Department
for Environment
Food & Rural Affairs

Risk assessment for Bluetongue Virus (BTV-8): risk assessment of entry into the United Kingdom

Updated Qualitative Risk Assessment

May 2017

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Summary

This document is an update of the risk assessment of the likely incursion of BTV-8 into the UK produced in 2016. It looks at the pattern of disease spread in the past few months, the pathogenicity and impact of the virus and the likely introduction of disease into the UK over the next few months from infected midges.

All updates in the main document are shown in red.

Bluetongue virus serotype 8 (BTV-8) re-emerged in 2015 in Central France, despite being undetected in mainland EU for at least five years. As of 5th May 2017, France has reported over 2,300 detections, relatively concentrated in the centre of the country and mainly affecting cattle, albeit with mild or no clinical signs and very low prevalence. As a result of these detections, restriction zones have been put in place to ensure only vaccinated or naturally immune BTV susceptible animals can move out of the zone. This restricted region now covers a large area of mainland France, as far as the North Coast and the region around Calais. The nearest positive detection was made earlier in 2017, but is located more than 150 km from the English coast.

On the risk of incursion via infected midges, it is difficult to predict at this stage, as it is highly dependent upon the level of disease on the Continent, the proximity to the UK and the climate. As an approximation and with a high level of uncertainty, in 2016 we considered the risk of an incursion in a cool spring (ie with average temperatures of less than 12-15^{o}C) to be between 5 and 10%; later in the summer at between 33 and 60% and by the end of the summer at 60-80%. This was based purely on expert opinion (including work from several workshops carried out at Defra in 2014) and relied on successful re-emergence and spread in France in 2016. In reality, infection did not spread outside the heavily affected central regions, except occasional sporadic cases, most likely due to movement of infected animals within the large restriction zone. Therefore throughout the summer of 2016 the risk level for incursion of BTV-8 from France **was never greater than medium**. Short summaries of the situation and risk level were produced on gov.uk at https://www.gov.uk/government/publications/bluetongue-virus-btv-8-in-france

The risk levels for this year are currently estimated at being very similar and again will change (giving lower uncertainty) as the year progresses and as we understand more about the level of vaccination and the temperature in France and Southern England. Not every incursion will lead to an outbreak as a single infected midge arriving at the UK coast will not necessarily go on to bite and infect an animal and lead to viral circulation. The work done last year to investigate the potential for using the bulk milk test for an early warning system in cattle demonstrated a high proportion of seroconverted animals which was considered to indicate a certain level

of immunity and which could reduce the level of transmission. A cool summer will also reduce the number of vectors and the level of virus circulation in the vectors.

The 2016 Qualitative Risk Assessment (QRA), modelling results, expert opinion and peer-reviewed literature suggested that a pre-emptive vaccination level of 80%, 50% or even 25% in bovine and ovine species carried out and giving full protection by May 1st 2016 would have a significant impact on the rate of spread of disease that year even if used as the only control measure but the impact varies according to where and when the first incursion happens. In an average year, when daily temperatures are lower and vectors less active, movement controls will have an impact on slowing down the spread from an incursion early in the season. However, using movement controls alone in an unusually hot year may not significantly slow down the spread during the vector season, as there would be greater vector activity and they would not prevent midge movement, but movement controls may reduce the country-wide impact, but as trade restrictions across a wider region would not apply.

Although the conclusions reached were to a certain extent as expected, there were also some recommendations which emerged which are insightful, such as movement controls alone are not effective to prevent spread if it is an unusually hot year and that even a low level of residual herd immunity may reduce the level of spread. We will monitor temperature against climatology to see if this year will be warmer or cooler than average. Now that the restriction zone has reached the north coast of France, we need to be aware that the legal movement of viraemic cattle or sheep from affected areas to premises near the coast could occur and therefore estimate the significance of this. These factors will be taken into account as we move into the transmission season.

There is no evidence of significant impacts of BTV-8 in sheep flocks or cattle herds in France during 2015 or 2016. It is difficult to assess whether the same would occur in the UK. It is likely in the absence of vaccination that the clinical outcome of infection in the majority of naïve British sheep would be similar to those seen previously in Northern Europe 2006-2008. The often quoted high case fatality rate in sheep in the second year was frequently in small flocks and therefore was skewed and it should be noted that prevalence was still low even in countries such as Germany where for sheep, it was estimated at ~6% in both 2006 and 2007 and in cattle at 2% in both years even though there was a significantly higher number of animals infected.

This risk assessment will remain a living document and will be updated as and when more information becomes available.

Introduction

Bluetongue (BT) is a notifiable disease of ruminants, most commonly associated with clinical disease in sheep but also occasionally and less severely in cattle. It is caused by infection with the bluetongue virus (BTV), an orbivirus of the *Reoviridae* family (1). There are currently at least 27 known serotypes (2-4, 52) and viruses are usually transmitted in Europe via the bites of infected *Culicoides* midges.

The virus is present in Southern Europe, where BTV serotypes 1, 2, 4, 9 and 16 have all been identified in the Mediterranean basin (5), but only BTV serotypes 1, 8 and 25 and three vaccine strains of BTV-6, BTV-11 and BTV-14 had previously been identified in Northern Europe; BTV-8, BTV-1 and BTV-14 are known to have circulated efficiently in *Culicoides* (6, 7). The BTV-8 virus reached the UK during 2007, the second year of the epizootic in Northwest Europe when infection rates were very high in Continental Europe and BTV-1 reached Northern France (8-10). The disease, if not controlled, has the potential to have a considerable economic impact for the cattle industry in particular, albeit mainly because of the trade restrictions which need to be put in place, the cost of vaccination and the reduced milk yield (3, 6, 43).

A previous risk assessment looked at the possible pathways and likelihood for incursion of BTV-4 into Northern Europe and the UK. (44). This document is looking at BTV-8 which has re-emerged in France in late 2015 and how different vaccination strategies may or may not control spread in the UK should an incursion happen in the coming year. The UK has published a disease control strategy for bluetongue and this confirms that the most appropriate control will be through vaccination, but that this should be an industry-led voluntary action which farmers should choose in consultation with their vets. This document is therefore to look at the risk of introduction of BTV-8 from France and the best control options which can be government or industry led.

The re-emergence of BTV-8 in France in October 2015 led to concerns that an epizootic across North Europe may develop again in the following year or so, leading to significant losses of livestock as seen in 2007/2008 in some areas. Genetic analyses of the virus have shown that it is almost identical to the previous Northern European strain of BTV-8 (2006-2009) and may have been circulating at a low level in the intervening years. As a vector borne disease, vaccination is the best control option. This was not available in the UK or Europe until 2008, by which time many animals had already been infected and were therefore immune. It was thought likely that vaccine induced immunity is greatly reduced now and that a substantially naïve population is now present in Europe.

Risk question

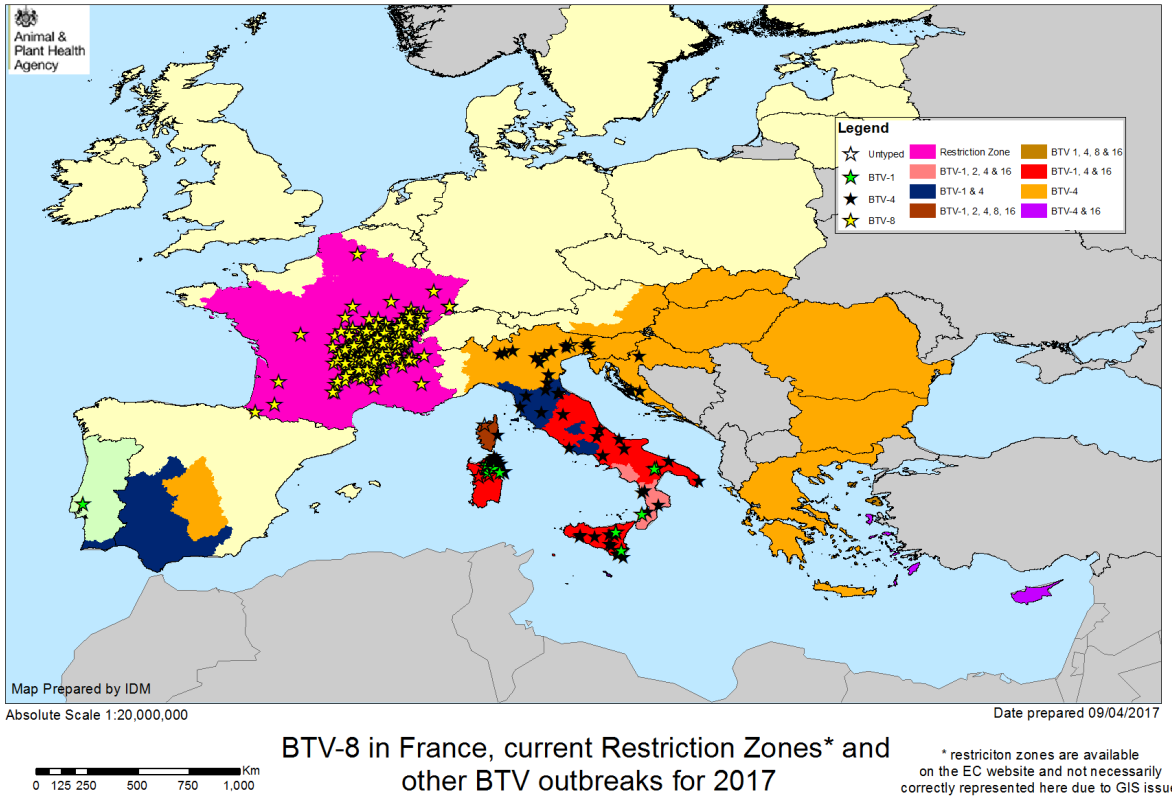
Within this QRA, we review the risk of BTV-8 entry to the UK during 2017, via infected midges as the primary route, but also via infected animals. The subsequent economic impact in the absence or presence of different vaccination strategies has been addressed in an additional analysis. As such, the specific risk question is:

What is the risk of BTV-8 being introduced from France in 2017?

Hazard identification

The hazard is identified as BTV-8, which has re-emerged in Central France (52). To date, over 2320[1] outbreaks have been reported, as a result of pre-export testing, clinical report cases or wide regional surveillance in cattle. The French authorities have tested tens of thousands of animals and the disease has remained relatively restricted to the centre of France, with a slow spread south and occasional cases reported in the northern regions. Vaccine supplies are limited and therefore France is targeting animals destined for export, animals moving out of the restriction zone or animals in high value genetic breeding programmes. According to data in the Animal Disease Notification System, of the 2,327 reported cases, 2,312 were reported in cattle, 18 in sheep flocks and 2 in goat herds. Only 18 report cases had animals showing clinical signs – 15 in cattle, 2 in sheep and 1 in goats. The majority of cases have been detected in the context of national surveillance, which has been designed to detect a 2% prevalence with 95% confidence by testing 60 animals from 30 herds in each department.

[1] As of 30/04/2017, according to the European Commission Animal Disease Notification System



BTV-8 in France, current Restriction Zones* and other BTV outbreaks for 2017

* restriciton zones are available on the EC website and not necessarily correctly represented here due to GIS issues

Source of infection

The source of infection is still not fully understood. Possible reasons for re-emergence are:

1. Silent circulation since the epizootic in 2006/2008. During those two years, France reported just 6 outbreaks in 2006, over 15,600 outbreaks in 2007 and 38,000 outbreaks in 2008. Mandatory vaccination was carried out in 2008 to 2010 resulting in a high proportion of immune animals (estimates at between 50 and 90%; [47]) and the final outbreak was in June 2010, therefore France was declared free of BTV-8 in 2012 (46). With the level of surveillance required for disease freedom, it was considered the likelihood of continuing circulation to be unlikely. However, this is currently the most likely reason for re-emergence of disease, as virus sequence shows close but not 100% homology with the virus circulating in 2007 and wildlife were still testing seropositive in 2012. This is supported by the EFSA Scientific Opinion published in 2017 (51, 52).

2. A new introduction through imported animals, germplasm or infected midges. However, according to the French Authorities, there had been no recent imports into the first identified affected farm. But if this were not the index case, there may have been import elsewhere into France and resulting virus circulation occurring. It is possible that the clinical signs of BTV-8 have not been reported as they are not as severe as in the previous epizootic and therefore livestock keepers and attending

veterinarians have not reported disease (see reference to immune animals in point 4 below).

3. Wildlife reservoirs. Wildlife were not vaccinated and therefore could have acted as reservoirs for disease in the intervening years. In Spain, red deer were tested positive (PCR) for BTV in areas where there were no clinical cases in livestock. However, this is not thought to be a major factor in disease transmission, as viral RNA can still be present many months after infection. In North America, bluetongue cycles every one to three years in deer populations in endemic areas and every eight to ten years in epidemic areas, but outbreaks in livestock would be expected given the co-habiting ranges of the animals in Europe (45).

4. Undetected infection in vaccinated animals. The vaccination programme in France was mandatory between 2008 and 2010 and then became voluntary in 2010, but there is no information on how many farmers continued with it. It is therefore possible that animals' herd immunity has significantly waned and they are at risk from exposure. However, given the immune response is understood to last as long as 4.5 years (Expert opinion), that the majority of animals in this area are beef cattle and are replaced less frequently than dairy animals, there may be animals present which were vaccinated in the original programme. New infection with BTV-8 will therefore act as a "booster" so mild clinical signs could be missed when infection re-emerged or was re-introduced. Natural immunity is believed to be life-long.

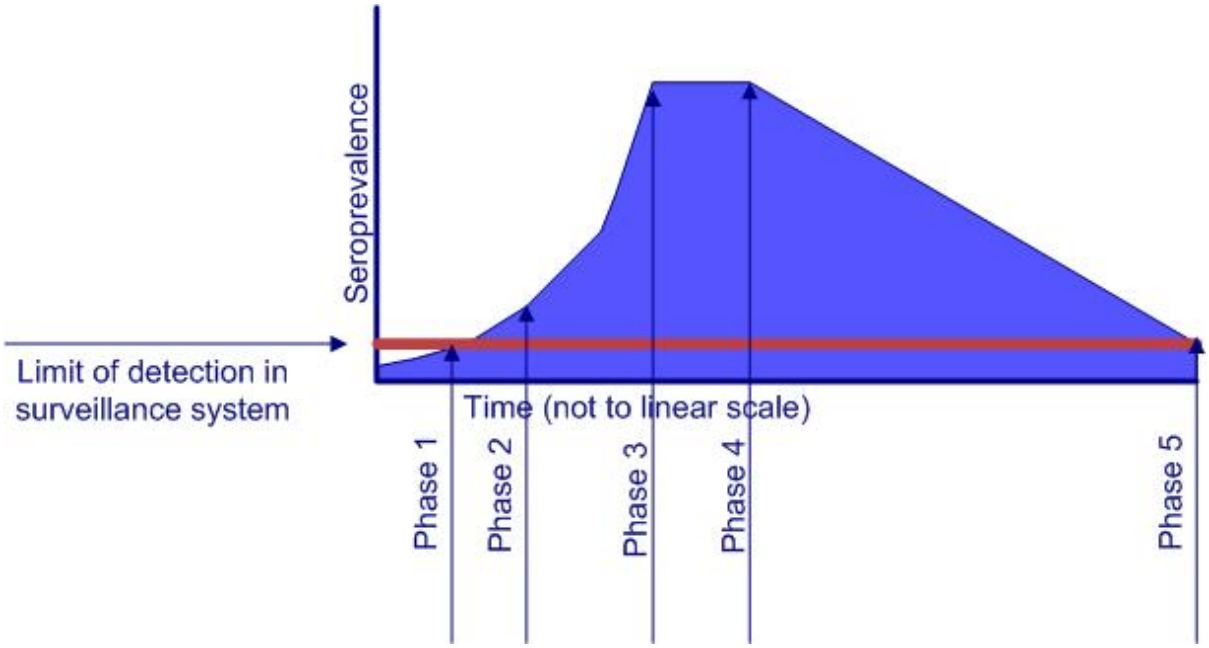
5. Transplacental spread. BTV-8 is capable of being transmitted transplacentally. It is not thought likely that vaccinated animals were capable of harbouring the virus in lymph nodes to then be transmitted to the foetus causing new outbreaks. If the disease were still circulating in livestock and transplacental transmission occurred, not all calves born to viraemic dams would survive and not all would be virus positive.

6. The source for the original BTV-8 outbreaks in Northern Europe in 2006 was never discovered. The virus is related to strains from sub-Saharan Africa, but it is uncertain how it originally arrived in Northern Europe. Therefore, it is not possible to rule out a similar event occurred in Central France this year given the uncertainty and that similar incursion events are possible in years to come. This presumes the source of disease is different to that in option 1.

7. Vaccine strains have been reported in the EU in the past (BTV-6, BTV-11 and BTV-14) possibly due to illegal use of an attenuated live vaccine. Sequence information has ruled out the possibility that the current outbreak strain could be derived from a live attenuated vaccine strain, showing that apart from a few nucleotide changes, the entire genome of the current strain is the same as that of the previous Northern European Strain of BTV-8.

In the previous epizootic of 2006/2008, there were distinct patterns of population dynamics which could be drawn from the epidemiology of disease (50). Five phases

can be seen: firstly, in a naïve population, the disease may not be detected as there are so few infected animals. In phase 2 the prevalence rises rapidly until phase 3 when prevalence plateaus. In phase 4, which can last several years, endemicity is reached or disease prevalence may drop again and phase 5 is where there is disease freedom, but still a history of disease can be found and again, is dependent on the surveillance system sensitivity. Given BTV is also a seasonal disease, the apparent increase in the second year of infection is not surprising. See the figure below. The duration of the phases depends on the circulation of the virus and therefore in winter, phase 4 may start but as there are still naïve animals present, phase 5 is not reached, and the increase continues in the following year.



Clinical impact of BTV-8

Reports vary as to the impact of this strain of BTV in terms of the clinical signs and morbidity and mortality (3, 4, 6, 43). While it was widely reported in 2006-2007 to have had a devastating effect on sheep and cattle populations, it was very variable and clearly depended on the proportion of ruminants infected. Experimental infection of sheep with BTV-8 has shown only mild clinical signs (53), while some retrospective work on French cattle and the incidence of early calving also shows only slight increase above what is expected (54). Therefore the mortality seen in the field in NW Europe may have been because the animals were repeatedly infected over a short period of time. The lack of clinical signs seen in the current French epizootic may be related to only a small number of animals testing positive in each herd and the rapid, albeit local, vaccination response, but equally it could be partly related to the low level of reporting which is driven by the lack of compensation available to farmers. The virus from the current outbreak has been sequenced and shown to be very closely related, enough so that expert opinion suggests there are not enough changes to show a difference in pathogenicity. Nevertheless, sometimes

pathogenicity is associated with only very few mutations in a virus and therefore this is still a possible theory.

Risk assessment

This risk assessment was conducted following the OIE framework (14). The following risk levels are used:

Risk Level	Qualitative statement	Quantitative level
Negligible	Event is so rare that it does not merit to be considered.	<0.01%
Very low	Event is rare but cannot be excluded.	0.01% – 10%
Low	Event is rare but does occur.	10% - 30%
Medium	Event occurs regularly.	30% - 60%
High	Event occurs very often.	60% - 80%
Very High	Event occurs almost certainly	80% - >100%

It should also be noted that a recent expert elicitation for the incursion of BTV in 2014 (and causing an impact) was given as 20% (low) with a lower and upper bound of between 10% (very low) and 70% (high). A similar piece of work by Gosling et al, 2012 also gave similar levels of likely incursions (49), but in both cases this was carried out at a time when the threat to the UK was lower as there were no outbreaks in NW Europe. The risk levels provided in this document therefore correspond to these results, but with the uncertainty around the time of year and disease situation in France applied.

Entry assessment

The presence in the UK of a BTV-8 infected animal may result from:

- an infectious vector reaching the UK and thus infecting an animal;
- entry via animal import; or
- use of infected germplasm.

Spread will depend upon the presence, activity and survival of vectors when the animal arrives or becomes infected and whether the animal is or becomes viraemic. Not every midge arriving from France will be infectious; not every infected vector will lead to an infected animal and; it is possible more than one animal is infected when many infected midges arrive in a single period.

The risk pathway for the entry of BTV-8 into the UK is shown in Figure 1. The pathway highlights the two key routes of entry; namely, the importation of infected animals, or the windborne spread of infected midges. Germplasm is not included in the pathway as it is considered lower risk, due to the statutory requirements for production of germplasm in AI centres in the EU.

It is also important to note that we define disease entry as “the presence of a BTV positive animal in the UK,” as opposed to the presence of an infectious vector. This is based on the assumption that a cloud of vectors arriving from an affected area to the UK is likely to include infectious individuals but not all will be infectious or lead to transmission. The 2 main routes for disease incursion end at one of several end points. Disease will be declared if there is onward transmission to UK susceptible animals. The likelihood of circulation of virus in the midge population depends upon the time of year and the likelihood of transmission via midges to other livestock depends on their immune status. Occurrence of indigenous cases in animals will be evidence for disease circulation leading to disease confirmation, although cases may be detected through laboratory testing and not necessarily as clinical cases per se.

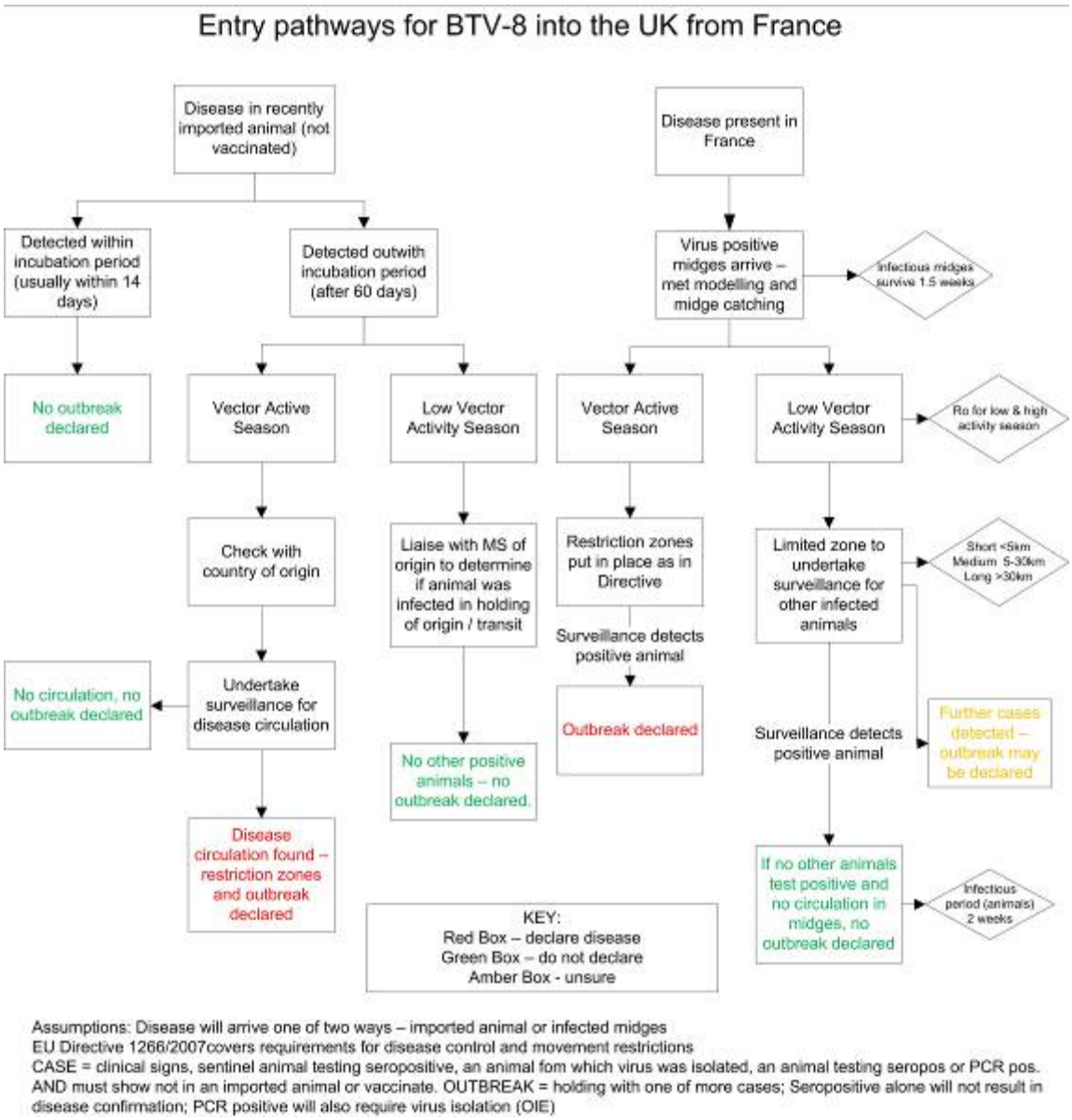


Figure 1: Risk pathway for entry of BTV-8 into the UK. Note: 1.5 weeks may be extended during cooler weather, however midges would not survive 1.5 weeks once in UK; 10 d is the longest period between blood meals. Declaration of a BTV zone in the UK has only occurred after the discovery of several clinical cases indicating that it is very likely that indigenous transmission has occurred (as happened in 2007). We do not use the results of the Met Office models to inform monitoring for infected *Culicoides* – the results of the model, in effect guide a need to raise awareness through clinical investigations in susceptible animals in that area. Vector surveillance is primarily relevant for indicating the vector free period during the winter months.

Overwintering of bluetongue virus

The cycle of bluetongue transmission has been well documented, with transmission occurring during peak vector activity periods, ceasing during the winter before re-emerging at the start of the next vector period (16). In Northern Europe, transmission occurs seasonally.

Under cool temperatures (<15^{o}C), both midge activity and virus replication are reduced (16), though the longevity of midges may increase (17). A mild winter, however, could increase the duration of suitable conditions for vector activity and virus replication. The exact time at which the disease may reappear can vary, however, this was estimated to be between April and May during the 2007/2008 outbreak, when the first new infections were detected in animals, but this will depend upon winter and spring temperatures in Northern Europe (18).

At temperatures below 12^{o}C virus replication ceases entirely, but the virus may persist in both the host and vector populations, and recrudesce should temperature increase (18, 20). It has been suggested that adverse (cold) weather conditions of 100+ days, could minimise BTV survival (3), but it should be noted this is for experimental data and BTV-8 replication in *C.obsoletus* has not been quantified.

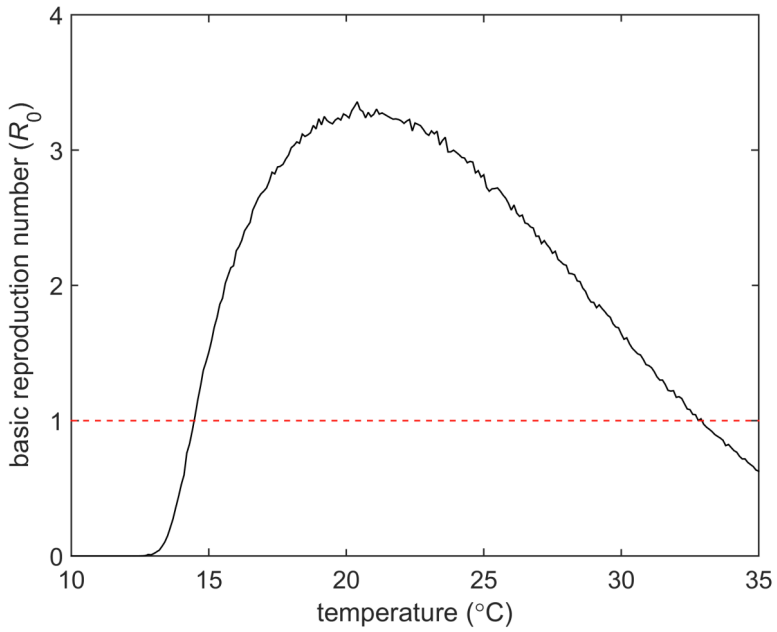


Figure 2 Basic reproduction number (Ro) for BTV as a function of temperature. The black line shows the mean for the uncertainty analysis used to calculate Ro (i.e. allowing for uncertainty in the underlying epidemiological parameters), while the red dotted line indicates the threshold at Ro=1. (courtesy of Simon Gubbbins)

Figure 2 shows the basic reproduction number (*R*0) for bluetongue as a function of temperature. The plot was generated using the uncertainty analysis presented in (38, 39), but using updated distributions for the underlying epidemiological parameters. From the plot, *R*0 exceeds one between around 15 °C and 33 °C, with a peak *R*0=3.3 at 22 °C.

A number of theories on how BTV overwinters exist, whereby BTV persistence could be due to the vector population or the host (cattle and sheep) population. Both horizontal and vertical transmission within the animal population have been suggested as mechanisms for BTV persistence (16); however the exact mechanisms

of overwintering remain largely unknown. BTV-8 is known to cause transplacental transmission in pregnant heifers (40, 41). Overwintering of vectors in livestock accommodation is a possible mechanism for maintaining disease transmission from year to year (13). Transovarial transmission of BTV in *Culicoides* has not been demonstrated in several laboratory based experiments. A recent EFSA opinion has described these mechanisms in more detail, but the conclusion was that the infection clearly overwinters successfully, and that disease eradication using vaccination would require several years of repeated vaccination of suspect animals, but the current surveillance levels required in EU legislation are not sensitive enough to detect low levels of circulation (51).

BTV-8 incursion via infected midges

The main route of BTV transmission is believed to be via infected midges (2), notably the *C. obsoletus* complex for the UK (5). In order for infected midges to reach the UK, a number of events must occur, such as successful overwintering of the virus and initial travel of infected midges over land to the coast, culminating in travel over the channel; such long distance travel is assisted by the wind, although active movement from the midge is required to stay airborne (22).

When France first reported BTV-8 in 2015, the Met Office carried out modelling of the likely wind borne distribution of midges from the area of the outbreak in the days leading up to reporting. The following figure describes the average wind direction and speed between late June and early August. Individual wind plumes were overlaid on a map of Europe and showed that the risk of wind borne transmission during this period was very unlikely. In the event of disease overwintering in France successfully, the risk of incursion from windborne vector movement will be predicted using such modelling. At present, we cannot predict the risk of incursion as the average daily temperature and wind direction cannot be determined so far in advance. Therefore this will be kept under review on a month-by month basis. The likelihood that temperature and rainfall conditions will be above or below average can be predicted up to three months in advance. Using the dispersion models must still be done only for real-time use and is not suitable for broad predictions. Nevertheless, if disease re-emerges in Central France in 2016, BTV transmission models (as used for spread within the UK) can be applied to the situation in France and used to predict the time from emergence to reaching the North Coast.

The risk of a windborne midge incursion will increase during the vector activity season – as the season progresses due to the increased likelihood of viraemic hosts in coastal areas of continental Europe. During an outbreak, the number of infected (and therefore viraemic) hosts increases and, as a consequence, the number of infected midges also increases and similarly the likelihood that one will be carried by

the wind as they will be close enough to the coast. It will also depend on there being present a high density of susceptible (naïve) animals in areas where infected midges arrive.

During the transmission season in 2016 the atmospheric dispersion model NAME (39) was used to provide daily forecasts of the potential incursion of midges to the UK from the French, Belgian, Dutch and Danish coastlines. The model releases 'midges' into the atmosphere when the meteorological conditions at the surface are optimal for their take-off; when wind speeds are low, there is no precipitation and conditions are warm. NAME then models their onwards transport and dispersion through the atmosphere using meteorological data provided by the Met Office's Numerical Weather Prediction model, the UM. Prior to a reported outbreak a set of hypothetical sources are used to indicate which days would have seen optimal conditions for the transport of midges to the UK. In the event of a reported outbreak the known location of the source would be used to initialise NAME, and forecasts could be used to predict which counties in the UK would be at most risk from an incursion of midges from the outbreak area. The Met Office also provided surface temperature forecasts and observations for northern France and southern England, which were used to assess whether conditions were optimal for midge transport. These data sets are then used to give qualitative risk levels and these as well as the average temperature data for several districts in either northern France of South England are represented in the following table.

Date	Temp in France§	Temp in England§	Closest case in N. France*	Risk of entry	Risk of exposure
5/9/2016	17 – 23 ºC	15 – 20 ºC	280 km from coast	Medium	Medium
26/9/2016	14 – 18 ºC	12 – 18 ºC	280 km from coast	Medium	Medium
10/10/2016	11 – 15 ºC	10 – 15 ºC	280 km from coast	Medium	Medium
26/10/2016	9 – 15 ºC	9 – 15 ºC	280 km from coast	Medium	Medium
8/11/2016	11 – 16 ºC	10 – 14 ºC	280 km from coast	Medium	Low
14/11/2016	10 - 12 ºC	10 - 12 ºC	160 km from coast	Low	Low

§ Temperatures taken from 2m above ground observations from weather stations

* The distance is measured from the geographic location of the infected case to the nearest point on the French coast.

The risk level during the 2016 transmission season (September to November) was considered to be medium dropping to low, based on the distance from the UK of the nearest case and the daily average temperatures.

Speed of vector movement

Movements of midges on the wind follow a different pattern over land compared to over water, whereby distances of 700km in a single movement could occur over

water, but not over land (25). Vector movement over land has been shown to intermittently stop and cause local disease spread at distances up to 10km / week, rather than long distance spread, which is unlikely to occur, despite suitable wind conditions (25). Meteorological data during 2006-2008 suggested that we could expect between 2.7 - 12 wind events per month suitable for *Culicoides* movement to the UK from northern France, but that midges will not fly in strong wind or heavy rain (28). Previous studies, looking at various sources, showed the south and south east coast of the UK to be more exposed to wind patterns that would be sufficient for vector movement (29).

Initial location of an infectious vector

It is important to note that while BTV-8 was able to reach the UK during the 2007/2008 outbreak, the foci of the originating outbreak was in the Netherlands and the point of entry was Suffolk / Essex (although it is likely that there were at least two separate incursions) (31). On the other hand, when we looked at the likely incursion of Schmallenburg virus into the UK using similar modelling and given the disease distribution across France, Belgium and Netherlands in 2010 (42) the whole South Coast of England was at risk.

Given the current location of BTV-8 and the level of surveillance being carried out in France, spread within Central and to northern France should act as a warning of increasing likelihood for disease entry to the UK.

As explained above, the nearest infected animals to the UK during the 2016 transmission season were located a considerable distance from the French coast and these cases did not necessarily represent a high number of infectious vectors. It is possible that some of the animals had been infected elsewhere and then moved while still viraemic, as opposed to an animal being infected by a local midge population. The wind assisted spread of BTV from these areas to the UK would have been unlikely. The risk level of medium which was reported last summer covers the uncertainty around the monthly surveillance being carried out in France in sentinel herds and the potential time lag in reporting new cases further north.

The expansion of the restriction zone to the North coast of France means that viraemic animals from the affected areas in Central France could move quite legally to other premises in the North. This may lead to new foci of transmission which would increase the likelihood of infected midges arriving along the coast of England.

Time period of risk

The time at which virus transmission re-occurs in France and then the time at which it spreads north are both likely to play crucial roles in the likelihood of BTV-8 entry to the UK. Cases can usually be expected to re-emerge in France around April to May, depending on the average daily temperature and the population of infected midges

and naïve animals, such that the R_o is greater than one (see Figure 2). This would clearly be towards the start of the vector period, but because of the uncertainty around this, three time periods were chosen for modelling – an incursion in May, July and September.

Generally, in Europe, BTV can be reported over the winter months in the southerly latitudes, where endemic disease is less seasonal. However in Europe, as in other countries (such as the USA) where BTV is seasonal, the main period of disease emergence is after July (54, 55).

Given the daily average temperatures observed over the summer and autumn of 2016, and that disease did not spread into Northern France during that period, the risk of incursion was no greater than medium at any time of the summer and autumn.

Our original assessment was assuming average seasonal temperatures, and that disease would spread to Northern France, we estimated the probability of incursion into the UK via infected midges at 5-10% (Low) in May, 33-60% (Medium) in July and 80% (High) in September, but that not all incursions will lead to an outbreak.

At present, we would consider the same likely risk levels to be applicable to the coming transmission season. The timing will depend on the temperature; it has been a mild winter across NW Europe and midge activity has started again, although temperatures are likely still too low for the extrinsic incubation period to be short enough for transmission to occur.

Incursion through imported live animals

The trade (from the EU) of live animals (cattle and sheep or goats) is governed by EU Legislation. All animals must be certified as fit to travel and not originating from a premises under control for a notifiable disease. If originating in a restriction zone for BTV, the animals are banned from leaving the zone, unless accompanied by a veterinary health certificate which confirms the animal moves under one of the agreements in Annex III of Directive 1266/2007/EC. The UK currently does not allow animals to travel under Annex III parts 1-4 (on vector protected establishments); however, animals may move if vaccinated against BTV-8 or if naturally immune. Animals originating outside the restriction zone do not require such guarantees but as this is presently an evolving situation, all such consignments are post import tested in the UK for BTV by PCR. During the 2016 transmission season, no animals originating in France tested positive for BTV by PCR.

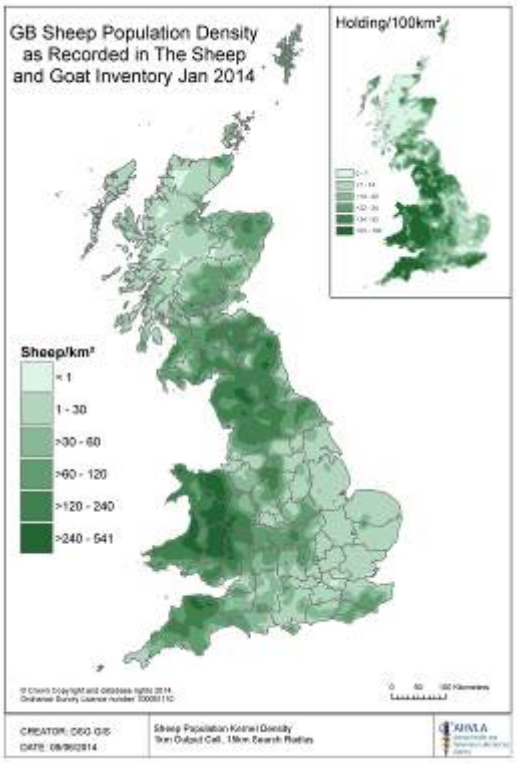
The likelihood of an incursion through movement of an imported animal is considered a low risk at present and is further reduced by the mitigation measures in place.

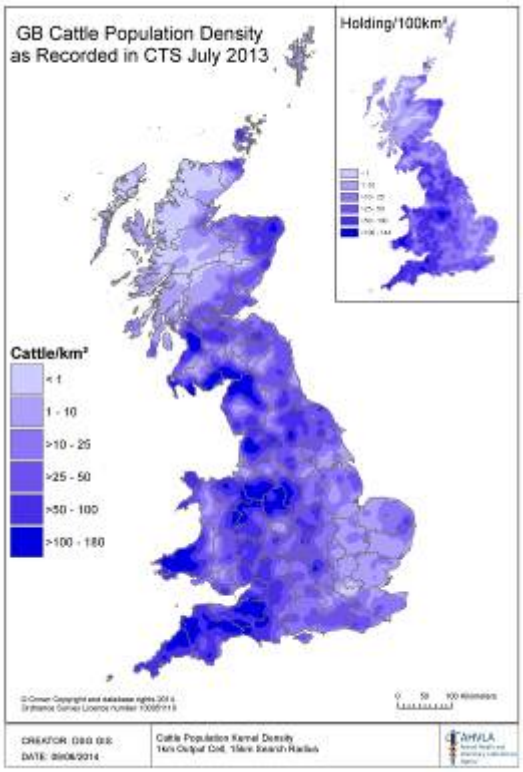
Exposure assessment

To consider the spread of BTV in GB once an incursion occurs (ie, an infected animal is detected) we used the modelling capability at the Pirbright Institute (TPI) with some additional information from models run by Scotland Government's Centre of Expertise on Animal Disease Outbreaks (EPIC) and at Liverpool University. We considered three incursion points and three incursion times, plus with movement restrictions and a low level of immunity (25%) which may result from prolonged immunity of animals (vaccinated or naturally immune) from the previous epizootic. The model was run for each scenario 100 times. The agreed scenarios were:

- Incursion via infected midges happening in spring (May), summer (July) or autumn (September).
- Incursion via infected midges happening at three locations: Hampshire, Kent and Suffolk, to account for differences in livestock demographics and proximity to Continental Europe.

The following maps (5&6) are livestock demographic maps for sheep and cattle livestock density in 2014. These are still considered suitable representations of our livestock populations.





Note: The maps were created using extracts from the Sheep & Goat Inventory (Jan 2014) and the Cattle Tracing System (July 2013). The density of sheep and cattle in GB was performed using the kernel density function in ArcGIS. The data are classified manually into six bins and the map is suitable only for demonstrating relative density across GB

Using the Pirbright model, incursion points of Hampshire, Kent and Suffolk and incursion times of May, July and September, were modelled.

No immunity in the livestock population

A baseline scenario with no controls showed that there was a high probability of an incursion taking place in May, July or September and leading to an outbreak developing as a result. Not all incursions will develop into outbreaks and not all outbreaks will lead to secondary spread. The Pirbright model used 2006 movement data and 2006 temperature data which was an exceptional year with high average temperatures in May. Models which use lower average annual temperatures suggest that not all disease incursions in May will lead to outbreaks and spread, but June is generally warm enough to lead to successful disease introduction into livestock. Of course if disease is spreading rapidly in France on the coast, it is likely that conditions are suitable in Southern England for similar spread.

The number of outbreaks which then occur during the year is greatest following incursions taking place in May and July (although not every incursion leads to an outbreak), while unsurprisingly, the opposite occurs in September, when an incursion leads to the least level of spread. This is of course related to the duration of the remaining vector period and the temperature under which BTV can replicate in the vector. There are differences between the incursion points, whereby an incursion in Hampshire leads to more outbreaks than Kent and in turn more than Suffolk – this is related to livestock density.

The models are still considered suitable to the current outbreak scenarios (S, Gubbins, pers comm).

Movement Controls

Movement controls are laid out in the Directive and require restriction zones of varying sizes (all centred on the infected holding/s, a 20 km Control Zone, a 100km Protection Zone and a 150km Surveillance Zone – collectively referred to as the Restricted Zone) to be put in place, from which animals may move from lower to higher risk zone without additional testing requirements but from higher to lower risk only with pre-movement testing (negative) and vector proof transport.

The modelling from Pirbright showed that in an unusually warm year (2006) with high vector activity, where there is a 150 km restriction zone around the incursion point, movement controls alone will not have a significant impact on preventing spread. As the majority of spread is due to vector-mediated transmission, this is not surprising. The same effect is seen with the modelling from Liverpool for the different years.

Using alternative modelling from EPIC and Liverpool, lower average temperatures and animal population data from 2010/2012, there is some reduction in disease

impact with the application of movement controls when an incursion occurs early in the season but the impact of an incursion would still be significant.

Further analysis using the Pirbright model has shown that a smaller restriction zone can have a significant impact on disease spread. However, this conclusion is sensitive to assumptions made about between-herd transmission via vectors and, in particular, the frequency of long-distance transmission events (56).

Pre-existing immunity

A level of 25% immunity was modelled to see whether this has any impact on preventing disease spread. While there is no information about the level of immunity in the current livestock population in these areas, it is possible that immunity from vaccination may last as long as 4 to 5 years (although vaccine recommendations are for boosters once a year to maintain a high level of immunity). The areas of the south and central England were known to have relatively high levels of vaccination coverage. To explore whether this is a reasonable scenario would require a level of surveillance in the livestock that is not a high priority at present.

The modelling results showed that in year with average temperatures, there is a significant impact of this low level of background immunity. Although it will not entirely prevent an incursion occurring, it will limit the size of the outbreak and therefore the impact.

Because the risk of incursion was medium throughout the summer of 2016 and given that the virus was not causing many clinical signs in animals, there was concern that disease was circulating undetected in cattle in the south and south east counties. Therefore a surveillance programme was developed to monitor disease incursion. As a pilot to this programme, bulk milk testing was carried out on cattle herds across the south and southeast of England. This method could detect BTV antibodies at relatively low prevalence (1 positive in 100 animals), albeit with low sensitivity and in theory, once suitable herds were identified, they could be tested on a monthly basis to look for seroconversion. In June 2016 ~200 randomly picked dairy herds were tested using the ID VET™ milk ELISA on bulk milk samples. The results showed a high proportion of herds (80%) tested positive for BTV antibodies. The test sensitivity is ~30% at 1% within herd seroprevalence and specificity for BTV antibodies is very high (99%). These results suggest that there was a high level of residual between-herd seropositivity in dairy cattle in these regions. There are four possible reasons for this:

- Animals were still present in the dairy herd which were infected with BTV during the 2007 / 2008 epizootic;
- Animals were still present in the dairy herd which were vaccinated against BTV during or after the 2008/2009 vaccination campaign in the UK;

- Animals had been imported into the herds from either areas with circulating BTV or from areas where vaccination was carried out;

- There had been circulating disease in the herds since the 2007/2008 epizootic.

There are no data that can be used to determine how the test results relate to the antibody titres for individual animals, nor whether these are protective, neutralising antibodies or another category of antibody not involved in antiviral activity.

Dairy cattle may still be present several years after either the disease was circulating, or after having been vaccinated, as the replacement rate for cattle ranges from 18% to 35% in the UK with an average lactation age of 3.03 and around 5% of the UK dairy herd being over eight years of age although that percentage has reduced in recent years.

Animals which are naturally infected are immune for life and will test positive for antibodies. Of the farms tested in 2016 (n=200), only eight had been previously tested in 2007/8 as part of surveillance programmes and four of those tested positive then and still tested positive for BTV antibodies in this study in 2016. The other farms had not been tested before.

Although vaccination is recommended to protect an animal for a single year, there are still likely to be residual antibodies as demonstrated by several authors and as confirmed by the OIE and EU Reference Laboratory (The Pirbright Institute) who demonstrated antibodies could be detected up to four years after vaccination (57, 58). Our own testing of animals destined for third country exports has also highlighted that vaccinated animals still express antibodies several years later. Only one bluetongue antibody positive animal needs to contribute to the bulk milk sample for the test to be positive in certain circumstances. This would depend on the strength of the individual animal's immune response and on the number of animals which contributed to the bulk milk sample. The BTV vaccination coverage in the South/ South East of England following the 2007/8 outbreak was very high (~90%). It is also possible that animals entered the herds from another country where vaccination was carried out since 2008. The ELISA used in this study will only detect BTV group-specific antibodies, not BTV strain-specific antibodies, so vaccination against BTV-1, BTV-2 or BTV-4 (which are currently present in Europe) could also produce a non-negative result in the ELISA.

We consider the likelihood of BTV-8 virus circulating in the years between 2007 and present day to be unlikely for several reasons: our scanning surveillance (investigation of all clinical cases or seropositive lab results reported to APHA) has not detected any cases; we continually monitor and assess the risk of incursions, and this risk level has been very low in the intervening years; all imported cattle from BTV-8 at-risk areas are tested for BTV and no infected animal has been imported

since this outbreak in France began; the small number of cases in the UK in 2007-8 in comparison to the Continent and the high level of vaccination in the North East Europe region meant multiple incursions through BTV-infected midges were very unlikely and the number of naïve livestock would have been too low to maintain infection (the R_0, or basic reproductive rate of BTV-8 infection in the UK would have fallen quickly below 1, meaning disease would have stopped spreading). Also, none of the recently increased number of BTV report cases that have been triggered by the greater level of awareness of BTV amongst vets and farmers, have proven to be positive.

The results from the survey should be treated with caution and may still only represent a small percentage of immune animals. Nevertheless, this low level of immunity in combination with a low number of infected midges arriving from France, the relatively low temperatures last summer could be sufficient to have prevented disease establishment if there had been an incursion.

Summary of key uncertainties

There are several key uncertainties in this assessment that impact on the estimate of the likelihood of disease entry. These uncertainties include:

- The level of vaccination used last year and into this year. The level of seroconversion in sheep populations and whether it is comparable to that observed in cattle.
- The suitability of the climate conditions in UK during 2017. The risk of BTV-8 incursion and spread could increase should climate conditions favour virus replication and high vector activity.
- The models differ in the assumptions they make, especially in the way they describe spread between farms, and in the demographic and climate data used.

Summary of key assumptions

The majority of the modelling was carried out using climatology data, livestock demographic data and movement data from 2006. The spring of 2006 was significantly warmer than previous and subsequent years therefore this represents the worst- case scenario. To make sure the model is compatible, all data were for 2006. Although the livestock demographics and movements will have changed considerably since 2006, the main changes are in number of premises (whereby there are now fewer, larger premises for dairy cattle). Hence this report uses an incursion point for Hampshire rather than further West, as restrictions already exist in that area.

Conclusions

At present, BTV-8 is still being reported from France as active cases (PCR positive), although the disease remains restricted in the main to the central regions. The closest case to the north coast of France has meant that restriction zones have now been expanded to include the regions around Calais and therefore there is unrestricted movement of animals within this zone, which could mean infected animals are moved to the north quite legally. However the sentinel surveillance which the French are carrying out does not suggest disease is widespread in this area, therefore **our risk level at present remains low**.

Our original assessment considered a level of vaccination which could equate to a level which may simulate residual immunity in older livestock or a level of compliance for high status livestock (breeding or export animals). Although the model used had temperature data from 2006, this represented a worst case scenario, when average daily temperatures were high in spring time and there were more and smaller livestock holdings. It is too early at present to forecast the likely temperatures in France and England this summer, but we will continue to keep these under review, as we did last year.

The model results suggest that even at a low level of immunity of just 25%, this would still have an effect on reducing the level of secondary spread. Our surveillance pilot study suggested at least 80% of herds in the south and southeast of England had at least one animal which was either vaccinated or naturally immune. The data for current levels of vaccination are not available, but the estimates provided by industry suggest last year very little vaccine was used. Therefore we do not consider the cattle and sheep population in southern England to be sufficiently protected against an incursion, should the weight of infection continue to rise in France or neighbouring northern countries.

It is quite possible that a cold spring and cold summer would mean a significantly lower chance of any spread taking place, even with multiple incursions. Equally, a delayed incursion and spread, later in the year, is possible. Predicting the likely incursion and spread is therefore difficult particularly given how disease did not spread widely from central to northern regions of France during the summer and autumn of 2016, and this new season will need to be monitored closely. Certain events will trigger close monitoring such as the first case reported in France to the northern area of the restriction zone, or a case reported near the north coast.

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