler	*Phylloscopus trochilus*	2 200 000	1 342 167	26
Wood Warbler	*Phylloscopus sibilatrix*	6500	22 579	0
Yellow Wagtail	*Motacilla flava*	15 000	79 179	2
Total		10 376 700	11 957 479	223

Table 2. Table of the parameters used in these analyses

Parameter	Symbol	Value	Source
Duration (days) of infection		triangle(4, 7, 5)	Komar et al. (2003)
Daily flight speed (km day^{-1})		pert(0, 0, 394, shape = 2.1)	Sussana et al. (2011)
Seroprevalence in infected area		beta(19, 374)	Jourdain et al. (2008)
Passerine death rate (per annum)	p_{surv}	0.55	Møller (2007), Durand et al. (2010)
Force of infection	p_{inf}	*prev*/166	
Probability of originating from:			
Camargue	p_{stop}	0.00082	Estimated from the data, details in the Figs S1 and S2
Grande Brière		0.00125	
La Brenne		0.00366	
Inflation factor for selecting wetland habitats	w_{ifn}	2.82	
Time from infection to departure (days)		unif(0, 1)	Wernham et al. (2002)
Total number of birds migrating to GB	n_{bird}	20 753 400	

4 Birds become infected at any point during their 24-h stopover in the wetland area, so the total time spent in flight with active infection is the infectious period minus the time between infection and departure. The 24-h stopover is based upon the average stop-off time for refuelling on migration and is representative of birds flying short migratory legs (as modelled here) over land with abundant refuelling opportunities (Wernham et al., 2002; Goymann et al., 2010).

5 The mean daily flight speed of the birds is a pert distribution (Vose, 2000), pert(0, 0, 394, shape = 2.1) derived from Sussana et al. (2011) (details in Figs S1 and S2). From this and the infectious period of the birds, we derive the number of infected birds that will travel the full distance between the infected area and GB. This is adjusted for the probability of the bird dying *en route*, based upon the life expectancy of the bird.

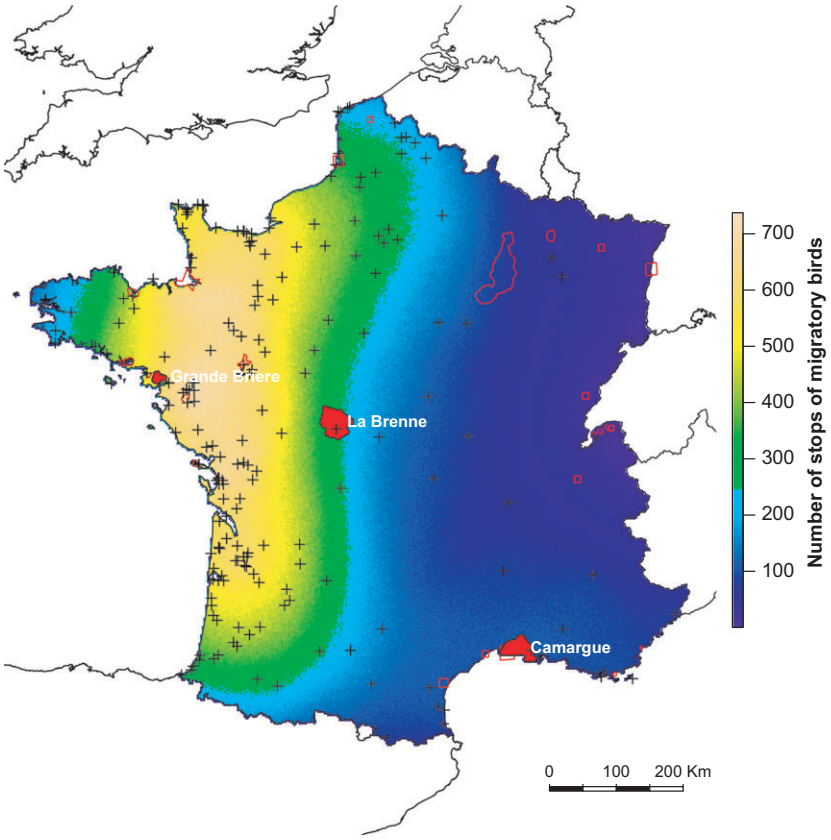

Fig. 2. The number of migrating birds stopping off in 2.5-km grid cells in France. Black crosses represent the locations of recovered ringed birds, the Camargue, Grande Brière and La Brenne marked (solid red polygons) and unfilled red polygons are other wetland areas.

6 The arrival point of these birds in GB is calculated from the bird species habitat data. These data allow us to calculate the probability that a bird of a given species selects a particular habitat type (Table 3). This is weighted such that the probability of a bird landing in a particular 1-km habitat data grid cell is dependent upon the distance of that cell from France normalized by the distribution of bird flight speeds.

The model

The model is a stochastic model with variability in the parameters incorporated by sampling from the parameter distributions. Based upon the population of migratory birds to GB (n_{bird}) and the probability of stopping in the wetland area (p_{stop}), we calculate the number of birds that stop in a wetland area as:

$$n_{\text{birdwet}} \sim \text{bin}(n_{\text{bird}}, p_{\text{stop}} \times w_{\text{inf}}).$$

The species of the birds in n_{birdwet} is sampled from the relative species preference for wetland (p_{wetA}) and an inflation factor representing the preference for wetland habitat (Figs S1 and S2) to create a vector of birds by species ($V_{\text{specieswet}}$) of length n_{birdwet}.

The force of infection is sampled as the force infection during that season

$$p_{\text{inf}} \sim \text{beta}(19, 374)/166$$

The number of birds that become infected is thus sampled:

$$n_{\text{birdinf}} \sim \text{bin}(n_{\text{birdwet}}, p_{\text{inf}})$$

The species of n_{birdinf} are sampled from the species of birds that stop in the wetland $V_{\text{specieswet}}$ to give a vector of the infected species V_{birdinf}. Given a 1 day stop off, the time to infection of each infected bird in V_{birdinf} is as follows:

$$V_{\text{timetoinf}} \sim \text{unif}(0, 1)$$

and the infectious period sampled for each bird

$$V_{\text{infperiod}} \sim \text{triangle}(4, 7, 5)$$

The duration of remaining infection after departure is

$$V_{\text{infremaining}} \sim V_{\text{infperiod}} - V_{\text{timetoinf}}$$

The vector of the flight speeds of each bird in V_{birdinf} is given by:

Table 3. Breakdown of the BTO habitat type classification and the LCM land cover classes broken down by the coverage of different habitats in the 1 km pixels of the LCM data and WNV vector suitability

BTO type	LCM type	Number of pixels	Number of birds	Birds/pixel	Vector suitability
Deciduous woodland	Broad leaf woodland	5733	453 755	79.1	0.366
Coniferous woodland	Coniferous woodland	14 705	1 035 948	70.4	0.306
Arable	Arable and horticultural	71 594	3 825 413	53.4	0.197
Pastoral	Improved grassland	60 953	4 249 110	69.7	0.234
Peatland	Semi-natural grassland	24 275	4 608 553	190	0.255
Heath Moorland Scrub	Mountain heath bog	38 898	4 633 473	119	0.293
Coastal	Coastal	6861	3 380 445	49.3	0.351
Rural Urban	Built up areas	14 233	805 274	56.6	0.254
Fen Reedbed	Fen marsh swamp	3632	861 829	237	0.373
Total			20 753 400		

$$V_{\text{flightspeed}} \sim \text{pert}(0, 0, 394, \text{shape} = 2.1)$$

and the distance travelled during the infectious period is given by:

$$V_{\text{distinf}} = V_{\text{infremaining}} \times V_{\text{flightspeed}}$$

Birds in V_{birdinf} will arrive in GB whilst infected depending upon the distance from the wetland to GB (d_{wet}) where

$$V_{\text{distinf}} > d_{\text{wet}}$$

and a proportion of the birds in V_{distinf} survive the journey according to $bin(V_{\text{distinf}}, p_{\text{surv}} \text{ x } V_{\text{infremaining}})$ where p_{surv} is the daily probability of survival.

Thus, the duration of infection and flight speed are sampled individually for each infected bird, whilst the force of infection is sampled once per model run (year).

The model was implemented in the base package of the R statistical environment (R Development Core Team, 2013) with a separate implementation for each sensitivity analysis. Each implementation was run for 1 000 000 iterations (convergence was inspected and was within 1% after 10 000 iterations), with each iteration being a single migration season.

Analysis

This model is used to calculate:

1 The probability of an infected bird arriving in GB based upon the proportion of model runs in which at least one infected bird arrived in GB.
2 The number of birds that are expected to arrive in GB with active infection.
3 The probability (and number) of bird(s) with active infection that are expected to arrive in an area of suitable WNV bridging vector habitat. This is calculated by multiplicatively overlaying the vector likelihood distribution surfaces onto the fitted distribution of WNV introduction risk. The sum of these cells gives a total expected number of introductions to at-risk areas.
4 For the arriving birds, the number of days of infection left and the number of birds that are still infected for at least 1 day.

Key assumptions

There are a number of assumptions and limitations in this study. These are as follows:

1 That birds of all passerine species are equally susceptible to infection with WNV and that the duration of viraemia is equal among all species. Evidence from North America suggests that susceptibility varies between species (Komar et al., 2003), but there is little data relating to the European species studied here; hence, we use parameters fitted to the passerine order.
2 The epidemic in the stop-off area will be widespread and spatially homogeneous at the time of stop off. It is possible that WNV incidence would be greater later in the year. Furthermore, we assume that birds will choose to stop off in a land cover type that is the preferred habitat for that species in GB.
3 That birds migrate along straight lines directly to GB, rather than following a random path. The literature indicates that this is a reasonable assumption (Bächler et al., 2010; Tøttrup et al., 2012).
4 That birds migrate independently of other members of that species and other species. If passerines migrate from France to GB in flocks, then this could create a large single introduction of WNV.
5 That infection with WNV does not affect the migratory speed of infected birds due to morbidity.

Table 4. The results of the baseline model and sensitivity analyses for the risk of WNV introduction

	Probability of introduction	Number of birds (median, 95% CIs)	Probability of a bird arriving and being infectious for >1 day	Days of introduction (median, 95% CIs)	Vector habitat introductions (95% CIs)
Baseline	0.881	2 (0, 6)	0.726	2.17 (0, 7.71)	0.384 (0.126, 1.37)
Sensitivity analysis – outbreak location					
Grande Brière	1.000	11 (4, 21)	1.000	25.8 (8.59, 50.1)	2.01 (0.659, 7.20)
La Brenne	1.000	27 (14, 46)	1.000	53.5 (25.3, 92.0)	4.79 (1.57, 17.1)
Sensitivity analysis – Flight speed					
Speed hyperparameter	0.878	2 (0, 6)	0.726	2.20 (0, 8.07)	0.386 (0.126, 1.39)
Sensitivity analysis – Longer duration of infection					
Duration of infection	0.917	2 (0, 7)	0.819	4.18 (0, 119.5)	0.453 (0.148, 1.622)
Sensitivity analysis – Duration of stop off					
Duration of stop off	0.951	3 (0, 8)	0.825	2.86 (0, 8.82)	0.559 (0.183, 2.00)
Sensitivity analysis – Prevalence					
50%	0.664	1 (0, 4)	0.464	0.829 (0, 5.08)	0.192 (0.063, 0.690)
25%	0.427	0 (0, 2)	0.261	0 (0, 3.50)	0.098 (0.032, 0.346)
10%	0.201	0 (0, 1)	0.112	0 (0, 2.39)	0.039 (0.012, 0.139)
Sensitivity analysis – Wetland stop-off likelihood					
50% Lower	0.664	1 (0, 4)	0.464	0.833 (0, 5.11)	0.193 (0.063, 0.690)
100% Higher	0.982	4 (1, 10)	0.933	4.71 (0.226, 12.3)	0.768 (0.253, 2.75)

Evidence suggests that birds that are infected with WNV in Europe remain largely asymptomatic (Hubálek and Halouzka, 1999) and so is a reasonable assumption.

6 That the probability of a ringed bird being recovered is spatially homogenous. Studies have demonstrated that there are significant biases in reencounter probabilities at the small scale (Korner-Nievergelt et al., 2010). However, the ringing recovery data used in these analyses are re-aggregated to a coarse national rather than a local scale which will have the effect of minimizing any bias.

7 The force of infection for a bird exposed to WNV can be estimated from seroprevalence data. Records of virus being detected in birds are few, so seroprevalence surveys were extrapolated to estimate the force of infection and so assume that birds with detectable WNV antibodies have been infected with WNV.

Sensitivity and uncertainty analysis

Each of the following will be evaluated in turn, comparing the change to the baseline:

1 Uncertainty in the flight speed by fitting a hyperparameter to the flight speed distribution (Figs S1 and S2).

2 A previous study has suggested that there may be a carrier state among some infected birds and virus can be detected for as long as 20–100 days from the organs of infected birds (Hubálek and Halouzka, 1999). Although it remains unclear whether these birds are infectious, we conduct sensitivity analysis with an infectious period of up to 100 days among 5% of infected birds.

3 Force of infection. The uncertainty in this parameter is that the force of infection will be lower during the period that the birds are in the Camargue as per Durand et al. (2010). To incorporate this, we reduce the force of infection by 50%, 75% and 90%.

4 To explore the proportion of migrating birds that stop in wetlands during migration, numbers stopping in wetlands are separately multiplied by 0.5 and 2.

5 Alternative wetlands. We explore the potential for stopping in wetland habitats further to the north – Grande Brière National Park and La Brenne Regional Park. Like the Camargue, the Grande Brière and La Brenne are large wetland areas but they are closer to GB (350 and 450 km compared to 900 km from GB). The Grande Brière is a small area, but on the route of migratory birds, La Brenne is larger and slightly east of the migratory flight route.

6 Duration of the stop off using a range 0–7 days of stop off per Moore and Kerlinger (1987), defined by a uniform(0,7) distribution.

Results

The results of modelling the introductions from the Camargue and the sensitivity analyses are presented in Table 4. Given an outbreak in the Camargue, there is a probability of 0.881 of a bird arriving whilst viraemic with a median 2 birds arriving (95% CIs = 0, 6) with a total of 2.17 days of active infection remaining (Table 4). Results of the sensitivity analysis indicate that there is a slight increase in risk of introduction from the Camargue if there is a carrier status among infected birds or if the birds stop in the risk area for longer than 1 day. The results are highly sensitive to the force of infection parameter, and a lower force of infection (as has been suggested for earlier in the transmission season) results in greatly reduced risk of introduction (Table 4). If there were an outbreak the Grande Brière or La Brenne, there is a large increase in risk with the potential for large numbers of introductions (Fig. 3).

The risk map for arrival locations of the WNV infected birds is shown in Fig. 4 and indicates that there are likely to be distinct clusters of high risk introductions, with the highest risk being in the south-east and patches of high risk of introduction in the south west.

Overlaying the distributions of WNV introductions (Fig. 4) on to the distribution of suitable bridging vectors shows a more scattered distribution of high risk areas (Fig. 5). The high risk areas are clustered in the south, specifically in areas closer to France. However, there are pockets further to the north and these sometimes coincide with the distribution of bridging vectors (Fig. 5).

Discussion

This study has demonstrated that if there is another outbreak of WNV in the Camargue, then it poses a threat to the human and equine populations of GB through infected migrating birds with the a probability of 0.881 that the disease will reach GB in migrating birds during a single migration season. However, there will be a relatively short period (2.17 days) of active infection remaining which could reduce the likelihood of establishment. If there disease moves to suitable vector habitats further to the north of France, then the risk increases.

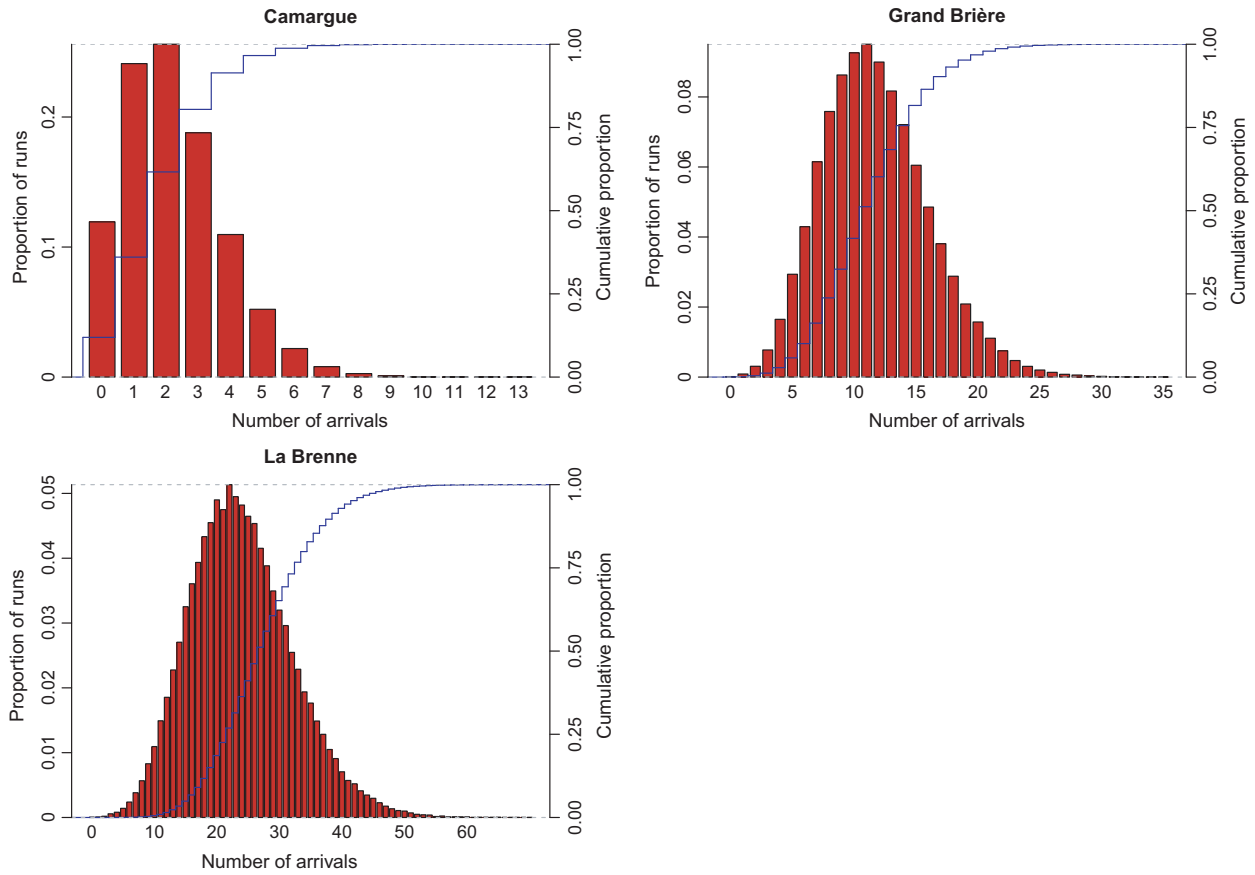

Fig. 3. Histograms and cumulative distribution plots of the number of infected birds arriving in the GB under the model runs in these analyses.

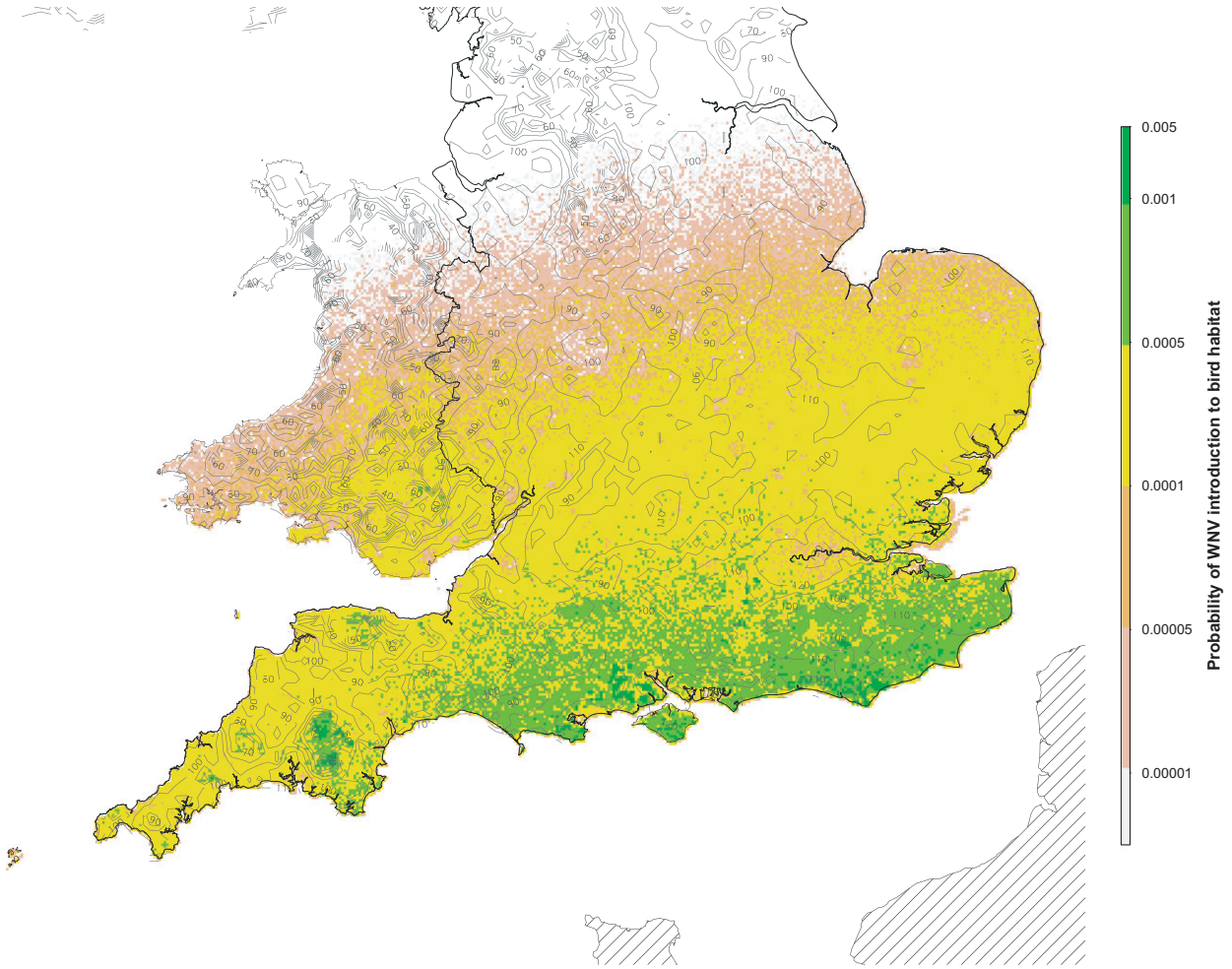

Fig. 4. Risk map for the south of England showing risk of introduction during a spring migration season from La Brenne into 1-km grid cells. Isopleths represent lines of the mean number of days with an average temperature above 14°C, derived from UKCIP data (Perry and Hollis, 2005) for the period 1990–2006.

If WNV is introduced into GB, then the presence of highly competent WNV vector species in GB (Golding et al., 2012) elevates the risk of establishment and the risk to public health as *C. modestus* can become infected when exposed to even a relatively low viraemia. However, the distribution of *C. modestus* in GB remains poorly understood. Thus, it is important to consider both the spatial distributions of likely arrivals of birds alongside the potential distribution of competent vectors (Fig. 5). Around one quarter of arriving infected birds will arrive in areas of WNV bridging vector habitat, and further work could be carried out to model the potential for spread and risk to human health following introduction. These sites are focussed on the New Forest area, Swanage and the Pevensey area. Avian surveillance could be carried out in these areas to monitor arriving birds, and vector surveillance could be enhanced to gain a better understanding of the vector populations and their dynamics in these areas. If introduced from the Grand Brière or La Brenne, then there is a longer period of infection following arrival during which infection can be transferred to the native vectors and so an increased risk of establishment. However, there is little published data on the vector suitability in the Grand Brière or La Brenne; hence, these were used as exemplars of risk.

The potential for establishment of WNV in GB is also dependent upon the climatic conditions and in particular whether the temperatures are high enough for within vector virus replication. Virus replication is very inefficient at temperatures below 14°C and efficiency of transmission increases at warmer temperatures (Cornel et al., 1993), and this raises the potential for greater WNV spread with global warming (Pradier et al., 2012). Furthermore, global warming would increase the suitability of the habitat for WNV in

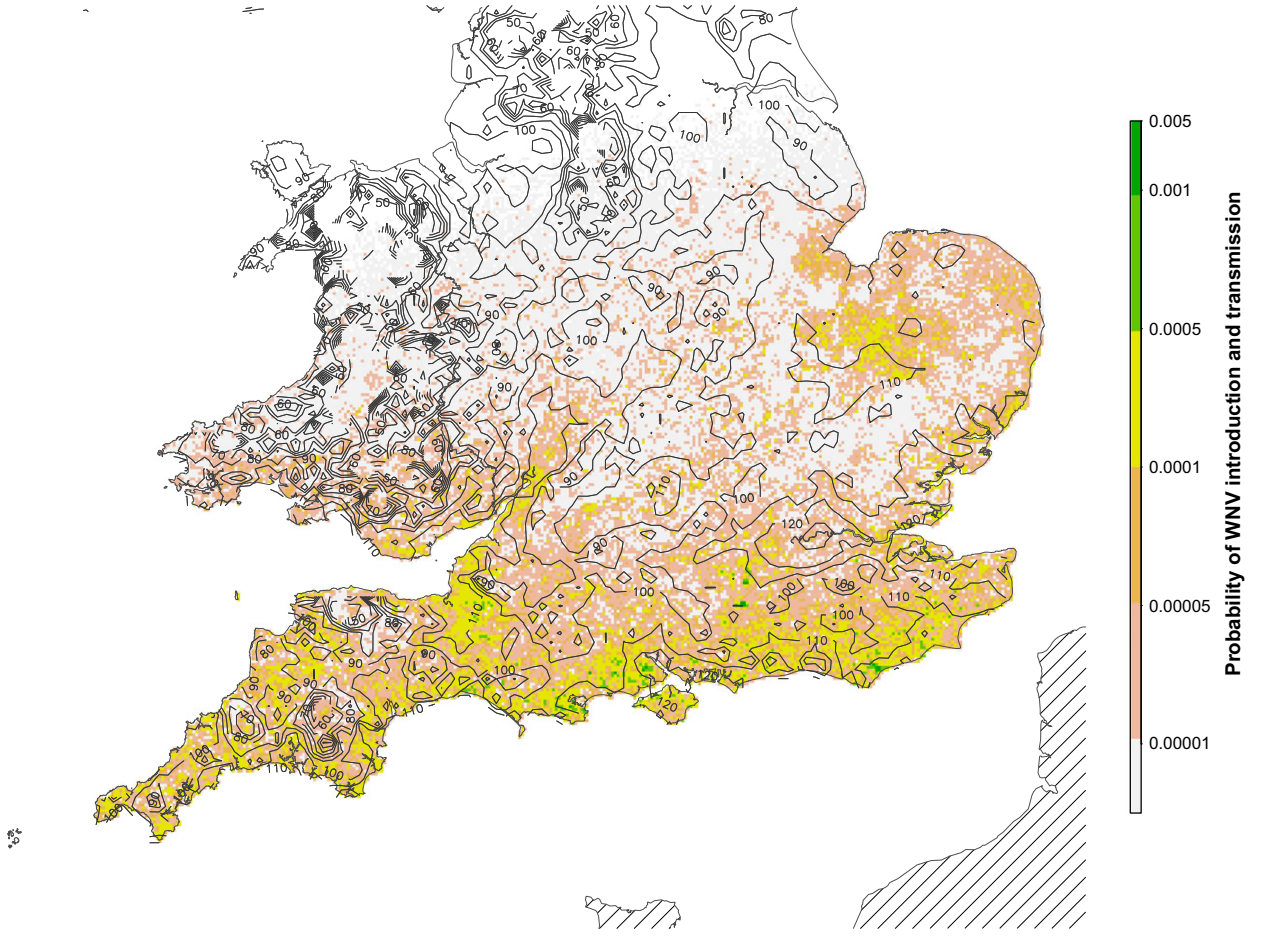

Fig. 5. Map of the distribution of risk of introduction into the south of England from La Brenne into 1 km given the probability of the presence of vectors. Isopleths represent lines of the mean number of days with an average temperature above 14°C, derived from UKCIP data (Perry and Hollis, 2005) for the period 1990–2006.

more northerly locations in Western Europe, so as WNV suitability increases in GB, the risk of establishment of WNV is also likely to increase (Paz and Semenza, 2013; Fischer et al., 2014; Schaffner and Mathis, 2014). However, the relationship with global warming may be detrimental to WNV vectors if temperatures and precipitation cause drying of habitats as forecast for areas of North America (Morin and Comrie, 2013). The impact of climate change on bird migration patterns remains less clear, but may be disruptive (Ovaskainen et al., 2013).

The model constructed here is limited by time, in terms of the requirement for the bird to cover the distance between the infected area and GB whilst still viraemic. However, sensitivity analysis exploring the potential effect of a carrier status among a proportion of birds (Hubálek and Halouzka, 1999) showed that this has relatively little effect. Instead, it is proximity to the wetland area, the force of infection in that area and the likelihood of a migrating bird stopping in that area that drive the risk of introduction. Whilst it has been suggested that a carrier status may exist in some birds, the virus was isolated from internal organs, so it is unclear whether these birds have a sufficiently high viraemia to infect the vectors (Hubálek and Halouzka, 1999). The model is also sensitive to the duration of the stop off in the WNV hot spot (Table 4). This is because the duration of the stop-off limits the number of birds that can become infected. This does not affect the risk of introduction from the Camargue where it is the distance to GB rather than the number of birds that become infected that determines the risk of introduction. A longer stop off of 0–7 days has only a small effect on the number of infected birds arriving from the Camargue. In this model, we only consider introductions by migrating passerines. Other migrating bird orders are susceptible to infection with WNV; however, their competence is lower and passerines are considered to be the principal risk (Komar et al., 2003; Jourdain et al., 2007). The different levels of competence in different species have not been defined in sufficient

detail to be incorporated into these analyses, so we focussed on passerines. Further quantification of the relative competence of different bird species could further inform this risk to GB.

These analyses are heavily dependent upon a number of parameters that were estimated from the literature. Of particular importance is the force of infection. As there were no data on surveillance for active WNV infection in birds, we used data on seroprevalence. Seroprevalence estimates from Spain, France and the Czech Republic all estimate seroprevalence to be approximately 5%. However, some migratory birds may have been infected outside Europe, so the actual prevalence during an outbreak in the Camargue is not yet known. As infection is transitory, but antibodies will remain in circulation for a prolonged period, we have adjusted for the lifespan of the bird and duration of viraemia. The migratory process and the resulting distribution of infections in the Camargue has been modelled by Durand et al. (2010) and demonstrate that infection in the Camargue is at its lowest at the start of transmission season. This means that the risk of introduction to GB may be very low as demonstrated by the sensitivity analysis. This could be further explored by longitudinal studies of the viral prevalence in affected areas.

The results in this study are also dependent upon the distribution of WNV epidemic areas in France. There have been multiple introductions and epidemics of WNV in the Camargue (Murgue et al., 2001b; Balenghien et al., 2006; Leblond et al., 2007; Jourdain et al., 2008) but no vector surveillance or disease surveillance other than that in the Camargue and the Dombes (Pradel et al., 2009), furthermore since 2004, there have been no incursions into the Camargue or the Dombes . The infrequency of incursions is possibly partly due to the northward migration occurring during the dry season (therefore lower transmission) in West Africa.

This study has demonstrated that the numbers of introductions of WNV from migrating birds from France are likely to be few and the likelihood of establishment is lower still. The potential for spread will be reduced as the infected birds would have to arrive at a time when temperatures are above those needed for extrinsic incubation and the birds are likely to arrive after their peak in viraemia when their infectiousness will be diminishing (Komar et al., 2003). The potential for establishment would be increased if competent vector species such as *Cx. modestus* continue to expand, as this vector species can become infected at relatively low viraemia. However, much of the introduction is likely to be early in the mosquito season when vector activity may be relatively low. This would reduce the risk of transmission and establishment and could be modelled further.

In addition to WNV, there are a number of arboviruses that infect birds and other species, and these viruses include Chikungunya, Usutu, Sindbis and Tahyna virus. Should such viruses continue to expand into new areas (Medlock et al., 2007), then this study has demonstrated that their risk of arrival in GB may increase. In addition to the expansion of the reservoirs explored in this analysis, the expansions of the geographical extent of vectors such as *Aedes albopictus* and *Ae. aegypti* that are vectors for Yellow Fever, Dengue and Chikungunya could also be considered. Thus, it is important to monitor hosts and vectors.

Acknowledgements

PRB and LAB are funded by the Scottish Government funded EPIC project. NG is funded by a grant from the Bill & Melinda gates Foundation (#OPP1053338). BMCB is supported by Institute Strategic Funding from the BBSRC. KRS and BVP are supported by the Natural Environment Research Council. The BTO Ringing Scheme is funded by a partnership of the British Trust for Ornithology, the Joint Nature Conservation Committee (on behalf of: Natural England, Natural Resources Wales and Scottish Natural Heritage and the Department of the Environment Northern Ireland), The National Parks and Wildlife Service (Ireland) and the ringers themselves.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Figure S1. Cumulative distribution function of the observed mean distance to the other recoveries (black line) and the fitted exponential distribution (red line).

Figure S2. The empirical probability function (red line) and cumulative probability of the pert(0,0,394, shape = 2.1) fitted to the points and associated 95% confidence intervals for these analyses.