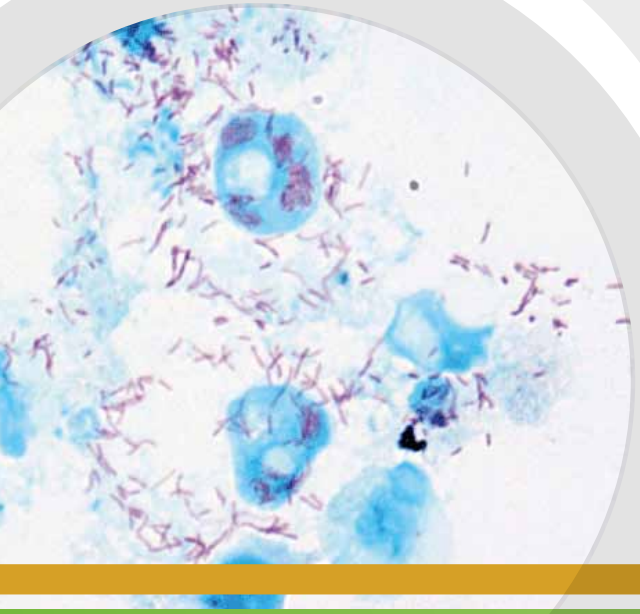

TECHNICAL REPORT

Epidemiological situation of rickettsioses in EU/EFTA countries

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ECDC TECHNICAL REPORT

Epidemiological situation of rickettsioses in EU/EFTA countries

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Abbreviations

DEBONEL	Dermacentor-borne necrosis erythrema and lymphoadenopathy
EFTA	European Free Trade Association
ELISA	Enzyme-linked immunosorbent assay
EQA	External Quality Assurance
EU	European Union
IFA	Immunofluorescence
IFD	Direct immunofluorescence
MSF	Mediterranean spotted fever
PCR	Polymerase chain reaction
TESSy	European Surveillance System
TIBOLA	Tick-borne lymphoadenopathy
WB	Western-blot

Executive summary

Rickettsioses are bacterial infectious diseases that occur in endemic areas across large regions of the world. They require the presence of competent reservoir hosts, vectors and the pathogen.

To obtain a better understanding of the current magnitude of tick-borne rickettsioses in the European Union (EU) and European Free Trade Association (EFTA) countries, the current project aimed to summarise existing information on the occurrence of tick-borne rickettsioses. The specific objectives were to characterise the different reporting systems for tick-borne rickettsioses in EU/EFTA countries; and to identify and assess the current epidemiologic situation of these diseases.

First, an online survey was distributed to nominated national surveillance experts requesting information on rickettsioses surveillance systems. From countries which implement surveillance for rickettsioses, surveillance data were requested for the period 2000–2010. Information on routinely collected surveillance data was supplemented with published and unpublished data on rickettsioses from environmental, animal and human sources, covering the period 2000–2010.

This report is a first effort to collect existing data on rickettsioses in EU/EFTA countries. The data covering the period 2000–2010 were collected from different sources using different case definitions, time scale and spatial units, and do not reflect the real picture and complexity of epidemiology of these diseases. These data do not allow prioritisation of disease-specific surveillance activities. As tick-borne pathogens are listed among emerging communicable diseases globally, they are expected to constitute an increasing burden to societies due to increasing travel, increasing cohorts of immunocompromised persons, and ageing societies. Recommendations for giving more attention to efficient monitoring of those pathogens at the local, national and international levels are provided.

Background

The etiological agents of human rickettsioses are obligate intracellular, very small Gram-negative coccobacilli from the order Rickettsiales. The genus *Rickettsia* contains 25 validated species [1] and a fast-growing number of "candidatus", whose taxonomic position is still unclear. They are classified into three groups: the spotted fever group associated mainly with ticks, and less frequently with fleas and mites; the typhus group which includes the agents of the epidemic typhus and murine typhus associated with lice and fleas; and a third group which includes *R. belli and R canadensis* [2]. Table 1 provides the list of the main *Rickettsia* species infecting humans with type of vector, disease and known area of geographic distribution. The circulation of *Rickettsia* in Europe has been widely documented including *R. conorii* and *R. massiliae* transmitted by *Rhipicephalus sanguineus* ticks; *R. helvetica* and *R. monacensis* by *Ixodes ricinus; R. slovaca* and *R. raoultii* by *Dermacentor marginatus* and *Dermacentor reticulatus*; *R. aeschlimannii* by *Hyalomma* spp. and *Rhipicephalus* spp.; and *R. sibirica mongolotimonae*, whose vector is still not identified in the EU, apart from other non tick-borne transmitted *Rickettsia* species such as *R. felis* or *R. akari.* Also*, Rickettsia* species of the typhus group, such as the louse-borne *R. prowazeki* and the flea-borne *R. typhi* (or *R. mooseri*), are found in selected areas of Europe [2]. Numerous published records of other *Rickettsia* species found in ticks with uncertain pathogenicity to humans complicate the definition of rickettsioses. Thus, rickettsial infections are probably not well recognised and there is a need to assess their magnitude at the EU level.

The traditionally most prevalent rickettsial disease in Europe is Mediterranean Spotted Fever (MSF) caused by *R. conorii* subspecies *conorii*, found mostly in Southern and Eastern Europe. The typical form of the disease includes flu-like symptoms, regional lymphadenopathies and the pathognomonic inoculation eschar ("*tache noire*") at the site of the tick bite, apart from a variable rash. The other two proposed *R. conorii* subspecies (*R. conorii* subspecies *israelensis* and *R. conorii* subspecies *caspia*) produce spotted fevers resembling MSF with different geographical distribution. Severity of MSF can be high, and in some parts of Portugal a fatality rate of 32.3% has been observed, associated with diabetes, dehydration and uraemia [3]. Other *Rickettsia* species can also cause a similar clinical picture such as *R. aeschlimannii* or *R. massiliae*.

Recently, new species have also been associated with human disease and diagnosed in the EU including *R. slovaca* and *R. raoultii*, both the cause of tick-borne lymphadenopathy and *Dermacentor*-borne necrosis lymphadenopathy (TIBOLA/DEBONEL) [4, 5] a mild rickettsiosis, *R. sibirica mongolotimonae*, etiological agent of the so-called Lymphangitis-Associated Rickettsiosis [2], and *R. monacensis*, which cause a MSF-like syndrome [6].

A human case of rickettsiosis is not always recognisable from its clinical picture as the typical symptoms may not always be present and at times the only apparent clinical sign is the presence of fever. A definitive diagnosis is made by serology, polymerase chain reaction (PCR) or culture [7], although serological cross-reactions among different species hamper a correct identification of the specific syndrome by serology. Selected *Rickettsia* species require BSL3 facilities for their cultivation, which is always fastidious. Consequently, isolates available from clinical samples are not frequent.

Ticks are considered reservoirs of most species of *Rickettsia* and the role of wild and domestic mammals as reservoirs is difficult to assess. Major variables that influence rickettsial transmission to humans are the abundance of ticks, their rate of infection by rickettsiae and the tendency of different tick species to feed on humans [2]. The pattern of appearance of this group of diseases follows the periods of activity of the vectors. Rickettsioses can be diagnosed all year around, taking into account that the periods of activity of the different tick species can vary between early spring to late fall, depending on the species, and that in areas of the EU with temperate climates, such as parts of Southern Europe, the period of activity may cover the whole year, with slight variations among seasons.

Doxycycline (usually 200 mg daily for 7–14 days for adults) is the conventional antibiotic of choice in the treatment of rickettsioses, although fluoroquinolones and other antibiotics such as josamycin, azithromycin and clarithromycin have also been proposed as possible alternatives to tetracyclines [2].

There is no vaccine available for *Rickettsia* and the only preventive measure is the surveillance of attached ticks after exposure, apart from the use of repellents. Therefore, to assess the risk of transmission, numerous studies on the distribution of rickettsia-infected tick species have been developed throughout Europe and have found a highly variable prevalence of *Rickettsia* species in ticks. Such is the case of *R. monacensis* in *I. ricinus*, whose prevalence were found ranging from 2.4% in Spain to 52.9% in Bulgaria [8].

To obtain a better understanding of the current magnitude of tick-borne rickettsioses in the European Union (EU) and European Free Trade Association (EFTA) countries the current report aimed to summarise existing information on the occurrence of tick-borne rickettsioses (Table 1). The specific objectives were to characterise the different reporting systems for tick-borne rickettsioses in EU/EFTA countries; and to identify and assess the current epidemiologic situation for these diseases covering the period 2000–2010.

Table 1. Overview of the currently recognised *Rickettsia* species

Species	Vector	Disease	Geographical distribution
Mentioned in this report			
R. aeschlimanii	Ticks	unnamed spotted fever	France, Morocco
R. africae	Ticks	African tick-bite fever	Sub-Saharan Africa, La Reunion Island, West Indies
R. conorii subsp. *conorii*	Ticks	Mediterranean spotted fever	Mediterranean area, Africa
R. conorii subsp. *indica*	Ticks	Indian tick typhus	India
R. conorii subsp. *caspia*	Ticks	Astrakhan fever	Chad, Kosovo, Russia
R. conorii subsp. *israelensis*	Ticks	Israeli spotted fever	Israel
R. felis	Fleas	flea spotted fever	worldwide
R. helvetica	Ticks	suspected agent of a rickettsiosis	Europe, Japan
R. honei	Ticks	Flinders Island spotted fever	Australia
R. massiliae	Ticks	Unnamed rickettsiosis	France
R. monacensis[1]	Ticks	Mediterranean spotted fever-like	Europe
R. prowazekii	body lice	Epidemic typhus	Africa, Russia, South America
R. raoultii	Ticks	TIBOLA or DEBONEL	France, Russia
R. sibirica subsp. *sibirica*	Ticks	Siberian or North Asian tick typhus	China, Russia
R. sibirica subsp. *mongolitimonae*	Ticks	Lymphangitis-associated rickettsiosis	Algeria, China, France, Greece, South Africa
R. slovaca	Ticks	TIBOLA or DEBONEL	Europe, Russia
R. typhi	Fleas	Murine typhus	Worldwide
Not covered by this report			
R. akari	Mite	Rickettsialpox	USA
R. asiatica	Ticks	unknown	Japan
R. australis	Ticks	queensland tick typhus	Australia
R. belli	Ticks	unknown	USA, Brazil
R. canadensis	Ticks	unknown	USA
R. heilongjingensis	Ticks	Far Eastern rickettsiosis	China, Russia, Thailand
R. japonica	Ticks	Oriental of japanese spotted fever	Japan
R. montanensis	Ticks	unknown	USA
R. parkeri	Ticks	unnamed rickettsiosis	USA
R. peacockii	Ticks	unknown	USA
R. rhipicephali	Ticks	unknown	Africa, Europe, USA
R. rickettsii	Ticks	Rocky mountain spotted fever	Brazil, Mexico, Panama, USA
R. tamurae	Ticks	Unknown	Japan

[1] *R. monacensis is not listed by Fournier and Raoult [1], but was included in the report.*

The report focuses on tick-borne rickettsioses and only limited information is provided on lice and fleas-borne rickettsioses. The table is adapted from [1].

Methods

The project was implemented through the application of the following data collection methods (a detailed description of the project is presented in Annex 1):

- on-line survey (questionnaire) regarding surveillance of rickettsioses, microbiological methods and other epidemiological data. The questionnaire was sent to all EU/EFTA countries
- a literature review of published data on rickettsioses epidemiology in Europe
- collection of surveillance data from countries.

Survey on rickettsioses data availability

The aim of the survey was to obtain an overview of surveillance systems on tick-borne rickettsioses in the EU and EFTA countries. The specific objectives of the survey were:

- to characterise the type and number of existing surveillance systems on rickettsioses, the type of data collected (case-based/aggregated), the data availability on surveillance sensitivity and case definitions adopted in surveillance systems
- to collect information on laboratory tests used to diagnose suspected rickettsioses cases, number of samples processed each year for diagnosis of rickettsioses cases in the country laboratories, presence of reference laboratories, information about External Quality Assurance (EQA) in relation to rickettsioses diagnosis
- to summarise information on reports of human cases of rickettsioses which are not available in Medline, collect information on reports of special studies on fever and rickettsioses prevalence in animals or ticks which are not available in Medline.

A standardised online questionnaire was developed (Annex 2). The questionnaire was tested by consortium members and ECDC project coordinators. The pilot study was conducted in February 2011, after which the questionnaires were reviewed and amended and the on-line survey was prepared with the assistance of EpiConcept in February 2011, and implemented on VoozaNoo platform in March 2011.

Cooperation was established between 27 EU Member States and three EFTA countries. The respondents were identified through existing research collaborative projects and networks: EDEN-TBD[i], VENICE II[ii], ENIVD[iii], and Med-Vet-Net[iv]. The list of initially selected respondents was sent to ECDC for approval. The nominated person could delegate part of the work to relevant experts.

Epidemiological rickettsioses data collection

During the implementation of the survey, respondents who indicated the implementation of at least one rickettsiosis surveillance system were contacted by the project coordinator, on behalf of ECDC, to ask whether they were willing to provide data collected through the described surveillance system. Following the discussion of potential concerns and clarification of details, the respondents were asked to provide case-based or aggregated data covering the period 2000–2010. To assure possible future integration of the data with the European Surveillance System (TESSy), the TESSy metadata specification was used. The TESSy team was consulted over the data format during February–March 2011.The specification for aggregated data was also used for the literature review/data extraction procedure.

[i] Emerging Diseases in a changing European Environment – research collaborative project funded by the European Commission Framework Programme 6 during 2005-2010 http://www.eden-fp6project.net/emerging_diseases/tick_borne

[ii] Vaccine European New Integrated Collaboration Effort. More information: http://venice.cineca.org/

[iii] European Network for Diagnostics of "Imported" Viral Diseases. More information: http://www.enivd.de/index.htm

[iv] European Network of Excellence for Zoonoses research funded by the European Commission Framework Programme 6 during 2004-2009

Literature review on rickettsioses data availability

The objective of the literature review was to identify and analyse published data on human rickettsioses occurring in Member States and EFTA countries, and to determine the publications providing important information on disease risk in humans.

The literature from 2000–2010 was searched using Medline, Embase, Global Health, Cochrane Database of Systematic Reviews, and CAB Abstracts linked databases, through the German Institute of Medical Documentation and Information[i] (DIMDI). The following search string was used to retrieve relevant papers: (*Rickettsia* spp. OR *Rickettsia conorii* OR *Rickettsia slovaca* OR *Rickettsia africae* OR *Rickettsia honei* OR *Rickettsia aeschlimannii* OR *Rickettsia helvetica* OR *Rickettsia raoultii* OR *Rickettsia massiliae* OR *Rickettsia monacensis* OR *Rickettsia typhi* OR *Rickettsia felis*) AND (surveillance OR epidem$ OR inciden$ OR prevalen$ OR outbreak$ OR cluster$).

Ten independent reviewers selected the abstracts that met the preliminary inclusion criteria and filled the summary table for each selected abstract.

Data from selected papers, including data on human cases, were retrieved using the TESSy-compatible aggregated format. All possible aggregation variables were retrieved, prioritising year of onset, region of residence, gender and age group.

In addition, supportive evidence on rickettsioses epidemiology in EU/EEA countries, including papers describing or evaluating rickettsioses surveillance systems, seroprevalence surveys of humans, animals, as well as vector studies, were selected as supplementary sources of information. Full papers were retrieved for all these studies.

Where no surveillance data were available from a particular country, the data captured from literature searches were used to assess the epidemiology of the disease. If surveillance data were available for a given country or region during specified period, the literature cases were omitted.

A complementary literature search was conducted to identify publications relevant for estimating the risk of rickettsioses in European countries that might have been omitted during the initial literature review. New articles were identified by reviewing the references of the previously identified publications. Their titles, year of publication and abstracts were screened. The articles were recognised on the basis of prior established inclusion criteria. Additionally, the countries were requested to provide references relating to their country. The identified publications were thoroughly analysed and a decision on their inclusion or exclusion was made. The included publications were assessed and categorised according to whether the extraction of data on human cases or provision of information that would be of assistance to analyse the risk of the tick-borne rickettsioses was possible.

[i] More information at: http://www.dimdi.de/static/en/index.html

Results

Survey on rickettsioses data availability

Among the 30 participating countries, 14 have developed surveillance systems for rickettsioses. Comprehensive surveillance exists in 12 countries and other surveillance types were implemented in two countries. A surveillance system is operating at the national level in 13 countries (43%), and in one country the surveillance system exists only in endemic areas. There is mandatory reporting in 13 countries (Figure 1, Table 2).

Figure 1. Overview of the rickettsioses surveillance implemented in EU/EFTA countries

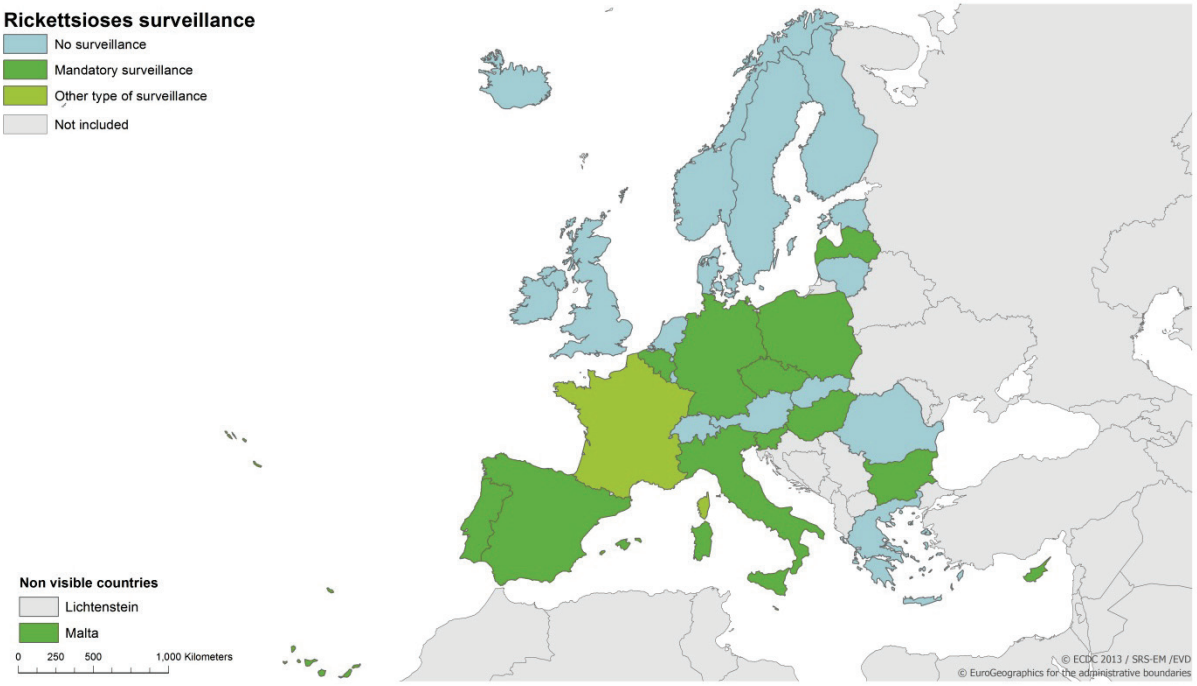


Table 2. Type of surveillance on rickettsioses in EU/EFTA countries

Country*	Type of surveillance	System operating	Type of reporting
Belgium	Comprehensive	At national level	Mandatory
Bulgaria	Comprehensive	At national level	Mandatory
Cyprus	Comprehensive	At national level	Mandatory
Czech Republic	University Hospital Infectious Diseases dept	At national level	Mandatory
France	National Reference Centre	At national level	Not well defined
Germany	Comprehensive	At national level	Mandatory
Hungary	Comprehensive	At national level	Mandatory
Italy	Comprehensive	At national level	Mandatory
Latvia	Comprehensive	At national level	Mandatory
Malta	Comprehensive	At national level	Mandatory
Poland	Comprehensive	At national level	Mandatory
Portugal	Comprehensive	At national level	Mandatory
Slovenia	Comprehensive	At national level	Mandatory
Spain	Comprehensive	Only in endemic areas	Mandatory

** The following countries have not developed surveillance systems for rickettsioses: Austria, Denmark, Estonia, Finland, Greece, Iceland, Ireland, Lithuania, Luxembourg, the Netherlands, Norway, Romania, Slovakia, Sweden, Switzerland and the United Kingdom*

Data for surveillance purposes are obtained from six sources: general practitioners, hospital physicians, reporting of deaths from infectious diseases, laboratories, hospital discharge records and death register records (Table 3).

Table 3. Sources of rickettsioses surveillance data in EU/EFTA countries.

Source of data						
Country	**Reporting by general practitioners**	**Reporting by hospital physicians**	**Reporting of deaths from infectious diseases**	**Laboratory reporting**	**Hospital discharge records**	**Death register records**
Belgium	✓	✓		✓		
Bulgaria	✓	✓	✓	✓		
Cyprus	✓	✓				
Czech Republic		✓	✓			
France				✓		
Germany				✓		
Hungary	✓	✓	✓	✓	✓	✓
Italy	✓	✓				
Latvia	✓	✓				
Malta	✓	✓	✓	✓		
Poland	✓	✓		✓		
Portugal	✓	✓				✓
Slovenia	✓	✓	✓			
Spain	✓	✓		✓		
Number of countries	11	12	5	8	1	2

Given the multitude of *Rickettsia* species the countries were asked whether all cases of rickettioses or only cases caused by selected species (*R. aeschlimanii, R. africae, R. conorii, R. felis, R. helvetica, R. honei, R. massiliae, R. monacensis, R. raoultii, R. slovaca, R. sibirica* subsp. *mongolotimonae* and *R. typhi*) are collected through their surveillance system. Nine countries report rickettsioses cases caused by all known *Rickettsia* species (Table 4). In three countries, cases caused by *R. conorii* are mandatorily reported and in one country only *R. typhi* is under surveillance. In Germany, Bulgaria and Slovenia cases caused by *R. prowazekii* are notified to the surveillance system.

Table 4. *Rickettsia* species collected by surveillance systems in EU/EFTA countries

Selected rickettioses				
Country	**All rickettsioses**	***R. conorii***	***R. typhi****	***R. prowazekii***
Belgium	✓			
Bulgaria		✓		✓
Cyprus			✓	
Czech Republic	✓			
France	✓			
Germany				✓
Hungray	✓			
Italy	✓			
Latvia	✓			
Malta	✓			
Poland	✓			
Portugal		✓		
Slovenia	✓			✓
Spain		✓		
Total	9	3	1	3

**Flea-borne* Rickettsia*; ***Louse-borne* Rickettsia

All clinical forms of rickettsioses are reported in 10 countries and only hospitalised cases in four countries (Table 5).

Table 5. Type of rickettsioses cases routinely reported in EU/EFTA countries

Type of cases routinely reported		
Country	**All cases including asymptomatic**	**Hospitalised cases**
Belgium	✓	
Bulgaria		✓
Cyprus	✓	
Czech Republic		✓
France	✓	
Germany	✓	
Hungary		✓
Italy	✓	
Latvia	✓	
Malta		✓
Poland	✓	
Portugal	✓	
Slovenia	✓	
Spain	✓	
Number of countries	10	4

There is no standardised European case definition for rickettsioses. Each country established a unique case definition for surveillance purposes. Surveillance case definition for rickettsioses is used in seven countries. In all of them each reported case is classified according to the applied case definition. Possible case classification is used in two countries, probable in five countries and confirmed in seven countries (Table 6).

Table 6. List of countries with case definition for rickettsioses used in surveillance systems indicating the starting date of the implementation and the case classification used

Case classification				
Country	**Year of implementation**	**Possible**	**Probable**	**Confirmed**
Bulgaria	2005		✓	✓
Cyprus	2008		✓	✓
Germany	Unknown		✓	✓
Italy	Unknown			✓
Malta	2004	✓	✓	✓
Portugal	1999	✓		✓
Spain	1996, revised 2010		✓	✓
Total		2	5	7

The detailed description of the case definition is described in Annex 3

In 11 countries, case-based surveillance data are collected. Detailed information on the type of the collected data is presented in Table 7. Additionally, in Cyprus information on predisposing conditions is collected and Hungary collects information on the date of onset of symptoms.

Table 7. Type of case-based data on rickettsioses collected in EU/EFTA countries

Type of case-based data	Number of countries
Notification source (GP, hospital, lab, other)	10
Date of notification	11
Presumed date of infection	7
Case classification (according to the case definition)	5
Demographic variables (age, gender)	11
Geographical location of residence: Eurostat NUTS1 (usually country regions)	8
Geographical location of residence: Eurostat NUTS2 (usually country provinces)	4
Geographical location of residence: Eurostat NUTS3 (usually districts or counties)	9
Geographical location of presumed exposure: Eurostat NUTS1 (usually country regions)	8
Geographical location of presumed exposure: Eurostat NUTS2 (usually country provinces)	2
Geographical location of presumed exposure: Eurostat NUTS3 (usually districts or counties)	4
Exposure to tick-bite(s)	5
Occupational exposures	5
Hospitalisation	9
Laboratory test details	5
Clinical signs/symptoms	5
Clinical complications	6
Outcome (dead/alive/disabled)	9
Imported case	7
Rickettsia species	8
Other	2

See Annex 4 for more information.

In three countries aggregated data on rickettsioses are collected (Table 8).

Table 8. Type of aggregated data on rickettsioses collected in EU/EFTA countries

Type of aggregated data	Country
Age group	Bulgaria, Spain
Gender	Bulgaria, Spain
Residence (e.g. urban/rural)	Spain
Period of time (e.g. season/month)	Bulgaria, Poland, Spain
Geographical location of residence: Eurostat NUTS2 (usually country provinces)	Poland
Case classification	Bulgaria, Spain
Hospitalisation	Bulgaria

In the survey, the countries were asked to assess the sensitivity of their tick-borne rickettiosis surveillance and provide the specific methods used to measure this attribute (capture-recapture analysis, mathematical modelling, and comparison of different sources). None of the countries assesses the sensitivity of the surveillance system. Out of 14 countries with surveillance system for rickettsioses, representatives from five countries subjectively assess their surveillance system as national with fair sensitivity, two countries as national with important regional differences in sensitivity, three countries as national with overall low sensitivity and one as regional with very low sensitivity (Table 9).

Table 9. Sensitivity of surveillance on rickettsioses assessed by the respondents to the questionnaire

Country	Surveillance sensitivity
Belgium	Other
Bulgaria	National, fair sensitivity
Cyprus	National, fair sensitivity
Czech Republic	National, important regional differences in sensitivity
France	National, overall low sensitivity
Germany	Unknown
Hungary	National, overall low sensitivity
Italy	Unknown
Latvia	National, fair sensitivity
Malta	National, fair sensitivity
Poland	National, overall low sensitivity
Portugal	National, important regional differences in sensitivity
Slovenia	National, fair sensitivity
Spain	Regional, very low sensitivity

Microbiological methods used for rickettsioses diagnosis

Among 30 participating countries, 21 used laboratory confirmation to ascertain rickettsioses cases in their countries. The most used assays are immunofluorescence (IFA) and PCR (Table 10).

Table 10. Laboratory test used for diagnosis of rickettsioses cases in EU/EFTA countries

	Indirect detection			Direct detection					Not specified
Country	IFA	CA - WB	ELISA	PCR	SEQ	Culture	HC IHC	IFD	
Belgium									✓
Bulgaria			✓						
Cyprus	✓	✓							
Czech Republic	✓			✓				✓	
Denmark	✓			✓	✓				
Finland	✓								
France									
Germany	✓	✓		✓	✓	✓	✓	✓	
Greece	✓			✓		✓	✓		
Iceland									✓
Italy									✓
Latvia	✓								
Luxembourg									✓
Malta									✓
Netherlands	✓			✓					
Poland	✓			✓	✓	✓			
Portugal	✓					✓			
Romania	✓								
Slovenia	✓			✓					
Spain	✓			✓	✓	✓			
Sweden	✓								
United Kingdom	✓			✓					
Total	15	2	1	9	4	5	2	2	5

IFA: immunofluorescence assay; IFD: direct immunofluorescence; CA-WB Cross-absorption - Western blot; PCR: polymerase chain reaction; SEQ: sequencing; HIC/IHC: histochemistry / immunohistochemistry.

In nine countries only one laboratory is available to perform a diagnostic test for rickettsioses, in five countries two to five laboratories, and in four countries there are more than five laboratories (Table 11). In nine countries there are reference laboratories for rickettsioses, of which six were officially nominated. The number of processed samples for rickettsioses diagnosis in each country laboratory ranges from less than 100 in six countries, to more than 1000 in three countries. Results of diagnostic tests are reconciled (linked) with epidemiological case reports and available at the national level in 12 countries.

Table 11. Number of laboratories and number of processed samples for rickettsioses diagnosis in EU/EFTA countries

Countries	Number of laboratories	Number of reference laboratories	Number of processed samples	Microbiological testing results reconciled with epidemiological case reports
Belgium	Don't know	Unknown	Unknown	Yes
Bulgaria	2–5	One	>1000	Yes
Cyprus	2–5	Unknown	250–<500	Yes
Czech Republic	2–5	N/A	<100	Yes
Denmark	1	N/A	100–<250	No
Finland	1	N/A	N/A	No
Germany	>5	One	250–<500	Yes
Greece	>5	One	Unknown	Yes
Italy	>5	More than one	Unknown	No
Latvia	1	One	<100	Yes
Luxembourg	Don't know	Unknown	Unknown	Unknown
Malta	1	N/A	<100	Yes
Netherlands	2–5	N/A	500–<750	No
Poland	1	One	<100	No
Portugal	>5	N/A	>1000	Yes
Romania	Don't know	One	Unknown	Yes
Slovenia	1	N/A	<100	No
Spain	2–5	More than one	>1000	Yes
Sweden	1	N/A	250–<500	No
United Kingdom	1	N/A	<100	Yes

In 14 countries, laboratories attempt to differentiate *Rickettsia* species. Germany, Poland, Portugal and Spain are able to differentiate all *Rickettsia* species under consideration (Table 12). Laboratories in Bulgaria, Latvia and Poland participated in EQAs in the previous five years.

Table 12. *Rickettsia* spp. differentiation in country laboratories in EU/EFTA countries

Country	*R. conorii*	*R. africae*	*R. honei*	*R. slovaca*	*R. aeschlimannii*	*R. helvetica*	*R. raoultii*	*R. massiliae*	*R. monacensis*	*R. typhi*	*R. felis*	*R. sibirica mongolotimonae*
Bulgaria	✓											
Cyprus	✓									✓		
Czech Republic	✓			✓						✓		
Denmark	✓									✓		
Finland	✓									✓		
Germany	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Greece										✓	✓	
Latvia										✓		
Netherlands	✓					✓				✓	✓	
Poland	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Portugal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Romania	✓											
Slovenia	✓									✓		
Spain	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Total	12	4	4	5	4	5	4	4	4	12	6	4

Surveillance data collection on tick-borne rickettsioses

Surveillance data were available in 14 European countries. During the current project, seven countries provided surveillance data (n = 9 663), of which 3 760 were sent in case-based format, which allows interpretation of data in terms of risk groups and seasonality (Table 13).

Table 13. Surveillance data availability on rickettsioses and transfer of surveillance data, EU/EFTA, 2000–2010

Country	Period for which rickettsioses data are available		Number of cases provided by the countries for the purpose of this report	
	Aggregated	Case-based	Aggregated	Case-based
Austria [a]				
Belgium		2000–2010		
Bulgaria [b]	2000–2010			
Cyprus		2000–2010		193
Czech Republic		2000–2010		
Denmark [a]				
Estonia [a]				
Finland [a]				
France [b]		2000–2010		
Germany		2000–2010		
Greece [a]				
Hungary		2000–2010		
Iceland [a]				
Ireland [a]				
Italy		2001–2009	4 609	
Latvia	2000–2006	2007–2010	15	79
Lithuania [a]				
Luxembourg [a]				
Malta		2000–2010	7	
Netherlands [a]				
Norway [a]				
Poland	2000–2010		3	
Portugal	2000–2001	2002–2010		2 837
Romania [a]				
Slovakia [a]				
Slovenia [b]		2000–2010		
Spain	2000–2004	2005–2009	1 269	651
Sweden [a]				
Switzerland [a]				
United Kingdom [a]				
Total number			5 903	3 760

[a] No surveillance on rickettsioses; [b] No data provided

Literature review on rickettsioses data availability

Among 1 522 selected abstracts on rickettsioses, 135 met inclusion criteria, 1 376 were excluded and 11 full texts were not available. The most common reason for exclusion was studies performed in non-European countries (Annex 5). During the complementary literature review a total of 12 publications were identified. The extraction of data was possible from five articles, one paper investigated rickettsioses risk using seroprevalence in humans and six papers discussed the prevalence of different *Rickettsia* species in animals and ticks.

In total, among the included articles: 61 provided data or significant information for interpretation of disease risk in humans (Table 14); 86 presented information on animals and vectors; and 14 were devoted to serologic surveys of humans. The majority of articles were referring to the risk of rickettsioses in Spain. Twenty-two articles provided data that were of assistance to interpreting the risk of disease in humans using prevalence studies in animals and ticks (Annex 5).

Table 14. Abstracts on rickettsioses fulfilled inclusion criteria by study type and subject of the study

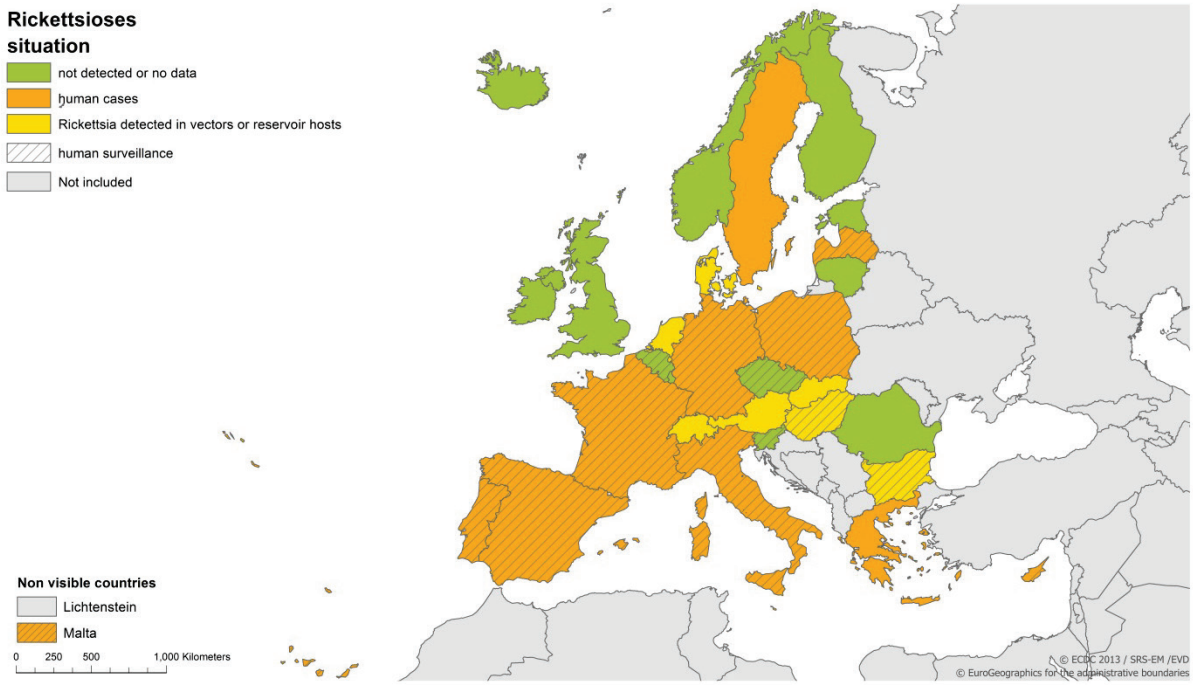
Study type	Abstract fulfilled inclusion criteria	Subject of the study	
		Rickettsial infections in human	*Rickettsia* in animals or vectors
Case report	20	20	
Case series	22	22	
Cross-sectional			
Cohort	1	1	
Case-control	1	1	
Serologic survey	29	14	15
Outbreak report			
Other (specify) or unknown	74	3	71
Total	147	61	86

Overview of tick-borne rickettsioses epidemiology in EU/EFTA countries

For the description of tick-borne rickettsioses epidemiology in Europe, we used surveillance data sent by countries (n= 9 663), summary figures provided by the countries for this report (n = 1 460) as well as data on rickettsioses cases retrieved from the literature review (n= 211). Of the 14 countries that developed a surveillance system for tick-borne rickettsioses, seven reported cases (Table 13). Furthermore, cases were described in the literature from four additional countries (France, Germany, Greece and Sweden) (Figure 2). Most of the cases are reported from Italy, Portugal and Spain. In these countries a decline in number of cases was reported during the study period (see individual country profiled below). In the most affected countries, rickettsioses cases commonly occurred among males. The age distribution of cases was variable with cases among persons younger than nine years and older than 60 years in Portugal and the older age groups more affected in Spain.

Summarised information for each country which implemented rickettsioses surveillance is presented in the country profiles section which follows. The country profiles have not been prepared for the countries where no rickettsioses surveillance was implemented during 2000–2010, and consequently no systematically recorded information on rickettsioses risk could be presented. These countries are Austria, Denmark, Estonia, Finland, Greece, Iceland, Ireland, Lithuania, Luxembourg, the Netherlands, Norway, Romania, Slovakia, Sweden, Switzerland and the United Kingdom. The figures prepared for each country reflect the level of detail provided by the country. In the case of two countries (Czech Republic and Portugal), summary figures that were provided for the purpose of the present report were used. During the literature review, 34 publications were identified that could help to estimate the risk of rickettsioses in countries where no surveillance system exists [9-42]. These articles provide information for Austria, Denmark, Greece, Ireland, Luxembourg, the Netherlands, Slovakia, Switzerland and the United Kingdom.

Figure 2. Current known situation of rickesstioses occurrence in Europe based on surveillance and literature data



Note: the map is based on the following data: Surveillance data submitted by the following countries: Cyprus (2000–2010, n=193), Italy (2001–2009, n=4,609), Latvia (2007–2010, n=79), Malta (2004–2010, n=7), Poland (2000–2010, n=3), Portugal (2002–2010, n=2,834), Spain (2005–2009, n=651).

Data retrieved from the literature for France (2001–2008, n=92), Germany (2002, n=2), Greece (2000–2004, n=19) and Sweden (2006, n=2).

The data on the occurrence of Rickettsia *in vectors or reservoir hosts is collected through the literature review (Annex 5).*

Country profiles

Belgium

The information in Table 15 is based on the rickettioses surveillance survey. The information of rickettsial infection in Belgium is very limited. During the literature search no articles on the risk of rickettsioses in Belgium were identified.

Table 15. Overview of rickettsioses surveillance in Belgium

Indicator	Description
Type of surveillance	comprehensive
Type of reporting	mandatory
Type of data recorded	case-based
Cases routinely reported	all cases
Rickettsia species under surveillance	*R.conorii, R. africae, R. honei, R. slovaca,R. aeschlimannii, R. helvetica, R. raoultii, R. massiliae, R. monacensis, R. typhi, R. felis, R. sibrica mongolotimonae*
Case definition	N/A
Provision of surveillance data	N/A
Estimated sensitivity of surveillance	N/A
Reference laboratory	N/A

Bulgaria

The information in Table 16 is based on the rickettsioses surveillance survey. A surveillance case definition was amended in 2005. There are between two to five laboratories offering rickettsioses diagnosis, processing more than 1 000 samples. One reference laboratory is located at the National Centre of Infections and Parasitic Diseases, NRL of Rikettsiae and Chlamydiae in Sofia.

One article provided interesting information on rickettsioses risk in Bulgaria. It aimed at identifying a group of pathogens (*Borrelia burgdorferi* sensu lato, *Anaplasma*, *Ehrlichia* species, and *Rickettsia* species) in ticks [43]. A total of 299 *Ixodes ricinus* ticks were collected in the area near the city of Sofia in May 2000 and May 2001. The prevalence of *Rickettsia* species was estimated at 67% in adult ticks and 19% in nymphs. Further investigation revealed that 59%, 58% and 17% of those adult ticks carried respectively *Rickettsia helvetica*, *Rickettsia* sp. IRS3 (now *R. monacensis*) and both species. Among nymphs, 65% carried *R. helvetica*, 88% carried *Rickettsia* sp. IRS3 and 53% were infected with both species. The results of the study suggest that simultaneous transmission of tick-borne pathogens to humans should be considered.

Table 16. Overview of rickettsioses surveillance in Bulgaria

Indicator	Description
Type of surveillance	comprehensive
Type of reporting	mandatory
Type of data recorded	aggregated
Cases routinely reported	hospitalised cases
Rickettsia species under surveillance	*R. conorii, R. prowazeki*
Case definition	Yes (2005)
Provision of surveillance data	Not provided
Estimated sensitivity of surveillance	national, fair sensitivity
Reference laboratory	National Center of Infections and Parasitic Diseases, NRL of Rikettsiae and Chlamydiae, Sofia http://www.ncipd.org/

Cyprus

The information in Table 17 is based on the rickettsioses surveillance survey and case-based surveillance data provided by the country (Figure 3 and Figure 4). *Rickettsia typhi* infections are common in Cyprus. A surveillance case definition has been used since 2008. There are between two and five laboratories offering diagnosis of rickettsial infections, and processing between 250 and 500 samples annually. One reference laboratory is located at Nicosia General Hospital, Immunology Laboratory.

One publication provided data on human cases [44]. Two studies provided information significant for rickettsioses risk in Cyprus. In this study the presence of *Rickettsia* species infection was identified in animals and ticks [45, 46]. A total of 622 rats, 557 birds and 15 ticks were collected from different locations in Cyprus. The laboratory findings revealed that 241 of 496 (48%) and 209 of 500 (42%) rats sera were positive for *R. typhi* and *R. conorii*, respectively. The prevalence of *Rickettsia* spp. was estimated at 3% in birds and 20% in ticks.

Table 17. Overview of rickettsioses surveillance in Cyprus

Indicator	Description
Type of surveillance	comprehensive
Type of reporting	mandatory
Type of data recorded	case-based
Cases routinely reported	all cases caused by selected species
Rickettsia species under surveillance	*R. typhi*
Case definition	yes (2008)
Provision of surveillance data	case-based (2004-2010)
Estimated sensitivity of surveillance	national, fair sensitivity
Reference laboratory	Immunology Laboratory, Nicosia General Hospital, http://www.moh.gov.cy

Figure 3. Number of rickettsioses cases by year, Cyprus (n=193)

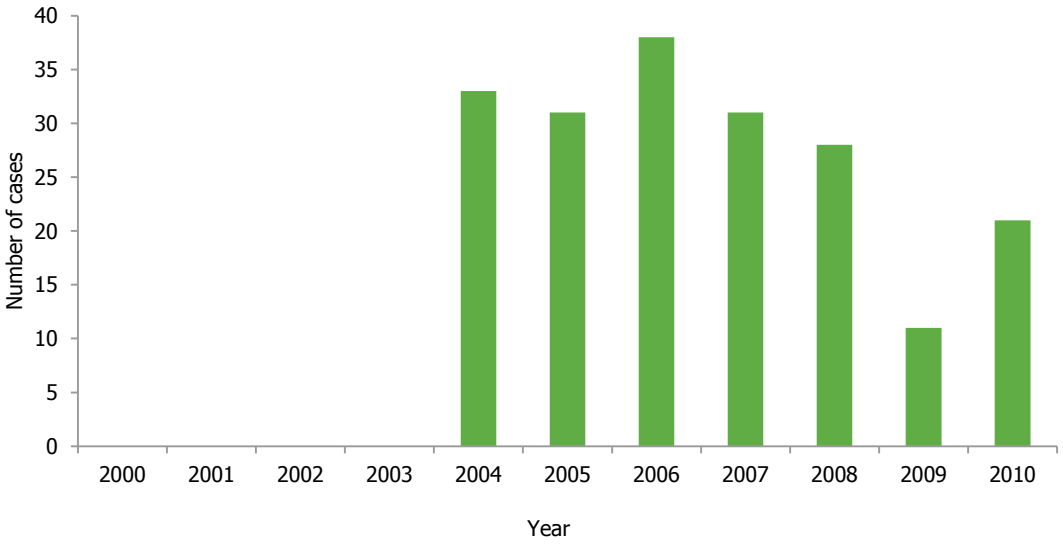
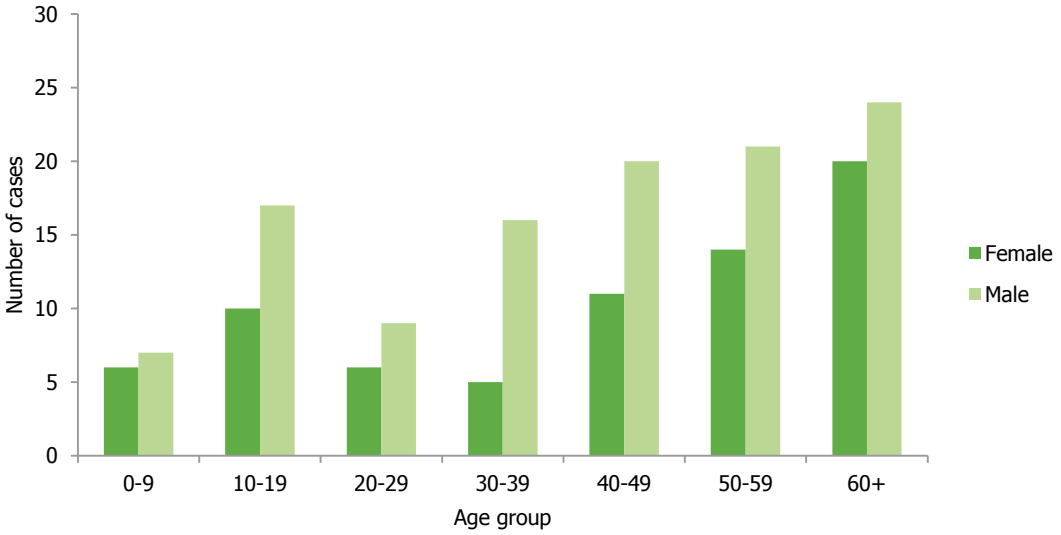


Figure 4. Number of rickettsioses cases by gender and age, Cyprus (n=186, data from 2004–2010 pooled)



Czech Republic

The information below is based on the rickettsioses surveillance survey (Table 18). Six cases of rickettsioses were reported to the Czech surveillance system during the period 2000–2010: four in 2002, one in 2003 and one in 2005, half of them among the 20–29 age group, two among 30–39 and one among 50–59. All detected cases over the last 10 years were imported from South Africa, Afghanistan, Croatia, Spain and Chile. There are between two and five laboratories offering diagnosis of rickettsial infections, processing less than 100 samples.

Table 18. Overview of rickettsioses surveillance in Czech Republic

Indicator	Description
Type of surveillance	other (University Hospital Infectious Diseases)
Type of reporting	mandatory
Type of data recorded	case-based
Cases routinely reported	hospitalised cases
Rickettsia species under surveillance	*R. conorii, R. africae, R. honei, R. slovaca, R. aeschlimannii,R. helvetica, R. raoultii, R. massiliae, R. monacensis, R. typhi, R. felis, R. sibrica mongolotimonae*
Case definition	N/A
Provision of surveillance data	no
Estimated sensitivity of surveillance	national, important regional differences in sensitivity
Reference laboratory	no

France

The information in Table 19 is based on the rickettsioses surveillance survey. Rickettsial infections are one of the most prevalent tick-borne diseases in France. The extraction of data on human cases was possible from nine articles [5, 47-55]. Seven studies provided information significant for interpretation of rickettsioses risk in France. Five of them aimed at estimating the prevalence of *Rickettsia* species in ticks. A total of 5 031 ticks were examined. The presence of *Rickettsia* species in ticks was estimated at 5.8% in Île de France [56], 1.9% in Pays de la Loire [57], 5.0% in Auvergne [58], 73.8% in Propriano [59] and 17.1% in Southern France [60]. The objective of the remaining two articles was to estimate the seroprevalence of bacterial agents in humans. A total of 2 978 serum samples taken from 930 homeless people and 467 controls [61], and 1 321 uveitis patients and 260 controls [62], were examined for the presence of *Rickettsia* species infection. The seropositivity was estimated at 2% for *R. conorii*, 0.54% for *R. typhi*, 0.2% for *R. akari* and 0.43% for *R. felis* among the homeless and 1% for *R. conorii*, 0.2% for *R.typhi*, 0% for *R. akari* and 0.6% for *R. felis* among the control patients. In patients with uveitis of unknown etiology and their controls, the seroprevalence for *Rickettsia* species was 0.6% and 0.8%, respectively.

Table 19. Overview of rickettsioses surveillance in France

Indicator	Description
Type of surveillance	other
Type of reporting	not well defined
Type of data recorded	case-based
Cases routinely reported	all cases
Rickettsia species under surveillance	*R. conorii, R. africae, R. honei, R. slovaca, R. aeschlimannii, R. helvetica, R. raoultii, R. massiliae, R. monacensis, R. typhi, R. felis, R. sibrica mongolotimonae*
Case definition	no
Provision of surveillance data	No data provided
Estimated sensitivity of surveillance	national, overall low sensitivity
Reference laboratory	N/A

Germany

The information in Table 20 is based on the rickettsioses surveillance survey. There are more than five laboratories offering rickettsioses diagnosis, processing between 250 and 500 samples annually. One reference laboratory is located at NRL on tick-borne pathogens, Friedrich-Löffler-Institute in Jena. The extraction of data of human cases was possible from one article [63, 64]. Ten studies investigated the risk of rickettsioses in Germany. One of them aimed at investigating the seroprevalence of *Rickettsia* species in an occupational group highly exposed to ticks [65]. A total of 286 hunters were enrolled in the study. Laboratory investigations revealed the presence of antibodies against different *Rickettsia* spp. for 18 individuals. Antibodies specific for *R. helvetica* and *R. aeschlimannii* were detected in two and six subjects, respectively. The other study discussed the prevalence of different vector-borne pathogens in dogs [66]. The antibodies to *Rickettsia* spp. were investigated in 58 out of 4 681 dogs enrolled in the study. The infection of *R. conorii* was determined in 20 subjects. The objective of the remaining eight papers was to assess the prevalence of *Rickettsia* species in ticks and animals. Overall, 7 801 ticks and 606 animals were examined for the presence of *Ricketttsia* species. The estimated prevalence in ticks was 2.7% for *Rickettsia* spp. in Thuringia in 2007 [67], 91.4% for *R. helvetica* and 8.6% for *R. monacensis* in Bavaria in 2006 [68], 12% for *Rickettsia* spp. in Bavaria [69], 23% for *Rickettsia* spp. in the northern and north-western parts of Germany in 2004 [70], 14.2% for *R. helvetica* in Berlin in 2003 [71], 14.7% for *Rickettsia* spp. in Thuringia in 2006 and 2007 [72], 30.3% for *R. raoultii* and 0.75% *for R. slovaca* in Baden-Wuerttemberg and Bavaria in 2006-2008 [73] and 7.3% for *Rickettsia* spp. in Mecklenburg-Western Pomerania [74].

Table 20. Overview of rickettsioses surveillance in Germany

Indicator	Description
Type of surveillance	comprehensive
Type of reporting	mandatory
Type of data recorded	case-based
Cases routinely reported	all cases caused by selected Rickettsia species
Rickettsia species under surveillance	*R. prowazeki*
Case definition	yes
Provision of surveillance data	N/A
Estimated sensitivity of surveillance	N/A
Reference laboratory	NRL on tick-borne pathogens, Friedrich-Löffler-Institute, Jena. http://www.fli.bund.de

Hungary

The information below is based on the rickettsioses surveillance survey (Table 21). The information on epidemiology of rickettsioses in Hungary is very limited. One study provided information on rickettsioses risk in the country. It reported on the molecular detection of *R. helvetica* and *R. monacensis* infection in *Ixodes ricinus* ticks collected in Hungary [75]. A total of 452 ticks were removed from carcasses of red foxes in 2002. *R. helvetica* was found in 12 out of 112 pools of investigated ticks (11%) and *R. monacensis* was detected in four pools.

Table 21. Overview of rickettsioses surveillance in Hungary

Indicator	Description
Type of surveillance	comprehensive
Type of reporting	mandatory
Type of data recorded	case-based
Cases routinely reported	hospitalised cases
Rickettsia species under surveillance	N/A
Case definition	no
Provision of surveillance data	N/A
Estimated sensitivity of surveillance	national, overall low sensitivity
Reference laboratory	N/A

Italy

The information below is based on the rickettsioses surveillance survey (Table 22) and aggregated surveillance data provided by the country (Figure 5, Figure 6, and Figure 7). Tick-borne rickettsioses are occurring endemically in Italy. A surveillance case definition has been used since 1990. There are more than five laboratories offering diagnosis of rickettsial infections. There is more than one reference laboratory, one national and several serving particular regions. The extraction of data on human cases was possible from eight articles [50, 76-82]. Seventeen studies provided information useful for the interpretation of rickettsioses risk in humans. Two of them discussed the seroprevalence of antibodies against *Rickettsia* in humans. Their results ranged from 37% in Sicily [83] to 4% in Friuli-Venezia Giulia [84], reflecting well the differences in human risk between the North and South of Italy. Five studies investigated the prevalence of anti-rickettsial antibodies in a total of 13 283 household animals mostly from Southern Italy [85-89]: 0.14% [88] to 10.13% [87] animals were found seropositive. Nine studies were identified investigating prevalence of rickettsial DNA in a total of 7 826 ticks [90-98]. Five studies, investigating 2 666 ticks, were conducted in the South of Italy (Sicily and Sardinia islands), and found 1.5% [96] to 35.2% [95] ticks positive for rickettsial DNA. *Rickettsia* species was determined only in one study, where *R. conorii*, *R. aeschlimannii*, *R. africae* and *R. slovaca* were found in different tick species [90]. Four studies investigating 5 160 ticks were conducted in the Northern and Central regions of Italy (Belluno, Friuli Venezia Giulia and Tuscany) [91, 92, 94, 97]. In these studies, prevalence of rickettsial DNA in ticks ranged from 1.6% in Belluno [94] to 37.9% in Tuscany [97]. Three studies allowed identification in the following *Rickettsia* species: R. *helvetica, R. monacensis, R. raoultii* and *R. slovaca*. Available evidence indicates that Mediterranean spotted fever cases are relatively well documented by human surveillance in Italy. Other rickettsial infections however may not be sufficiently diagnosed and reported.

Table 22. Overview of rickettsioses surveillance in Italy

Indicator	Description
Type of surveillance	comprehensive
Type of reporting	mandatory
Type of data recorded	case-based
Cases routinely reported	all cases
Rickettsia species under surveillance	*R. conorii, R. africae, R. honei, R. slovaca, R. aeschlimannii, R. helvetica, R. raoultii, R. massiliae, R. monacensis, R. typhi, R. felis, R. sibrica mongolotimonae*
Case definition	yes (1990)
Provision of surveillance data	aggregated (2001-2009)
Estimated sensitivity of surveillance	N/A
Reference laboratory	Department of Infectious, Parasitic and Immune Mediated Diseases, Istituto Superiore di Sanità, Rome, http://www.iss.it

Figure 5. Number of rickettsioses cases by year, Italy (n=4 609, data available over the period 2001-2009)

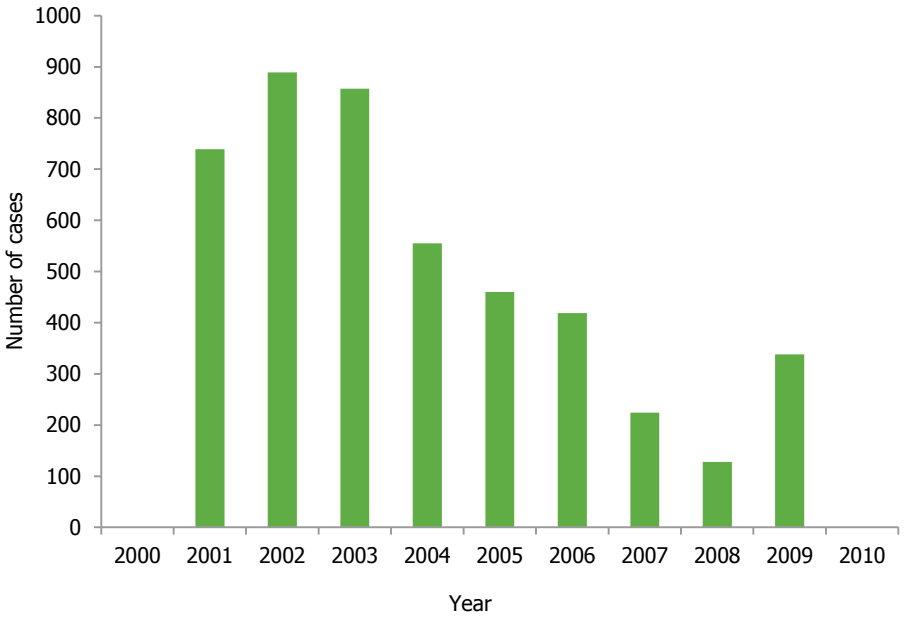


Figure 6. Number of rickettsioses by NUTS2, Italy (n=4 609, period 2001–2009)

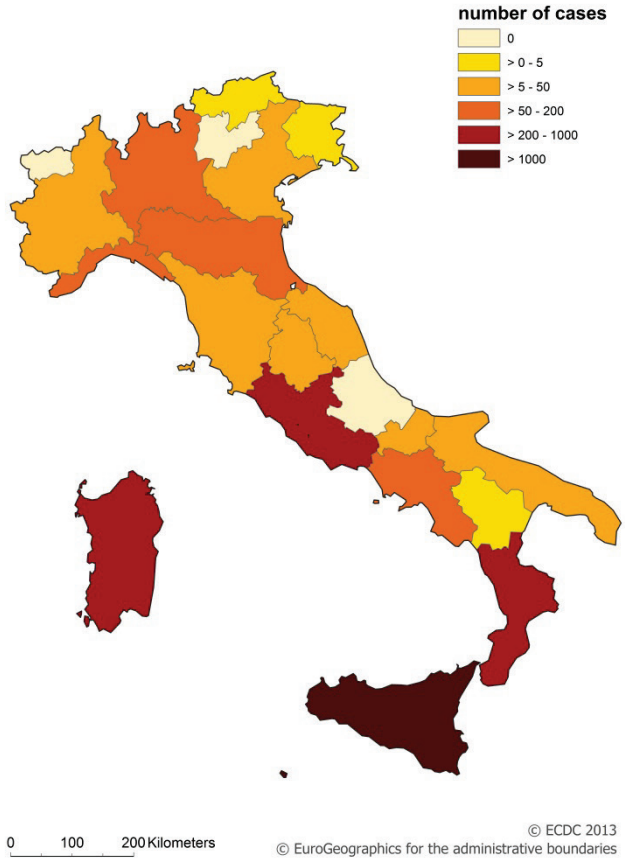
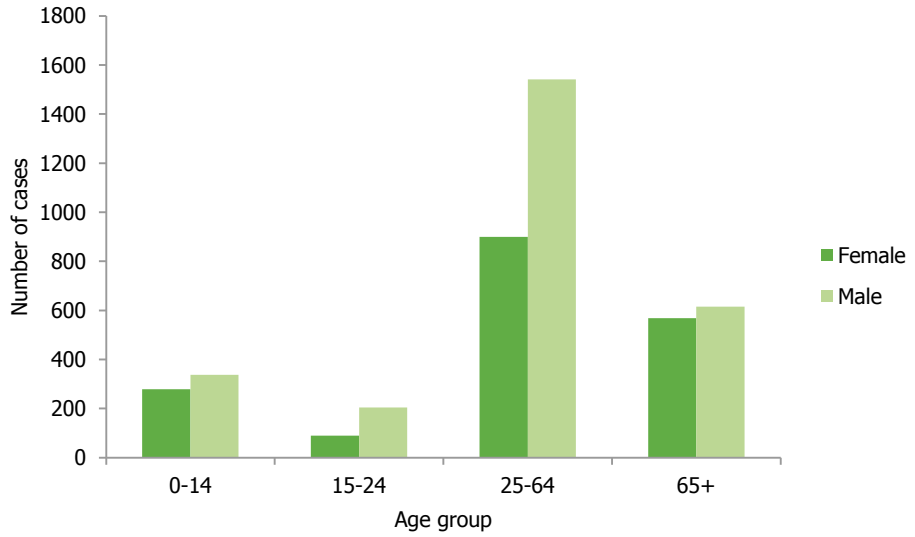


Figure 7. Number of rickettsioses cases by gender and age, Italy (n=4 532, period 2001–2009 pooled)



Latvia

The information below is based on the rickettsioses surveillance survey (Table 23) and case-based and aggregated surveillance data provided by the country (Figure 8, Figure 9, and Figure 10). The information on epidemiology of rickettsioses in Latvia is very limited. There is only one laboratory offering rickettsioses diagnosis, processing less than 100 samples annually. The reference laboratory is located at the Infectology Centre of Latvia in Riga. During the literature search no articles on the risk of rickettsioses in Latvia were identified.

Table 23. Overview of rickettsioses surveillance in Latvia

Indicator	Description
Type of surveillance	comprehensive
Type of reporting	mandatory
Type of data recorded	case-based
Cases routinely reported	all cases
Rickettsia species under surveillance	*R. conorii, R. africae, R. honei, R. slovaca, R. aeschlimannii, R. helvetica, R. raoultii, R. massiliae, R. monacensis, R. typhi, R. felis, R. sibrica mongolotimonae*
Case definition	no
Provision of surveillance data	aggregated (2000-2006) case-based (2007-2010)
Estimated sensitivity of surveillance	national, fair sensitivity
Reference laboratory	Infectology Centre of Latvia, Riga http://www.lic.gov.lv

Figure 8. Number of rickettsioses cases by year, Latvia (n=94)

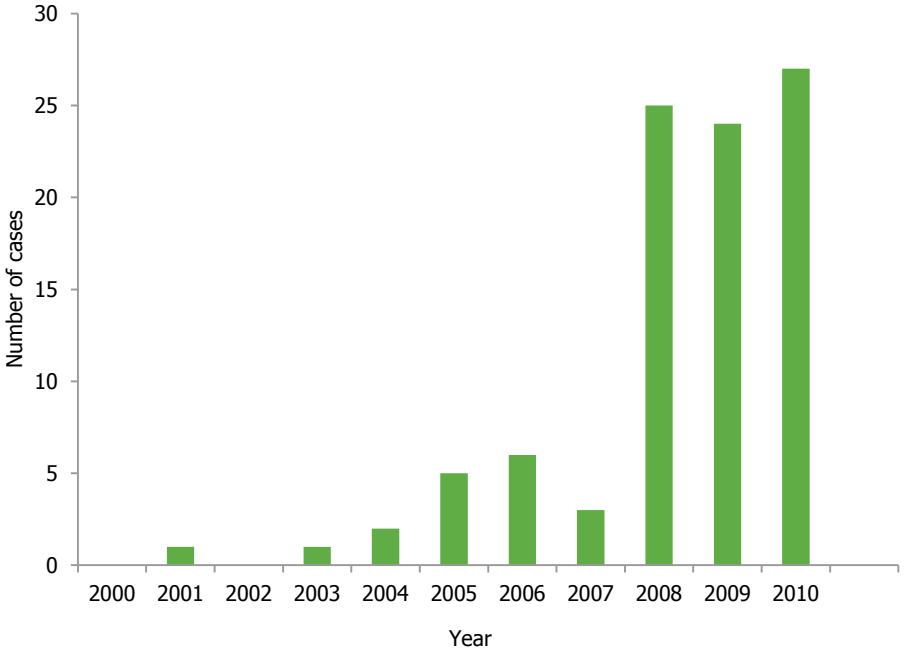


Figure 9. Number of rickettsioses by NUTS3, Latvia (n=79, period 2000-2010)

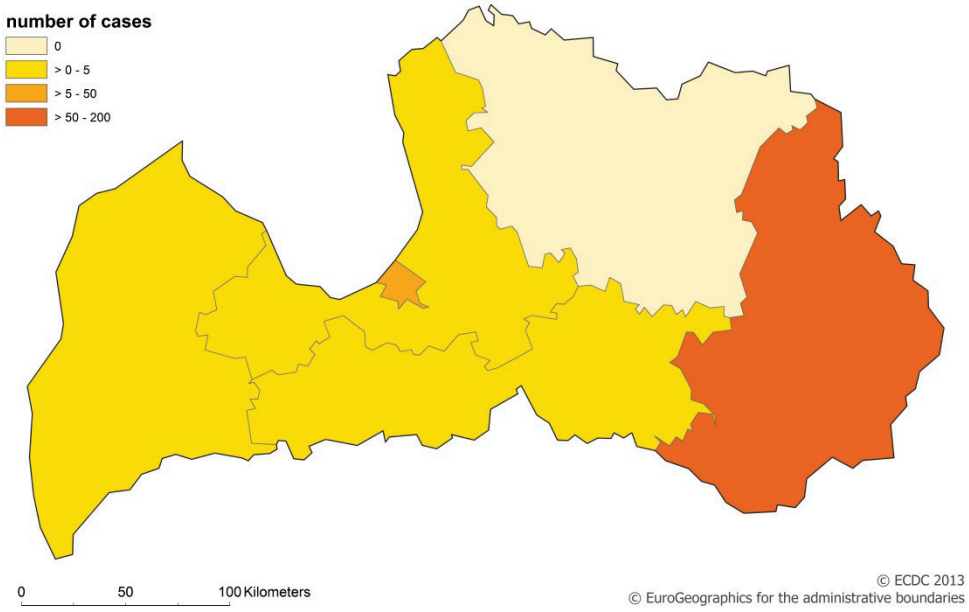
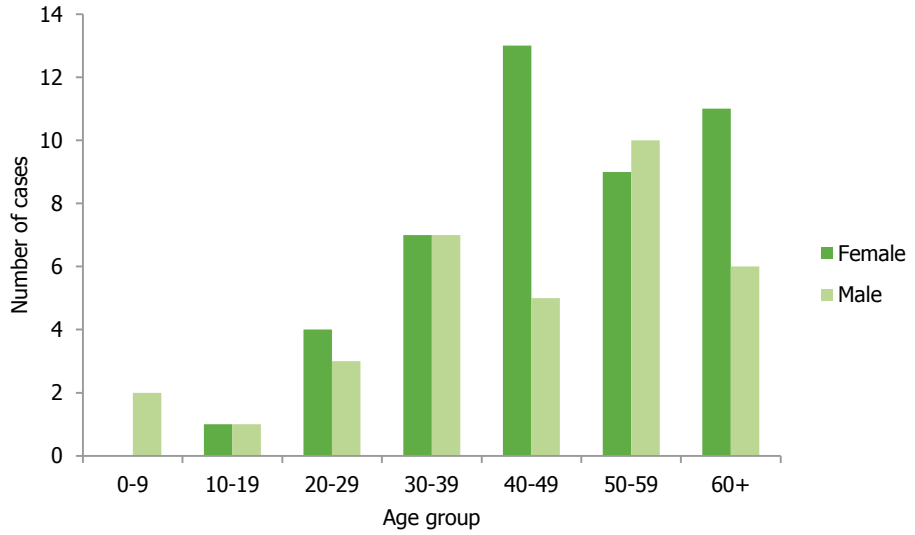


Figure 10. Number of rickettsioses cases by gender and age, Latvia (n=79, period 2000-2010 pooled)



Malta

The information below is based on the rickettsioses surveillance survey (Table 24) and aggregated surveillance data provided by the country. Spotted fever rickettsiosis occurs endemically in Malta. Seven cases were reported during the 2000–2010 study period: two in 2004 and 2005 and one in 2006, 2008 and 2010. A surveillance case definition is used since 2004. There is only one laboratory offering diagnosis of rickettsial infections, processing less than 100 samples annually. The extraction of data on human cases was possible from one article [99]. The objective of the study was to characterise the causative agents of rickettsioses and analyse the epidemiology of 33 cases of rickettsial disease.

Table 24. Overview of rickettsioses surveillance in Malta

Indicator	Description
Type of surveillance	Comprehensive
Type of reporting	mandatory
Type of data recorded	case-based
Cases routinely reported	hospitalised cases
Rickettsia species under surveillance	*R. conorii, R. africae, R. honei, R. slovaca, R. aeschlimannii, R. helvetica R. raoultii, R. massiliae, R. monacensis, R. typhi, R. felis, R. sibrica mongolotimonae*
Case definition	yes (2004)
Provision of surveillance data	aggregated (2000-2010)
Estimated sensitivity of surveillance	national, fair sensitivity
Reference laboratory	No

Poland

The information below is based on the rickettsioses surveillance survey (Table 25) and case-based surveillance data provided by the country. In Poland tick-borne rickettsioses are reported sporadically. During 2000–2009, three cases were reported. Only one laboratory offers diagnosis of rickettsial infections, processing less than 100 samples annually. One study investigated 11 dogs referred to a veterinary clinic, all of them being negative for rickettsial DNA [100]. Five studies investigated the prevalence of *Rickettsia* in ticks collected from different Polish regions [101-105]. DNA of *Rickettsia* spp. was found in 3% to 32.7% ticks. Detection of *Rickettsia* species from *Ixodes ricinus* ticks confirmed *R. helvetica* in four studies (5.5–12.7%), as well as *R. raoulti* (23.4%) and *R. slovaka* (2.1%) in one study. *Rickettsia raoulti* was detected in 3–57% *Dermacentor reticulatus* ticks collected from two Polish regions. Those sporadic reports confirmed the risk for tick-borne *Rickettsia* infections in Poland.

Table 25. Overview of rickettsioses surveillance in Poland

Indicator	Description
Type of surveillance	comprehensive
Type of reporting	mandatory
Type of data recorded	case-based
Cases routinely reported	all cases
Rickettsia species under surveillance	all tick-borne Rickettsia, including unspecified
Case definition	no
Provision of surveillance data	aggregated
Estimated sensitivity of surveillance	overall very low
Reference laboratory	National Institute of Public Health-National Institute of Hygiene, Warsaw http://www.pzh.gov.pl

Portugal

The information below is based on the rickettsioses surveillance survey (Table 26) as well as summary figures (2000–2001) and case-based surveillance data (2002–2010) provided by the country (Figure 11, Figure 12, and Figure 13). Rickettsioses caused by *R. conorii* occur endemically in Portugal mainly in eastern rural areas, not frequently in coastal regions. The highest risk has been linked with young children and the elderly, as they have common contact with tick habitats and animals due to common outdoor activities all year round. On the other hand, elderly people constitute the majority of inhabitants of rural areas. The surveillance system has been operating since the 1950's. The current case definition has been used since 1999. There are more than five laboratories offering diagnosis of rickettsial infections, processing more than 1 000 samples annually. The extraction of data was possible from five articles [81, 106–109]. Four papers looked at rickettsioses risk in humans. Three of the articles investigated the prevalence of *Rickettsia* species in ticks [110–112]. A total of 386 ticks were tested for the presence of *Rickettsia* species infection. The sampling was conducted in the southern and north eastern parts of Portugal. The prevalence was: 34.5% for *R. slovaca* and 65.5% for *Rickettsia* sp. RpA4 (now *R. raoultii*) in Alentejo in 2003–2004 [112], 55.1% for *Rickettsia* spp. in Alentejo in 2006–2009 [110] and 17.1% in Norte in 2004 [111]. The remaining article aimed at detecting the presence of *Rickettsia* species in animals [113]. Overall, 51 blood samples taken from cats living in Lisbon and Alentejo were tested for the presence of different pathogens. *R. conorii* specific antibodies were found in seven cats (14%).

Table 26. Overview of rickettsioses surveillance in Portugal

Indicator	Description
Type of surveillance	comprehensive
Type of reporting	mandatory
Type of data recorded	case-based
Cases routinely reported	all cases caused by selected species
Rickettsia species under surveillance	*R. conorii*
Case definition	yes (1999)
Provision of surveillance data	case-based (2002-2010)
Estimated sensitivity of surveillance	unknown
Reference laboratory	N/A

Figure 11. Number of rickettsioses cases by year, Portugal (n=4 291)

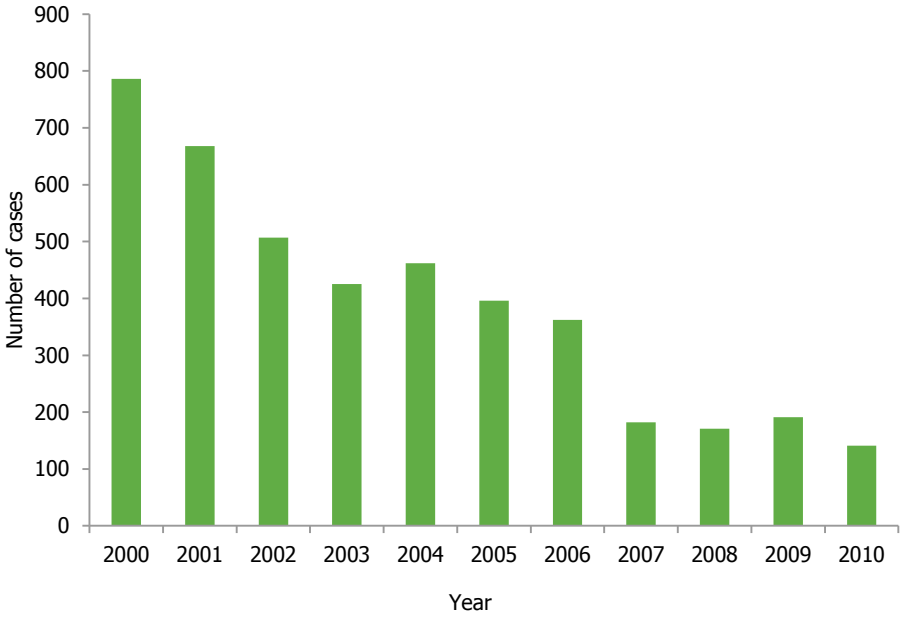


Figure 12. Number of rickettsioses cases by NUTS3, Portugal (n=2 834, period 2002–2010)

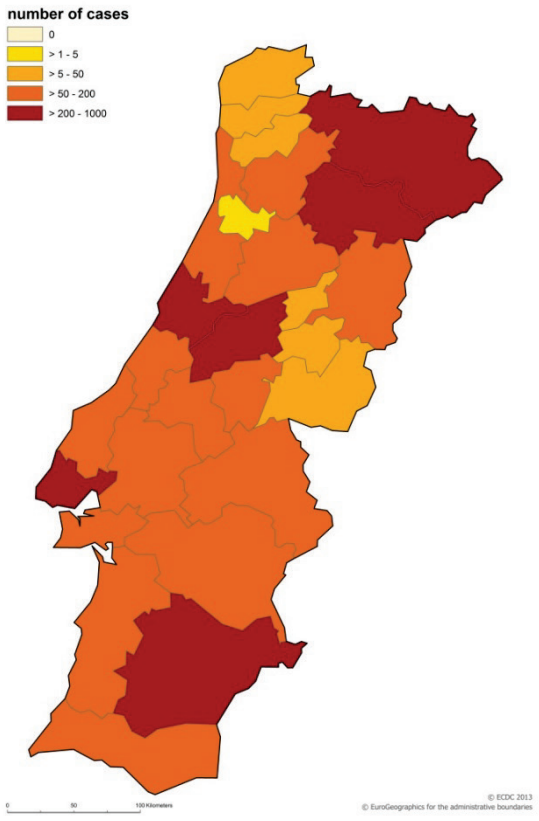
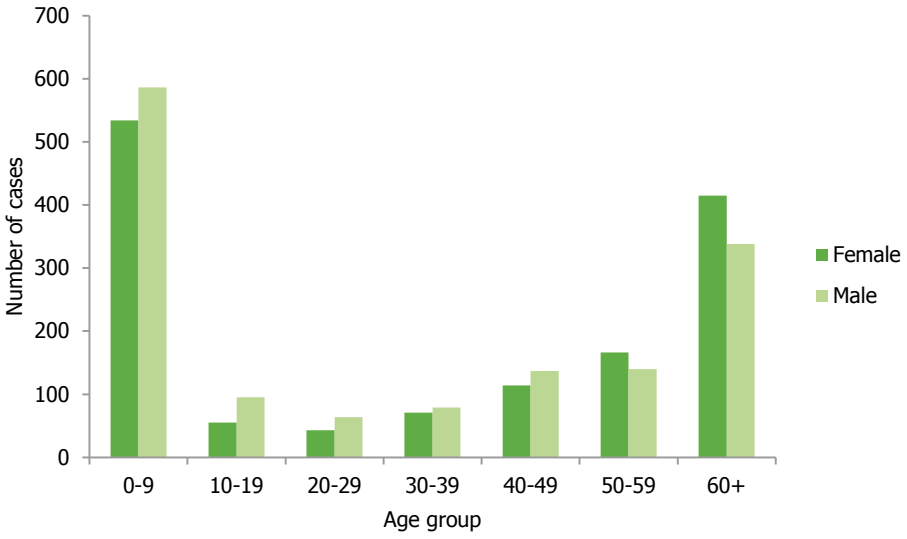


Figure 13. Number of rickettsioses cases by gender and age, Portugal (n=2 837, data from 2002–2010 pooled)



Slovenia

The information below is based on the rickettsioses surveillance survey (Table 27). Only one laboratory offers diagnosis of rickettsial infections, processing less than 100 samples annually. No cases of rickettsioses were reported to Slovenian surveillance system from 2000 to 2010. During the literature search no articles on the risk of rickettsioses in Slovenia were identified.

Table 27. Overview of rickettsiosis surveillance in Slovenia

Indicator	Description
Type of surveillance	comprehensive
Type of reporting	mandatory
Type of data recorded	case-based
Cases routinely reported	all cases
Rickettsia species under surveillance	*R. prowazekii*
Case definition	no
Provision of surveillance data	N/A
Estimated sensitivity of surveillance	national, fair sensitivity
Reference laboratory	no

Spain

The information below is based on the rickettsioses surveillance survey (Table 28) and aggregated and case-based surveillance data provided by the country (Figure 14, Figure 15, Figure 16). Tick-borne rickettsioses are endemic in Spain. A surveillance case definition has been used since 1996 and revised in 2010. There are between two and five laboratories offering diagnosis of rickettsial infections, processing more than 1 000 samples annually. There is one national reference laboratory located at Centro Nacional de Microbiología-Instituto de Salud Carlos III, Laboratorio de Espiroquetas y Patógenos Especiales, and several serving particular regions. The extraction of data was possible from seventeen articles [4, 6, 63, 81, 114-126]. Among others, 26 papers provided information important for the interpretation of rickettsioses risk in humans. Four of them reported results of seroepidemiological population-based studies of *Rickettsia* species infections. Past infection with *R. typhi* was investigated among 1 238 healthy subjects in Andalusia (Southern Spain), 143 inhabitants of Madrid community (Central Spain) and 217 inhabitants of Catalonia (North-Eastern Spain), and was detected in 3%, 4-18% and 9%, respectively [127-130]. Antibodies specific to *R. conorii* were detected in 9% of inhabitants in Catalonia and 5% of inhabitants in Madrid. Evidence of past infection with *R. felis* was detected in 7% inhabitants of Andalusia. One study investigating patients with hypertransaminemia from Madrid established prevalence of antibodies against *R. conorii* in 11% patients and against *R. typhi* in 7% patients [128]. Apart from classical studies on *R. conorii* in humans, six studies confirmed by molecular methods and/or culture the presence of different *Rickettsia* species in patients: *R. typhi* and *R. felis* in the Canary Islands [120, 124], *R. felis, R. slovaca* and *R. raoultii* in La Rioja [4, 123], *R. monacensis* in La Rioja and the Basque Country [6], or *R. sibirica mongolotimonae* in the Basque

Country [116]. Six studies investigated the prevalence of antibodies against *Rickettsia* spp. in domestic animals including 1 491 dogs and 268 cats mostly from the North-Eastern regions of Spain [131-137]. Evidence of past infection with *R. conorii* was detected in 30% of dogs from Galicia [131], 53–65% dogs, as well as 44% of cats from Catalonia [133–135] and 51% cats from the Balearic Islands [134]. Studies attempting detection of rickettsial DNA in domestic animals did not find evidence of current infection [136, 137]. One study investigated the prevalence of antibodies against *R. typhi* and *R. felis* in dogs from Catalonia and found evidence of past infection caused by these pathogens in 10% and 51% of dogs, respectively [132]. Three papers reported studies investigating tick-borne *Rickettsia* in wild animals. Evaluation of 334 rodents in the Basque Country and 150 wild rabbits in the Canary Islands did not allow detection of rickettsial DNA [138, 139]. Evidence of past infection with *R. conorii* and *R. slovaka* was found in wild boar hunted in Catalonia, with prevalence of antibodies 83% and 52%, respectively [140]. Thirteen papers reported results of rickettsial DNA detection in ticks [140-152]. In those studies a total of 7 106 ticks were collected from 7 of the 17 autonomous communities in Spain. The prevalence of *Rickettsia* spp. in ticks ranged from an average of 14% ticks in two studies carried out in La Rioja [150, 151] to an average of 19% found in Madrid and of 25% ticks infected found in four studies carried out in Andalusia [145-148, 153] and an average of 42% infected ticks found in two studies from Catalonia [140, 149]. In all studies identification of *Rickettsia* species was done. The following species were identified: *R. aeschlimannii, R. conorii, R. felis, R. helvetica, R. massiliae, R. monacensis, R. raoultii, R. sibirica mongolotimonae, R. slovaca*, as well as strains Bar 29, DnS14, DnS28, JL-02, and Candidatus *R. rioja*. The evidence cited above indicates that rickettsial infections are carefully monitored in Spain. Human surveillance covers only infections caused by *R. conorii.*

Table 28. Overview of rickettsiosis surveillance in Spain

Indicator	Description
Type of surveillance	comprehensive
Type of reporting	mandatory
Type of data recorded	case-based
Cases routinely reported	all cases caused by selected species
Rickettsia species under surveillance	*R. conorii*
Case definition	yes (1996, revised in 2010)
Provision of surveillance data	Aggregated; case-based (2005-2009)
Estimated sensitivity of surveillance	regional, very low sensitivity
Reference laboratory	Centro Nacional de Microbiología, Instituto de Salud Carlos III, Madrid http://www.isciii.es

Figure 14. Number of rickettsiosis cases by year, Spain (n=1 920, no data available for 2010)

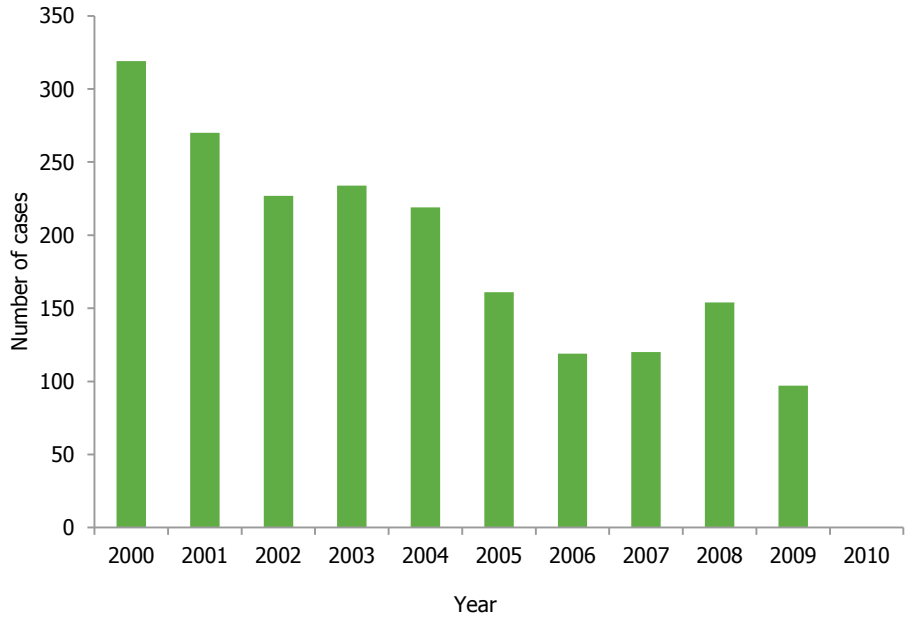


Figure 15. Number of rickettsiosis cases by NUTS2, Spain (n=651)

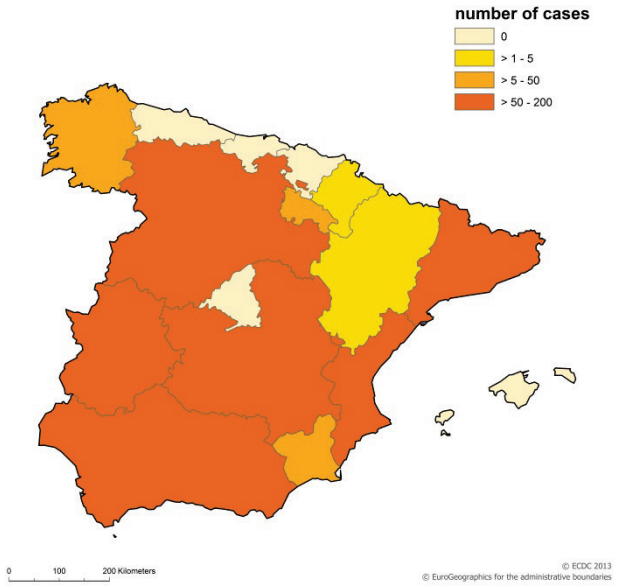
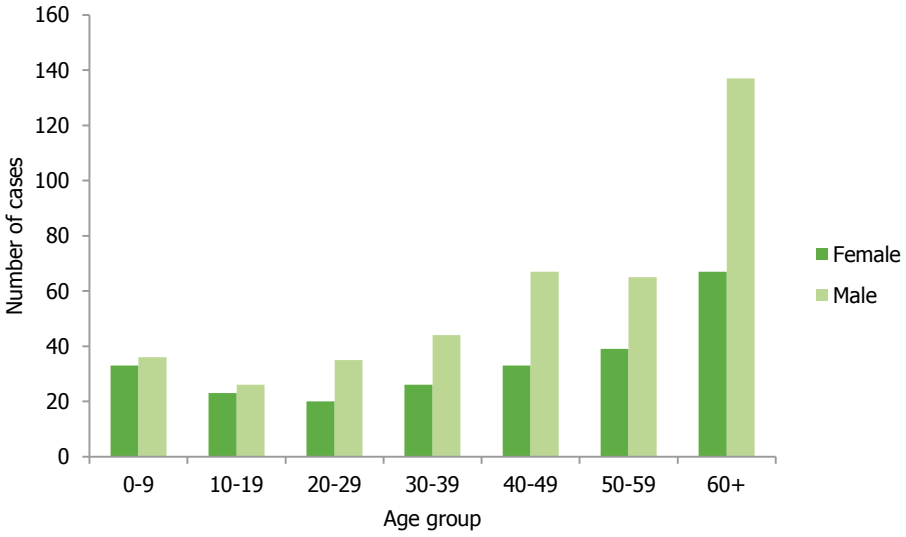


Figure 16. Number of rickettsiosis cases by gender and age, Spain (n=651, data from 2000–2009 pooled)



Discussion

Rickettsioses surveillance is implemented in 14 countries of the EU/EEA. Laboratory diagnosis of suspected rickettsial infection is primarily implemented in three countries in the Mediterranean Basin namely Italy, Portugal and Spain. In these three countries, Mediterranean spotted fever caused by *R. conorii* is well recognised by physicians, and therefore more reliably reported. In other countries the reported number of cases is limited and *Rickettsia* infections seem not to be of primary importance. Interestingly, while laboratories in Latvia analysed a relatively low number of samples per year (<100), an average of 25 cases in the period 2008–2010 were reported. From published papers, the presence of *Rickettsiae* belonging to the Spotted Fever Group (SFG) in wildlife across all European regions was confirmed in 17 countries suggesting a potential widespread risk of infection for humans. This indicates that data from human cases should not be the only source of information to determine risk areas for infection.

Currently there is no case definition at EU level for rickettsial infection: only seven countries have adopted case definitions in their country and even in these countries there are no standardised criteria for case classification. Moreover, apart from pathogens causing MSF and murine typhus, in the last years different *Rickettsia* species have been described and identified as new pathogens for humans in Europe [5, 6, 51]. The increasing diversity of these *Rickettsia* bacteria as published in recent years should be considered both for surveillance and for development of appropriate laboratory capacity to detect human cases. In addition, physicians should receive information about the occurrence of these diseases and related clinical symptoms in order to increase their awareness and ask for laboratory diagnostic confirmation if needed. Furthermore, since only four out of 14 countries are capable of identifying *Rickettsia* at the species level, there is a need for improvement and standardisation of methodology in all European countries.

Based on the very incomplete picture regarding surveillance data and published investigations, the high risk for tick-borne rickettsioses is limited to the Southern European regions. A decrease of cases was observed in the study period 2000–2010 in Italy, Portugal and Spain. The cause of this decrease is intriguing and factors altering tick dynamics such as changes in the management of livestock, climatic factors or improved specificity of clinical suspect and diagnostic tools should all be investigated. The groups at highest risk for rickettsioses are the youngest and oldest age groups. Healthy adults are less likely to exhibit symptoms of rickettsial infections. Further investigations both at clinical and immunological level are needed to improve the prevention of these emerging diseases.

As a result of the present evaluation, important gaps were identified in epidemiological information available on tick-borne rickettsioses. No systematic investigation of suspect cases is performed in the majority of European countries. This hampers a valid monitoring of rickettsioses risk and implementation of efficient interventions directed to both inhabitants of endemic regions as well as tourists visiting endemic regions.

As with many diseases under surveillance in Europe, there is a need to prioritise surveillance activities. In comparison with tick-borne encephalitis less consistent data for rickettsioses are collected in European countries, and less priority for surveillance of human and animal cases is given. Since rickettsioses are poorly understood and considered as emerging diseases in Europe, this situation creates a vicious circle. Without reliable date on disease risk because of their low priority, it will not be possible to prioritise them properly, since we will not know their burden to the involved societies. Due to the emerging nature of currently known tick-borne pathogens, an increasing burden factor due to increasing travel, expanding cohorts of immunocompromised subjects, and ageing societies may be expected. Therefore there is a need to give more attention to efficient monitoring of those pathogens at local, national and international levels.

Recommendations

Based on this thorough overview of epidemiological situation of rickettsioses in EU/EFTA countries, the following recommendations are suggested:

- There is a need for improvement of rickettsioses surveillance throughout Europe, with emphasis on obtaining comparable data at EU level or at least regional level.
- Data collection at sub-national levels, at least at NUTS-3 geographical level should be encouraged. Collection of data at country level is not relevant for a European approach to rickettsioses risk assessment, as it needs to take into account several geographically variable biotic and abiotic determinants of disease risk.
- The use of diagnostic methods allowing comparison of results should be encouraged, i.e. through promotion of implementation of reference laboratories in all EU/EFTA countries. The reference laboratories should have the appropriated diagnostic tools available, including methods for distinguishing among *Rickettsia* species.
- Due to the zoonotic nature of the evaluated diseases, it is recommended to strengthen continuous cross-information exchanges between different sectors such as the World Organisation for Animal Health and European Food Safety Authority, according to the Directive 2003/99 on the monitoring of zoonoses and zoonotic agents. This process will facilitate a proper risk assessment procedure based on the combination of surveys in the vector, in the reservoir animals, in sentinel animals and in humans with the development of predictive models and high resolution diseases risk maps.
- For tick-borne rickettsioses surveillance the following is recommended:
  - the development of a harmonisation of case definition for the most important *Rickettsia* species (presently MSF and *R. typhi*) primarily for the Mediterranean Basin
  - considering more comprehensive assessment of human risk in all EU/EFTA countries, i.e. through systematic monitoring of ticks and of pathogens in ticks in different European regions.

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Annex 1 – General description of the project

The main goal of the project was to summarise existing data on rickettsioses. To achieve these goals, a consortium of experts was created, with expertise in communicable disease surveillance, tick biology, microbiology, and clinical medicine. First, a thorough literature review was performed in order to identify gaps in knowledge on the burden of rickettsioses. Secondly, surveys were prepared to evaluate the implementation of surveillance systems in particular countries, laboratory methods used, and data availability. As a final step, collected data were assessed in terms of completeness, and possibility to fill data gaps.

The following steps were taken to achieve the goals:

Identification of experts – respondents of the survey

Respondents to the survey on *surveillance of rickettsioses and availability of data* were identified in the preparatory phase, through an existing network of experts EU-FP6 EDEN or Med-Vet-Net. Consortium members assured appropriate links with existing or past networks. The head of the ECDC Surveillance Unit approved the list of experts and the invitations were sent by the ECDC Surveillance Unit through ECDC competent bodies in each country

Literature review

The consortium members shared the task of collecting all published evidence on risk for rickettsioses based on infection in humans, wild hosts and ticks. First, a set of keywords were agreed during the initial teleconference performed in November 2010. The period of the review was limited to 2000–2010. The information on disease risk was extracted from papers identified by the reviewers and entered into standardised tables. Ten independent reviewers selected the abstracts that met the preliminary inclusion criteria and filled the summary table for each selected abstract.

The inclusion criteria adopted for the literature review were:

- time limits: years 2000–2010
- geographical limits: EU and EFTA countries (27 Member States and three EFTA countries - Switzerland, Norway and Iceland). Cases imported from other countries were excluded
- language: English, French, Italian, Czech, German, Hungarian, Polish, Russian, Slovak, Slovenian, Spanish, Swedish. If there were abstracts written in languages that were not understandable for the reviewers then the person from the particular country was asked to review the text.

Inclusion criteria for papers were as follows:

- includes numbers (human case counts) which can be extracted with geographic reference
- the data source (surveillance system, special "ad hoc" study…) is described
- provides information important for interpretation of disease risk in humans:
  - serologic survey of humans or animals
  - predictive model using environmental variables
  - other information on pathogen occurrence.

Exclusion criteria for papers were as follows:

- incompatible time period
- different disease
- country not on the list
- only imported cases
- non-understandable language
- not addressing the aim of the study
- other

For each included article the full text was retrieved. Reference lists of the selected papers, as well as citation of selected articles in Google Scholar were used to identify papers not included by the original query.

In order to verify the applied methods a pilot study of summary tables was conducted. The reviewers were to evaluate the first 30 abstracts and send the results to project co-ordinator. The co-ordinator team checked summary tables' compliance with procedure and provided feedback to the reviewers. Any additional identified paper was reviewed. Published papers and reports provided by the respondents of the survey were also reviewed using the same criteria.

Development of questionnaires

The survey addressed issues on surveillance of rickettsioses data availability; surveillance contact people were asked to provide information on unpublished evidence on risk of rickettsioses at tick, animal, and human levels.

Web-based survey administration

The technical co-ordinator prepared the questionnaires in an electronic form, and used the platform VoozaNoo (http://www2.voozanoo.net/fr). EpiConcept was subcontracted to provide technical assistance in designing the on-line surveys, and solve technical problems during survey administration. The technical coordinator of the project was responsible for sending reminders to each contact point. Access to the survey was through username and password and the access rights varied between different user profiles. The respondents in each participating country entered data directly on-line.

Analysis of reporting systems

The availability of reporting systems was summarised, and selected indicators were evaluated. The possibility of under-reporting in view of type of surveillance system was discussed.

Analysis of epidemiological data

The EU and EFTA countries were requested to provide surveillance data on rickettioses. The data was then analysed and presented individually for each country and for the whole of Europe.

Working group constitution

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- Joanna Zajkowska, Białystok Medical University, Białystok, Poland.

Timeline

September 2010	Distribution of tasks for the questionnaire contents development and protocol for the literature review
December 2010	Development of the questionnaire contents and protocol for literature review
March 2011	Initiation of the online survey on TBDs data availability in EU/EFTA countries
May 2011	Review of abstracts selected for literature review on TBDs data availability in EU/EFTA countries
June 2011	Collection of survey from countries
	First call for surveillance data from countries consenting to provide their data
July 2011	Extraction of data on cases from articles selected by reviewers and through supplementary literature review
August 2011	Preparation of the final report for ECDC

Annex 2 – Questionnaire of tick-borne rickettsioses data availability in EU/EFTA countries

SECTION 1: SURVEILLANCE OF TICK-BORNE DISEASES

1. Which of the following diseases are subject to epidemiological surveillance in your country at national or sub-national level?

- Tick-borne encephalitis
- Tick-borne rickettsioses
- Q fever
- Lyme borreliosis

SECTION 2: SURVEILLANCE OF TICK-BORNE RICKETTSIOSES

2.1. Is there one or more surveillance systems for tick-borne rickettsioses operating in your country?
- One system
- Two systems
- Three systems
- Four systems
- Five or more systems

2.2. The type of surveillance system is:
- Comprehensive
- Sentinel
- Other (please specify …….)

2.3. This surveillance system is operating:
- At national level
- At sub-national level (e.g. at regional level)
- Only in endemic areas
- Other (please specify …….)

2.4. Reporting in the surveillance system is:
- Mandatory
- Voluntary
- Not well defined

2.5. The sources of data used in the surveillance system are (check all that apply):
- Reporting by general practitioners
- Reporting by hospital physicians
- Reporting of deaths from infectious diseases
- Laboratory reporting
- Hospital discharge records
- Death registers records
- Other (please specify …….)

2.6. The surveillance system collects epidemiological information on Rickettsiosis:
- All cases of rickettsioses
- Cases caused by selected Rickettsia species

2.6.1. Please check all that apply:
  - R. conorii
  - R. africea
  - R. honei
  - R. slovaca
  - R. aeschlimanii
  - R. helvetica
  - R. raoultii
  - R. massiliae
  - R. monacensis
  - R. sibirica mongolotimonae
  - R. typhi
  - R. felis
  - Other

2.7. Which cases are routinely reported within the surveillance system?
- All cases (including asymptomatic)
- Hospitalized cases
- Only cases with central nervous system involvement
- Other (please specify …….)

2.8. Is there a case definition for tick-borne rickettsioses used in the surveillance system?
- Yes
- No
- Don't know

2.8.1. Is this surveillance case definition used to classify each reported case?
  - Yes
  - No
  - Don't know

2.8.2. How are reported cases classified?
  - Possible (typically only clinical criteria)
  - Probable (typically clinical criteria with epidemiological link or confirmation using less specific laboratory test)
  - Confirmed (typically require laboratory confirmation)

2.8.3. Please provide the current surveillance case definition for tick-borne rickettsioses.

2.8.4. In which year was the above surveillance case definition implemented and eventually revised?

2.9. How is data recorded at the highest level of the surveillance system operation?
- Case-based
- Aggregated
- Don't know

2.9.1. If case-based, what data are collected?
  - Notification source (GP, hospital, lab, other)
  - Date of notification
  - Presumed data of infection
  - Case classification (according to the case definition)
  - Demographic variables (age, gender)
  - Geographical location of residence
  - Eurostat NUTS1 (usually country regions)
  - Eurostat NUTS2 (usually country provinces)
  - Eurostat NUTS3 (usually districts or counties)
  - Geographical location of presumed exposure
  - Eurostat NUTS1 (usually country regions)
  - Eurostat NUTS2 (usually country provinces)
  - Eurostat NUTS3 (usually districts or counties)
  - Exposure to tick-bites
  - Occupational exposures
  - Hospitalization
  - Laboratory test details
  - Rickettsia species
  - Clinical signs/symptoms
  - Clinical complications
  - Outcome (dead/alive)
  - Import related case
  - Other (please specify…..)

2.9.2. If aggregated, which aggregation levels are used?
  - Age group (please provide the age groups used)
  - Gender
  - Residence (urban/rural)
  - Season/month
  - Case classification
  - Geographical location of residence
  - Eurostat NUTS1 (usually country regions)
  - Eurostat NUTS2 (usually country provinces)
  - Eurostat NUTS3 (usually districts or counties)
  - Rickettsia species
  - Hospitalization
  - Outcome (dead/alive)
  - Importation status
  - Other (please specify……)

2.10. Where there any attempts to measure the sensitivity of the surveillance system (i.e. estimation of under reporting)?
- Yes
- No
- Don't know

2.10.1. If yes, what method was used:
  - Capture-recapture analysis
  - Mathematical modelling of disease burden
  - Simple comparison among different sources
  - Other (please describe…..)

2.10.2. Please provide the estimate of tick-borne rickettsioses surveillance sensitivity:
  - <50%
  - 50-75%
  - >75%

2.10.3. Please provide below the appropriate references or links to the sensitivity assessments.

2.11. How would you assess the surveillance system sensitivity?
- National, fair sensitivity
- National, important regional differences in sensitivity
- National, overall low sensitivity
- Regional, fair sensitivity
- Regional, very low sensitivity
- Other (please describe….)
- Don't know

2.12. Is another case definition for tick-borne rickettsioses used for the clinical management of cases, other than the previously described surveillance case definitions?
- Yes
- No
- Don't know

2.12.1. If yes, please describe.

2.13. If surveillance data are available for your country, could you provide them to ECDC in the framework of this project (note; data format will be provided)
- Yes
- No

SECTION 3. MICROBIOLOGICAL METHODS FOR RICKETTSIOSES

3.1. Is laboratory confirmation used to ascertain rickettsioses cases in your country?
- Yes
- No
- Don't know

3.2. What laboratory tests are used to confirm rickettsioses cases ?
- IFA (immunofluorescence assay)
- Cross-absorption (CA) and WB (Western blot)
- PCR (polymerase chain reaction)
- SEQ (sequencing)
- IFD (direct immunofluorescence)
- Histochemical and immunohistochemical methods
- Culture
- Don't know
- Other- specify……

3.3. How many laboratories perform diagnosis of suspected rickettsioses cases in your country?
- 1
- 2-5
- >5
- Don't know

3.4. Could you estimate how many samples are processed each year for diagnosis of rickettsioses cases in the country laboratories?
- < 100
- 100 -< 250
- 250 -< 500
- 500 -< 750
- 750 -< 1000

- 1000
- Don't know

3.5. Are laboratories in your country attempting to differentiate the following Rickettsial species?
- No differentiation (Rickettsia spp.)
- R. conorii
- R. africea
- R. honei
- R. slovaca
- R. aeschlimanii
- R. helvetica
- R. raoultii
- R. massiliae
- R. monacensis
- R. sibirica mongolotimonae
- Don't know

3.6. Are the microbiological testing results for rickettsioses reconciled (linked) with epidemiological case reports at the national level?
- Yes
- No
- Don't know

3.7. Is there a reference laboratory for rickettsioses diagnosis operating in your country?
- Yes
- No
- Don't know

3.7.1. How many?
  - One
  - More than one (please specify the number…..)

3.7.2. Is the laboratory officially nominated to provide reference microbiological methods for the local laboratories?
  - Yes
  - No

3.7.3. What reference methods of rickettsioses confirmation are performed in the reference laboratory?
  - IFA (immunofluorescence assay)
  - Cross-absorption (CA) and WB (Western blot)
  - PCR (polymerase chain reaction)
  - SEQ (sequencing)
  - IFD (direct immunofluorescence)
  - Histochemical and Immunohistochemical Methods
  - Culture
  - Don't know
  - Other- specify……

3.7.4. Did the reference laboratory participate in international External Quality Assurance in relation to rickettsiosis diagnosis?
  - Yes
  - No
  - Don't know

3.7.5. How often did the reference laboratory participate in international External Quality Assurance (EQA) during 2005-2010?
  - >5
  - 5
  - 2-4
  - 1
  - 3.7.6. When was the latest EQA exercise performed?
  - 2010
  - 2009
  - More than 2 years ago

3.7.7. Could you please, provide the addresses of reference laboratories. (postal address, contact name, email, telephone number)

Annex 3 – Rickettsioses case definitions used in surveillance systems in EU/EFTA countries as reported through the rickettsia survey

Bulgaria	BOUTONNEUSE FEVER Clinical description Disease characterised by the formation of a primary affect at the tick-bite site, i.e. "Tache noire" (rounded infiltrate covered by a necrotic slough), with fever, chills, headache, myalgia, maculo-papular rash on the whole body, including palms and feet. Laboratory criteria - Demonstration of specific antibodies in the patient serum - Isolation of the agent in clinical specimens Case classification Suspected: N/A Probable: A clinically compatible and epidemically linked case Confirmed: A clinically compatible case that is laboratory confirmed. EPIDEMIC TYPHUS Clinical description A disease, characterised by an immediate onset, high fever and chills, strong toxic and infectious syndrome, roseola petechial rash and change in the sensorium (status typhosus). Laboratory criteria - Demonstration of specific antibodies in the patient serum - Isolation of the cause in clinical specimens Case classification Suspected: N/A Probable: A clinically compatible and epidemically linked case Confirmed: A clinically compatible case that is laboratory confirmed.
Cyprus	Any person meeting the clinical and the laboratory criteria for rickettsioses so as to be classified either as probable or confirmed case (depending on the laboratory criteria)
Germany	Clinical description Clinical presentation of acute typhus, defined as - Fever Laboratory criteria Positive result with at least one of the following five methods: A) Direct detection of pathogen: - Nucleic acid detection (e.g. PCR) - Antigen detection by IFA only in tissue samples (e.g., spleen, lung) B) Indirect (serological) confirmation: - IgM antibody detection (e.g., ELISA), - Significant change in IgG titre between two samples (e.g. ELISA, IFT) - Significant antibody titre change between two samples using complement fixation test. Epidemiological link Epidemiological link with a laboratory-confirmed infection in a human through a common source of exposure (e.g. lice) considering the incubation period. Case classification: Clinical case with epidemiological or laboratory confirmation
Italy	Clinical + laboratory confirmation
Malta	Clinical description Acute onset of fever, with headache, generalised pains, prostration and a dull maculo-papular rash. Cough may also be present. Defervescence within 48 hours following tetracycline (or doxycycline) therapy strongly suggests rickettsial aetiology. The presence of an eschar suggests tick-borne typhus. Laboratory criteria Positive *Rickettsia* enzyme immunoassay

Portugal	Clinical criteria A disease characterized by sudden onset with fever, arthralgia and myalgia, and subsequent appearance (3 - 5 day) of non-pruritic maculopapular rash usually affects the palms and soles. A primary lesion in the skin often appears at the start, the site of the tick bite, with the appearance of ulcers 2-5 mm in diameter with a central zone and a dark red halo accompanied by regional lymphadenopathy. Laboratory criteria - Isolation of *R. conorii* in cell culture or - Detection of serum IgM antibodies *R. conorii* by indirect immunofluorescence or - 4 times increase in the IgG antibody titer between acute and convalescent phase by indirect immunofluorescence or ELISA or complement fixation reaction Case classification suspected case: compatible clinical description of the case confirmed case: case compatible with clinical description and confirmed by the laboratory
Spain	Clinical criteria and at least one of the following laboratory criteria: a. Isolation of *Rickettsia conorii* in skin biopsy. b. Detection of *Rickettsia conorii* genome in skin biopsy. c. Antigen of *Rickettsia conorii* in skin biopsy. d. Detection of serum IgM antibodies *R. conorii* by indirect immunofluorescence or detection of increased fourfold or greater antibody titer by indirect immunofluorescence

Annex 4 – Variables collected for rickettsioses cases by EU/EFTA countries

Country	Belgium	Cyprus	Czech Republic	France	Germany	Hungary	Italy	Latvia	Malta	Portugal	Slovenia
Notification source (GP, hospital, lab, other)	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓
Date of notification	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Presumed date of infection	✓		✓		✓		✓	✓	✓	✓	
Case classification (according to the case definition)		✓			✓		✓		✓	✓	
Demographic variables (age, gender)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Geographical location of residence: Eurostat NUTS1 (usually country regions)			✓	✓	✓	✓	✓	✓		✓	✓
Geographical location of residence: Eurostat NUTS2 (usually country provinces)					✓	✓	✓	✓			
Geographical location of residence: Eurostat NUTS3 (usually districts or counties)	✓	✓	✓	✓	✓	✓	✓	✓		✓	
Geographical location of presumed exposure: Eurostat NUTS1 (usually country regions)	✓	✓	✓		✓	✓	✓	✓		✓	
Geographical location of presumed exposure: Eurostat NUTS2 (usually country provinces)					✓		✓				
Geographical location of presumed exposure: Eurostat NUTS3 (usually districts or counties)					✓		✓	✓		✓	
Exposure to tick-bite(s)	✓			✓				✓	✓	✓	
Occupational exposures	✓					✓		✓	✓	✓	
Hospitalisation	✓	✓			✓	✓	✓	✓	✓	✓	✓
Laboratory test details	✓				✓			✓	✓	✓	
Clinical signs/symptoms	✓			✓	✓				✓	✓	
Clinical complications	✓	✓			✓			✓	✓	✓	
Outcome (dead/alive/disabled)	✓	✓			✓	✓	✓	✓	✓	✓	✓
Imported case	✓	✓	✓		✓	✓		✓	✓		
Rickettsia species	✓	✓	✓	✓		✓		✓		✓	✓
Other		✓				✓					

Annex 5 – Literature review on rickettsioses data availability - additional information

Summary of literature review on rickettsioses

Abstracts on rickettsioses		Number
Total abstracts reviewed		1522
Selected abstracts	Human	41
	Animals and vectors	80
	Serologic survey	14
Excluded abstracts	Country not on the list	831
	Incompatible time period	63
	Different disease/vectors	67
	Not addressing the aim of the study	305
	Non-understandable language	10
	Only imported cases	59
	Duplicated	27
	Other	14
Other	Not available	11

Rickettsioses data availability from literature search by country

Country	Abstracts on animals and vectors	Abstracts on humans	Cases retrieved from articles
Austria	1	--	--
Belgium	--	--	--
Bulgaria	1	--	--
Cyprus	2	--	--
Czech Republic	--	--	--
Denmark	2	--	--
Estonia	--	--	--
Finland	--	--	--
France	6	9	154
Germany	9	2	2
Greece	--	5	19
Hungary	1	--	--
Iceland	--	--	--
Ireland	1	--	--
Italy	14	--	--
Latvia	--	--	--
Lithuania	--	--	--
Luxembourg	1	--	--
Malta	--	1	33
Netherlands	2	--	--
Norway	--	--	--
Poland	6	--	--
Portugal	4	--	--
Romania	--	--	--
Slovakia	12	--	--
Slovenia	--	--	--
Spain	22	--	--
Sweden	2	2	2
Switzerland	1	--	--
UK	--	1	1
Total	87	20	211