Public Health England

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Human Animal Infections and Risk Surveillance (HAIRS) group

Qualitative assessment of the risk that newly emerging tick-borne bacteria present to the UK population

V1.0/ November 2016

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About the Human Animal Infections and Risk Surveillance group

This document was prepared by Public Health England (PHE) on behalf of the joint Human Animal Infections and Risk Surveillance (HAIRS) group.

This cross-government group is chaired by the PHE Emerging and Zoonotic Infections section. The HAIRS group acts as a forum to identify and discuss infections with potential for interspecies transfer (particularly zoonotic infections).

Members include representatives from PHE, Department for the Environment, Food and Rural Affairs (Defra), Department of Health (DH), Animal and Plant Health Agency, Food Standards Agency, Public Health Wales, Welsh Government, Health Protection Scotland, Scottish Government, Public Health Agency of Northern Ireland and the Department of Agriculture, Environment and Rural Affairs for Northern Ireland.

About this risk assessment

Information on the HAIRS Group risk assessment processes can be found on the Public Health England website. https://www.gov.uk/government/collections/human-animal-infections-and-risk-surveillance-group-hairs

Date of this assessment	5 October 2016
Version	1.0
Reason for update	Increasing evidence in Europe for the emergence of tick-borne bacterial pathogens and their presence in UK tick populations, and the need to document the implications for UK public health
Completed by	HAIRS scientific secretariat and members
Date of previous risk assessment	N/A
Date of initial risk assessment	N/A

Summary of risk assessment for newly emerging tick-borne pathogens in the UK population

Note: This risk assessment considers *Borrelia miyamotoi*, *Rickettsia helvetica*, *R. massiliae* and *R. raoultii* only.

Overview	A number of tick-borne bacterial pathogens are present in the UK, the most significant being *Borrelia burgdorferi* sensu lato (causative agent of Lyme disease). This risk assessment focuses solely on four other bacterial species that have recently been detected in UK ticks and which have been reported to cause clinical disease outside the UK. These are *Borrelia miyamotoi*, *Rickettsia helvetica*, *R. massiliae* and *R. raoultii*. There is currently little information available on the clinical importance of these tick-borne bacterial pathogens.
	All four bacterial species have been detected in UK ticks in a number of locations across the UK, so it is possible that humans are being exposed to infected ticks through tick bites and may therefore become infected. Although there are no published cases of *Borrelia miyamotoi* in humans in the UK, one possible case of *Rickettsia massiliae* has been reported, possibly acquired in southwest England but diagnosed in Greece[1].
	None of these pathogens have routinely been tested for in individuals who have not travelled overseas and there is currently no standardised diagnostic test in the UK for the detection of *Borrelia miyamotoi* cases. Improved diagnostic tests for *Borrelia* infections are currently in development (by PHE as part of the Health Protection Research Unit).
	The continued emergence of tick-borne infections across Europe demonstrates the plausibility of similar situations developing in the UK. Continued expansion of important tick hosts in the UK (such as deer), land use changes and climate adaptation strategies (such as increasing urban green space) may contribute to changes in UK tick distributions and their associated disease epidemiology. Monitoring the impact of such changes is therefore very important.

Qualitative assessment of the risk that newly emerging tick-borne bacteria present to the UK population

Assessment of the risk	Probability	Low/Moderate
	Impact	Very Low/Low
Level of confidence in assessment of risk	Good	
Action(s)/ Recommendation(s):	- continued tick surveillance via established PHE Tick Surveillance Scheme which brings together data on tick species distribution, seasonality and host associations - continued targeted sampling of the main tick-borne disease vector in the UK (*Ixodes ricinus*) in order to further understand tick-borne disease ecology - tick pathogen analysis (for *Borrelia* and other potential emerging infections, perhaps including genomics to identify unknown potential pathogens) should be carried out across and within landscapes to identify high risk areas (this should include urban areas that may support ticks) - investigate the role of other tick species in the transmission of emerging pathogens (such as *Ixodes hexagonus*) - information on emerging tick-borne pathogens should be made available to GPs and others who may be treating patients with tick-bites to increase awareness - investigate whether or not the UK population are being exposed to these pathogens (serological survey).	

Assessing the risk to the UK population from new and emerging infections

Step One: Assessment of the probability of infection in UK population

The likelihood of an infectious threat causing infection in the UK human population. Where a new agent is identified, there may be insufficient information to carry out a risk assessment and this should be clearly documented. Please read in conjunction with the probability algorithm following the boxes shaded green. Where the evidence may be insufficient to give a definitive answer to a question, the alternative is also considered with the most likely outcome shown in solid colour and the alternative outcome in hatched colour.

QUESTION	OUTCOME*	QUALITY OF EVIDENCE
i) Are these recognised human diseases?	Yes	Overall evidence: good

Yes. Both *Borrelia miyamotoi* and the *Rickettsia* species considered in this risk assessment have been associated with cases of infection in humans.

B. miyamotoi was first implicated as the cause of clinical disease in humans in 2011 in Russia and since then in the US, Europe (Netherlands) and Japan. It belongs to the relapsing-fever group of species in the spirochaete genus *Borrelia*, which are related to, but distinct from, the *Borrelia* bacteria which cause Lyme borreliosis. Immunocompetent patients typically present with headache, fever, chills, fatigue, and myalgia[2] whereas immunocompromised patients have not been febrile but had a chronic meningoencephalitis with declined mental status and disturbed gait developing over several months. Of the known cases, relatively few have presented with relapsing fever[3]. Knowledge of the geographic distribution of human infection with *B. miyamotoi* is limited, but is likely to be similar to the distribution of Lyme borreliosis. Although the risk of infection with *B. miyamotoi* would be expected to be lower than *B. burgdorferi* s.l. due to its lower prevalence in ticks[3], a small study of persons who had been bitten by infected *Ixodes persulcatus* found that 2/24 developed symptomatic PCR and serologically confirmed infection[4], suggesting that the risk of infection may be as high as *Borrelia burgdorferi* s.l.

The *Rickettsia* species considered within this risk assessment are within the spotted fever group of rickettsiae.

Rickettsia helvetica is thought to cause a Mediterranean spotted fever (MSF)-like illness which is self limiting and associated with headache, myalgias, rash or eschar. Small numbers of human infections in Europe have been reported from Austria, Denmark, France, Italy, Slovakia, Sweden and Switzerland[5-9]. Some were confirmed via PCR detection. However, most were diagnosed by serology. A recent study in the Netherlands also provided evidence of increased seroprevalence of spotted fever group rickettsiae in Lyme borreliosis patients compared to healthy blood donors, and the detection of rickettsial DNA in CSF[10]. In the Netherlands, *R. helvetica* is the most commonly reported rickettsial species found in *Ixodes ricinus*[10]. *R. helvetica* has also been linked to a case of meningitis and a separate fatal case of acute perimyocarditis, both in Sweden[11] but further evaluation and isolation of the bacterium from clinical samples are needed to confirm its pathogenicity[10,12].

R. raoultii is associated with a syndrome characterised by scalp eschars and neck lymphadenopathy, "SENLAT". This syndrome is most commonly caused by *R. slovaca*[9]. *R. raoultii* was detected by PCR in a *Dermacentor marginatus* tick removed from a patient in France who developed SENLAT, and was also found by PCR in the blood of a patient with SENLAT in Spain[12]. It has since been identified serologically as the cause of infection in a number of cases in France (four probable cases diagnosed serologically or based on compatible symptoms and feeding ticks testing positive by PCR)[13]. Cases elsewhere in Europe include Slovakia (one molecularly confirmed case)[6] and Poland (probable case diagnosed serologically)[14].

R. massiliae is thought to cause an MSF-like illness with single cases (molecularly confirmed) reported in Sicily, France and Spain (the latter imported from Argentina).[11] The first confirmed human case was detected in 2005 from a sample taken 20 years previously in Sicily[15]. Serological evidence of infection has also been reported in forestry workers in Poland, however no clinical signs of illness were reported at the time of the survey[9].

Due to cross-reactivity between rickettsial bacteria found within the Spotted Fever group, any serological case reports should be carefully interpreted[10,16].

ii) **Are these diseases endemic in the UK?**	**No**	**Overall evidence: Poor**

There is no current evidence in the UK of clinical disease in humans caused by *B. miyamotoi* and only one possible UK-acquired rickettsial infection has been reported to date[1]. However, current routine diagnostics in the UK would not detect cases of *B. miyamotoi* and tests used for *Rickettsia* would not indicate which rickettsial species caused the infection[17].

Diagnostics for emerging tick-borne pathogens that are present in the UK tick population are currently under development. Individuals presenting with a tick-borne infection would not routinely be tested for *Rickettsia* unless they reported a travel history. Since 2013, an extended panel of serological tests has been used by the PHE Rare and Imported Pathogens Laboratory (RIPL) for patients who tested negative for Lyme disease but still display symptoms of illness (includes screening for *Rickettsia*, *Anaplasma*, tick-borne encephalitis virus and *Coxiella*)[18].

iii) Are there routes of introduction into the UK?	Yes	Overall evidence: Good

All of the bacterial pathogens included in this risk assessment are already present within the UK tick population with several detected in the most ubiquitous tick *Ixodes ricinus*. Introductions via the movement of infected ticks on animal hosts (including travelling companion animals) is however also possible and evidence of this has been found in ticks submitted to PHEs Tick Surveillance Scheme from recently travelled/imported pet dogs. Of 85 *Rhipicephalus sanguineus* ticks tested for spotted fever group bacteria, six tested positive and two were sequenced to be *R. massiliae* (PHE MEZE personal communication). An increased number of records of imported ticks entering the UK via recently travelled/imported pet dogs has also been reported [19–22].

Recently, migratory birds have been identified as potential reservoirs of rickettsiae[23–25] and ticks removed from migratory birds elsewhere in Europe have been found infected with *B. miyamotoi*[26]. This may also serve as a route of introduction of infected ticks in the UK.

iv) Are there effective control measures in place to mitigate against these?	No	Overall evidence: Satisfactory

In response to increasing records of imported ticks on travelling and imported dogs (based on tick surveillance data held by PHE and APHA), a PHE information leaflet was developed to provide information to members of the public and vets who might be rehoming, travelling with or treating pet dogs with a recent history of travel. PHE also worked with the Chartered Institute of Environmental Health to disseminate information to pest control operators (PCOs) on this tick species (*R. sanguineus*), and have produced a guidance document.

v) Do environmental conditions in the UK support the natural reservoirs?	Yes	Overall evidence: Good

All of the above rickettsiae and *B. miyamotoi* are considered to be transmitted transovarially and transstadially[3,8], thus increasing their ability to be maintained in nature in tick vectors in addition to vertebrate hosts. There is limited information available on the animal reservoirs of rickettsiae[9] and *B. miyamotoi*[3].

The maintenance of *B. miyamotoi* via transovarial transmission alone is considered unlikely[27] and a number of animal reservoirs have been suggested including wild rodents[27,28,31-34] , roe deer and wild boar[35] and birds[29,30,35]. However, the role of wildlife in the transmission *of B. miyamotoi* is still unclear and requires further investigation.

No studies have been conducted in the UK to identify potential reservoir hosts for *B. miyamotoi.*

Ticks are important reservoirs of rickettsial infection[36] and it is possible that all tick stages of the tick may play a role in transmission to humans[37]. Co-feeding transmission is also thought to occur[17,38] and infected male ticks are able to sexually transmit rickettsiae to females[38]. Ticks are found in many habitats in the UK but more information on pathogen prevalence in both ticks and their hosts is needed to ascertain which host species and which areas might be important for the transmission of these pathogens. Although vertebrate hosts are thought to play a role in the maintanence of *Rickettsia*, there is very little information available on this[9] and many unanswered questions regarding transmission cycles[17].

Mice, hedgehogs, roe deer, wild boar, lizards and birds have all been suggested as reservoirs of *R. helvetica*[23, 35,39-42] which has also been found in mammalian fleas, mites and louse flies[45-6]. However, recent studies (including xenodiagnostics) investigating the potential role of rodent tick hosts found no evidence to suggest that they may act as a reservoir of *R.helvetica*[31,43]*.*

R. raoultii could not be detected in rodent samples despite being found in 30% of ticks collected in the same area[47]. *Dermacentor marginatus* and *D. reticulatus* infected with *R. raoultii* have been removed from wild boar and European bison, but the role of these hosts as potential reservoirs requires further investigation[48,49].

R. massiliae-like DNA has been detected in cats[50] but not in a range of wild or domestic carnivores sampled in close proximity to peri-urban areas, despite these animals being infested with *R. massiliae* infected ticks[44]. *Rhipicephalus* ticks infected with *R. massiliae* have also been found on hedgehogs and foxes [51] but the role of such hosts as reservoirs is unclear.

No studies have so far been conducted in the UK to identify potential reservoir hosts for tick-borne rickettsiae.

vi) Will there be human exposure?	Yes	Overall evidence: Good
Yes. People acquiring tick bites in the UK may be exposed to a number of pathogens including those considered in this risk assessment. Not enough information is available on the seasonal prevalence of these bacteria within the UK tick population to indicate when incidence might be highest, but this may well coincide with the seasonal peaks in activity of *I. ricinus* or *D. reticulatus*. Tick exposure depends upon a number of factors such as tick habitat suitabililty, tick host presence, human behaviour and also knowledge and understanding of tick bite risks (eg 'tick aware' individuals are less likely to acquire an infection following a tick bite because they will have performed a tick check and removed any feeding ticks quickly, which is thought to reduce the risk of tick-borne bacterial transmission). *B. miyamotoi* is an emerging tick-borne pathogen in Europe and has recently been detected in UK ticks as part of PHE's ongoing vector borne disease risk assessments. Three of 954 *I. ricinus* from southern England tested positive and were collected from three geographically distinct locations across two time periods; suggesting that *B. miyamotoi* might be widespread in southern England and may have been present for a number of years[52]. Additional unpublished studies also reported *B. miyamotoi* in other parts of eastern, southern and south western counties of England, suggesting that it is widespread, albeit at low prevalence. *R. helvetica* was detected in 10 of 338 *I. ricinus* ticks collected between 2006-2009 from various locations in the UK (Hampshire, Ross & Cromarty, Gloucestershire and Devon)[53] and later in one of 61 *D. reticulatus* tick in Aberdovey, Wales in 2011[54]. *R. helvetica* has also been detected in female *Ixodes hexagonus* collected from UK hedgehogs[39]. The geographical spread and the finding of *R. helvetica* in various tick stages and species, suggests that this rickettsial species is widespread in the UK. *R. raoultii* was detected for the first time in the UK in ticks when 13 of 63 *D. reticulatus* ticks collected from Gwynedd and Essex in 2009-10 tested positive[53] and then later in two of seven *D. reticulatus* from Aberdovey, Wales in 2011[54].		

R. massiliae-like bacteria were detected in 6 *I. ricinus* collected from a dog in Wiltshire[53] and in two of 55 *Haemaphysalis punctata* from North Kent[54]. In addition, a suspected case of *R. massiliae* was reported in a patient who had acquired a tick-bite in Exmoor National Park and then returned to Crete[1]. One month later the patient was found to be seropositive (IgG only) for *R. massiliae*. The lack of IgM antibodies may have been due to late presentation after the tick-bite and cross-reactivity between rickettsiae meant that this case could not be confirmed. Tick species in Greece have tested positive for *R. massiliae,* so the patient may have acquired it previously, having not noticed a tick-bite.

Transmission of *B. miyamotoi* via blood-transfusion under experimental conditions using mice has also been demonstrated[55].

vi) Are humans highly susceptible?	Yes/No	Overall evidence: Poor

Yes/No. Over 50 *B. miyamotoi* cases but only a handful of infections due to *R. helvetica, R. raoultii,* or *R. massiliae* have been reported in Europe.
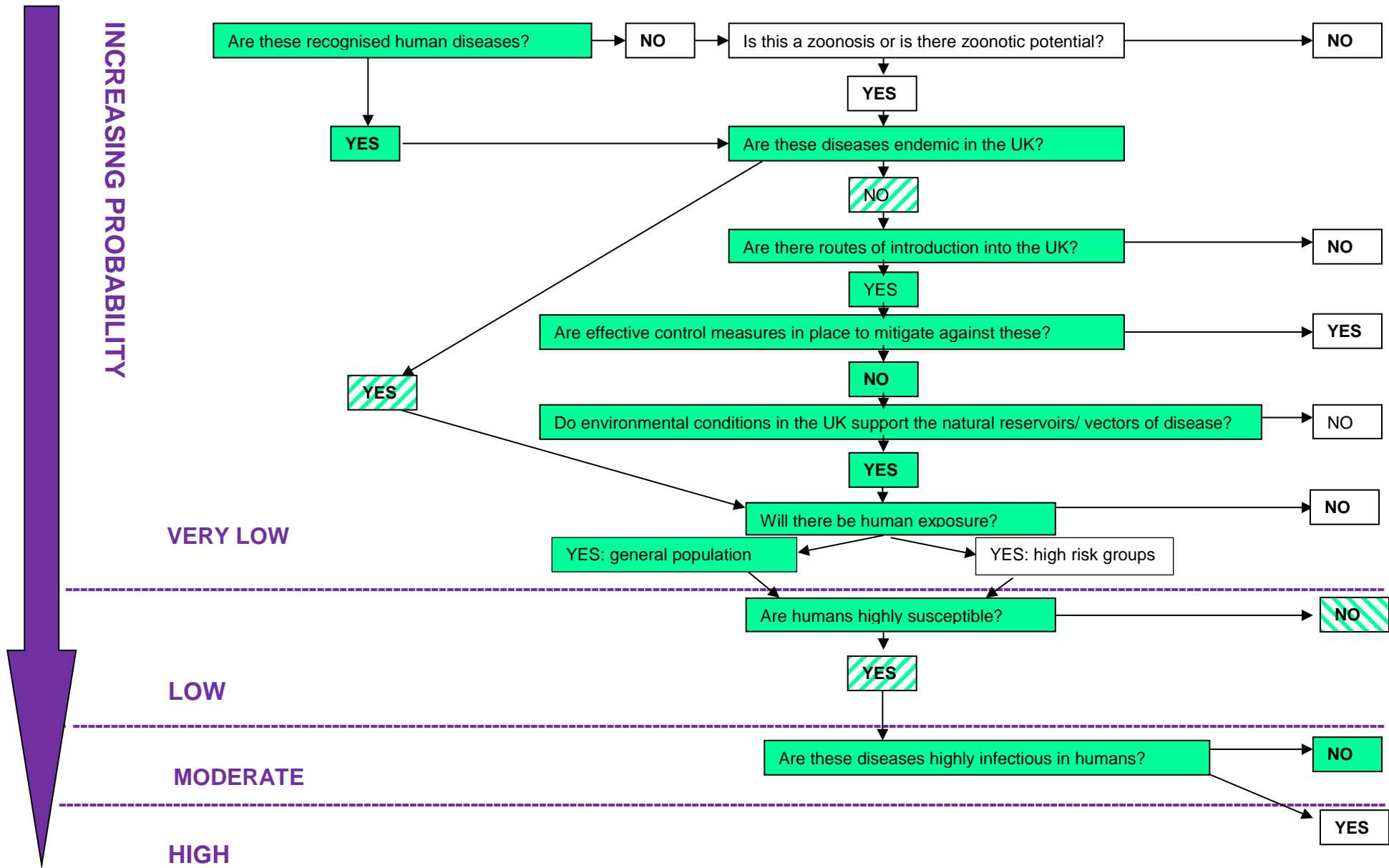
Humans are susceptible to infection but may remain undiagnosed due to the lack of available diagnostic tests for *B. miyamotoi* which are currently under development. In the UK, patients presenting with symptoms following a tick-bite who test negative for Lyme disease would be screened for *Rickettsia* (as well as a number of other tick-borne pathogens) so cases should be detected in this patient group. Of approximately 460 patients screened at the NHS Lyme disease clinic between 2013 and 2015, 115 seroconverted to Lyme disease and 27 had low level anti-*Rickettsia* titres. (PHE unpublished information)

vii) Is the disease highly infectious in humans?	No	Overall evidence: Good

No. *B. miyamotoi* and the rickettsiae included in this risk assessment are transmitted to humans via the bite of infected ticks. Humans are considered to be dead-end hosts, thus cases only occur after contact with an infected tick that successfully transmitted the bacteria (eg tick was not removed in time). Transmission of *B. miyamotoi* via blood-transfusion has been demonstrated experimentally in mice [55], but there is no evidence of human transmission via this route.

The **probability** of human infection with tick-borne bacteria in the UK population**: low / moderate**

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Step Two: Assessment of the impact on human health

The scale of harm caused by the infectious threat in terms of morbidity and mortality: this depends on spread, severity, availability of interventions and context. Please read in conjunction with the impact algorithm following the boxes shaded green. Where the evidence may be insufficient to give a definitive answer to a question, the alternative is also considered with the most likely outcome shown in solid colour and the alternative outcome in hatched colour.

Question	Outcome*	Quality of Evidence
i) **Is there human-to-human spread?**	**No**	**Overall evidence: Good**
No. *Borrelia miyamotoi* and the rickettsiae included in this risk assessment are transmitted via the bite of an infected tick. Transmission of *B. miyamotoi* via blood-transfusion has been demonstrated experimentally in mice [55], but there is no evidence of human transmission via this route.		
ii) **Is there zoonotic or vector borne spread?**	**Yes**	**Overall evidence: Good**
Yes. All are transmitted by ticks, including the common *I. ricinus*. Although the evidence for wild animal reservoir is limited, it is likely that all are zoonotic, involving wild animals.		
iii) **For zoonoses/vector borne disease is the animal host or vector present in the UK?**	**Yes**	**Overall evidence: Good**
Yes. *B. miyamotoi* has been detected in a number of tick species globally, including UK resident *I. ricinus*[56]. This is the most abundant tick species in the UK, being found in a variety of rural and urban habitats and is often found feeding on humans[57]. This species is also thought to be the main vector of *R. helvetica*[11] which in European studies has been found in ticks also infected with *Borrelia burgdorferi s.l.*[10]. For *B. miyamotoi* and *R. helvetica* the tick vector is widespread and highly abundant, with humans reporting high exposure to bites. *D. reticulatus* is also present in the UK (coastal north west Wales, a few foci in Essex, coastal Devon)[58], but in geographically distinct areas compared to *I.ricinus*. *Dermacentor* ticks are thought to be involved in the transmission of *R. raoultii*[11] and have also tested positive in the UK for *R. helvetica*[53,54]. There is minimal evidence that this tick actually bites humans in the UK with most reports from horses, dogs, cattle and sheep. However, in continental Europe it does bite humans[8].		

I. ricinus and *Haemaphysalis puncatata* in the UK have also tested positive for *R. massiliae*-like bacteria[53,54], but the main vectors thought to be involved in transmission of *R. massiliae* in Europe are those that form the *Rhipicephalus sanguineus* species complex[59]. *R. sanguineus* is a non-native tick[20] in the UK, but is imported on dogs through the Pet Travel scheme. Although there are so far no UK reports of human biting by this tick, they are known to bite humans in their endemic range in Europe.

H. punctata has a limited distribution in England, mainly in Kent and Sussex, where it has been reported to bite humans.

Tick species testing positive for the pathogens considered in this risk assessment does not confirm vector competence, but may indicate involvement in transmission cycles (both in nature and possibly to humans) that warrant further investigation.

iv)	Is the population susceptible?	Yes	Overall evidence: Good

Yes. Humans are susceptible via bites from infected tick species present in the UK. Most UK reports of tick bites are due to *I. ricinus,* therefore potential pathogens associated with this tick would appear more likely to pose a risk of infection.

v)	Does it cause severe disease in humans?	Yes/No	Overall evidence: Satisfactory

The most commonly reported clinical presentation of *B. miyamotoi* infection is a febrile illness with a relapsing or episodic presentation and fatigue, headache, chills, myalgia, arthralgia and nausea[56]. A more severe presentation with meningoencephalitis has been reported in immunocompromised patients[60]. All cases reported in the scientific literature to date made a full recovery following treatment with antibiotics.

Different *Rickettsia* species can cause different symptoms and severity of disease in humans and diagnosis can be challenging due to unfamiliarity of physicians with the nonspecific symptoms found during early stages of infection[9].

R. helvetica is a non-eruptive rickettsiosis where most patients present with an isolated fever without rash or eschar. Some more severe cases resulting in a rash, perimyocarditis and meningitis have been reported in Sweden[59].

R. raoultii has been implicated in cases of SENLAT which is characterised by a short incubation period, an inoculation eschar (up to 2cm) surrounded by erythema and is associated with painful lymphadenopathy. If the tick bite is not on the scalp, the erythema can resemble the erythema migrans associated with Lyme disease. Other symptoms can include rash,

facial edema and fever (but this occurs in less than 20% of cases)[59].

R. massiliae has been linked to acute spotted fever illness[1,9,11,59] but case reports are rare. One patient developed acute visual loss from which recovery was incomplete[9].

vi) **Would a significant number of people be affected?**	No	**Overall evidence: Satisfactory**

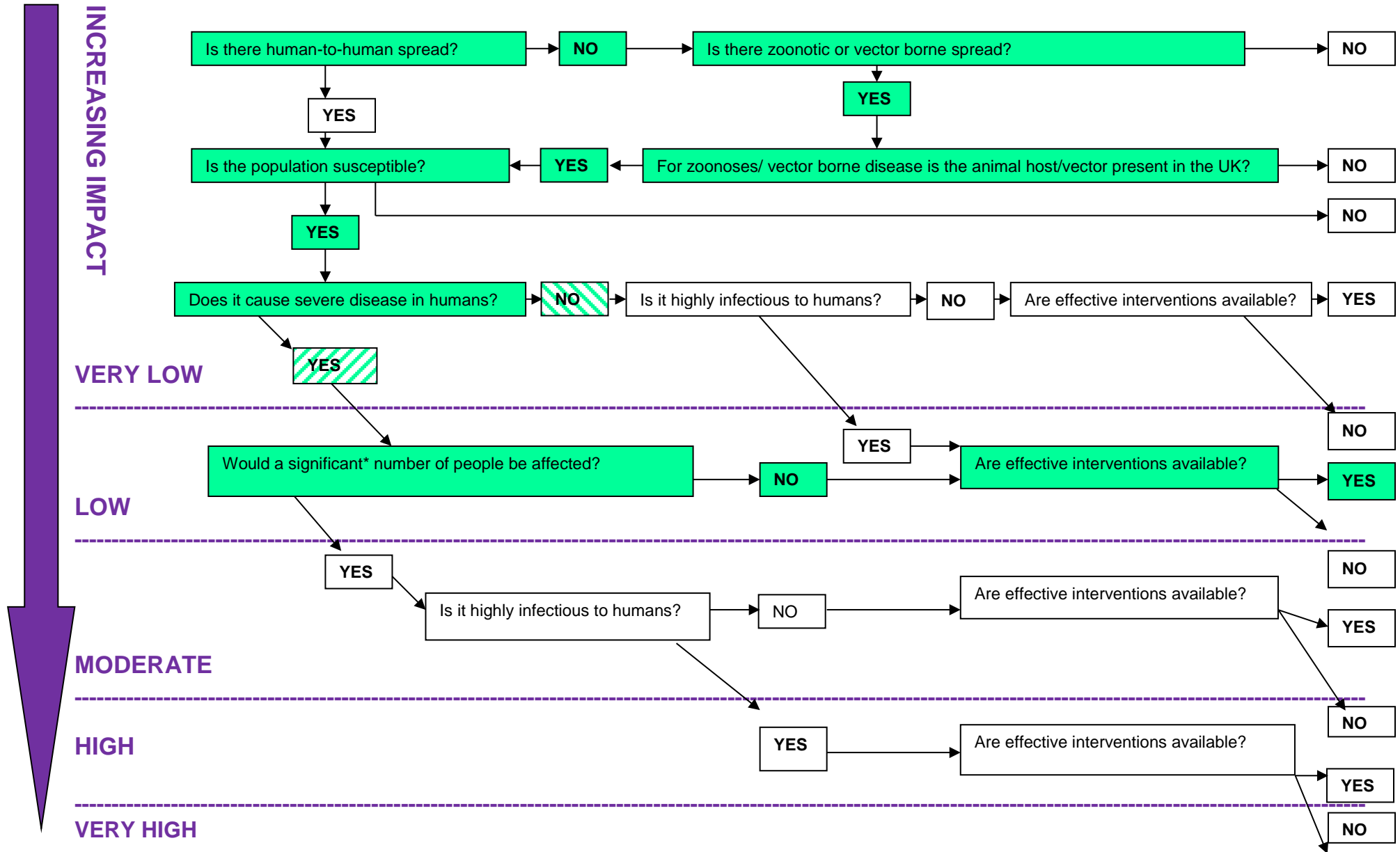The number of people affected would be contingent on the following factors:

(1) prevalence of the pathogen within the tick population

(2) presence of suitable habitat/microclimate and abundance of ticks and their hosts (including potential reservoir hosts)

(3) contact between humans and such habitats resulting in tick contact and acquiring a tick bite

(4) affinity of various tick species to feed on humans

(5) duration of tick feeding on a human host before it is removed

(6) likelihood of infection leading to clinical disease

vii) **Are effective interventions available?**	Yes	**Overall evidence: Satisfactory**

All of the infections in this risk assessment can be treated with antibiotics[9].

PHE have developed public health awareness materials that can be used during campaigns to educate members of the public and GPs about the risks posed by tick bites. Although these materials are currently focused on Lyme disease, the same control measures apply (e.g. carrying out a tick check after being outdoors, removing any ticks found promptly and visiting your GP if you experience illness following a tick bite).

However, recognition of disease and diagnostics are currently lacking so cases may remain untreated or may be treated as Lyme disease.

The **impact** of tick-borne bacteria on human health in the UK: **low / very low**

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INCREASING IMPACT

Is there human-to-human spread?	**NO** →	Is there zoonotic or vector borne spread? → **NO**

YES ↓ (from human-to-human spread)

YES ↓ (from zoonotic or vector borne spread)

Is the population susceptible? ← **YES** ← For zoonoses/ vector borne disease is the animal host/vector present in the UK? → **NO**

→ **NO**

YES ↓

VERY LOW

Does it cause severe disease in humans? → **NO** → Is it highly infectious to humans? → **NO** → Are effective interventions available? → **YES**

YES ↓

→ **NO**

LOW

Would a significant* number of people be affected? → **NO** → Are effective interventions available? → **YES**

YES (above Are effective interventions)

YES ↓

MODERATE

Is it highly infectious to humans? → NO → Are effective interventions available? → NO / YES

HIGH

YES → Are effective interventions available? → YES / NO

VERY HIGH

*.*This question has been added to differentiate between those infections causing severe disease in a handful of people and those causing severe disease in larger numbers of people. 'Significant' is not quantified in the algorithm but has been left open for discussion and definition within the context of the risk being assessed.*

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