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Ongoing outbreak of invasive listeriosis, Germany, 2012 to 2015

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Listeriosis patient isolates in Germany have shown a new identical pulsed-field gel electrophoresis (PFGE) pattern since 2012 (n = 66). Almost all isolates (*Listeria monocytogenes* serotype 1/2a) belonged to cases living in southern Germany, indicating an outbreak with a so far unknown source. Case numbers in 2015 are high (n = 28). No outbreak cases outside Germany have been reported. Next generation sequencing revealed the unique cluster type CT1248 and confirmed the outbreak. Investigations into the source are ongoing.

Since November 2012, a previously not observed pulsed-field gel electrophoresis (PFGE) pattern in human isolates of invasive *L. monocytogenes* serotype 1/2a has been detected in Germany with increasing frequency. Altogether 66 outbreak cases have been recorded, with 28 cases in 2015. Four cases were pregnancy-associated and six cases died in the course of the disease. Here we provide details of the ongoing outbreak.

Outbreak description

Since 2009, all German *Listeria* isolates submitted to the National Reference Centre (NRC) for Salmonella and other bacterial enterics at the Robert-Koch Institute (RKI) or to the Austrian-German binational reference laboratory (KL) for Listeria at the Austrian Agency for Health and Food Safety (AGES), have been tested with PFGE for clonal relationship. Submission of isolates is encouraged by public health authorities but is voluntary without legal obligation. Between November 2012 and November 2015, altogether 793 isolates from notified listeriosis cases were typed, which accounted for 45% of all cases in that period (n = 1,765). In southern Germany, this proportion was higher (ca 60%) and since 2012, human isolates of *L. monocytogenes* serotype 1/2a with the NRC internal nomenclature of the *Asc*I/*Apa*I pattern 13a/54 have been observed.

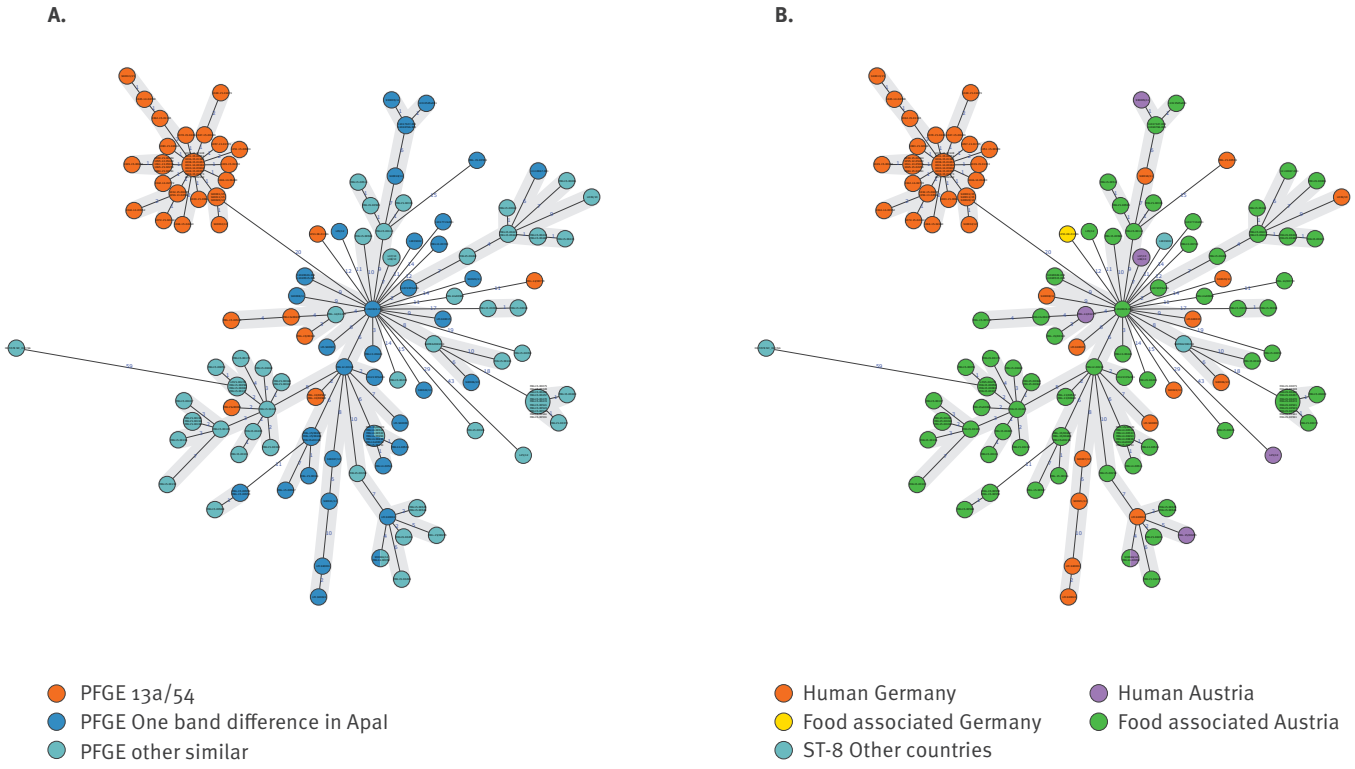
By 30 November 2015, the typing centres had received a total of 69 isolates with the 13a/54 PFGE pattern. Multilocus sequence typing (MLST) revealed sequence type 8 (www.pasteur.fr/mlst). After exclusion of three isolates (see below), next generation sequencing (NGS) was applied to 38 of 66 isolates using a published core genome MLST (cgMLST) [1]. All 38 patient isolates could be allocated to one cluster type (CT1248) (Figure 1).

We used the following case definition in our investigation: Possible outbreak cases were patients with the clinical picture of acute invasive listeriosis with onset since November 2012 with isolation of *Listeria* from normally sterile body fluids and detection of the characteristic PFGE pattern 13a/54. Confirmed cases were patients meeting the above criteria with isolates assigned to cluster CT1248 in NGS.

According to the Protection Against Infection Act of 2001, laboratory confirmation of *Listeria* from a normally sterile site is notifiable to local health departments which transmit information to RKI. Of the 69 isolates with the 13a/54 PFGE pattern, 66 could be assigned to surveillance cases reported in the mandatory notification system; of those, 38 were confirmed by NGS. Figure 2 illustrates the outbreak cases by month. There was a first peak in the second half of

Figure 1

Minimum Spanning Tree based on NGS allelic profiles of Listeria monocytogenes isolates, Germany, 2012–15 (n = 160)

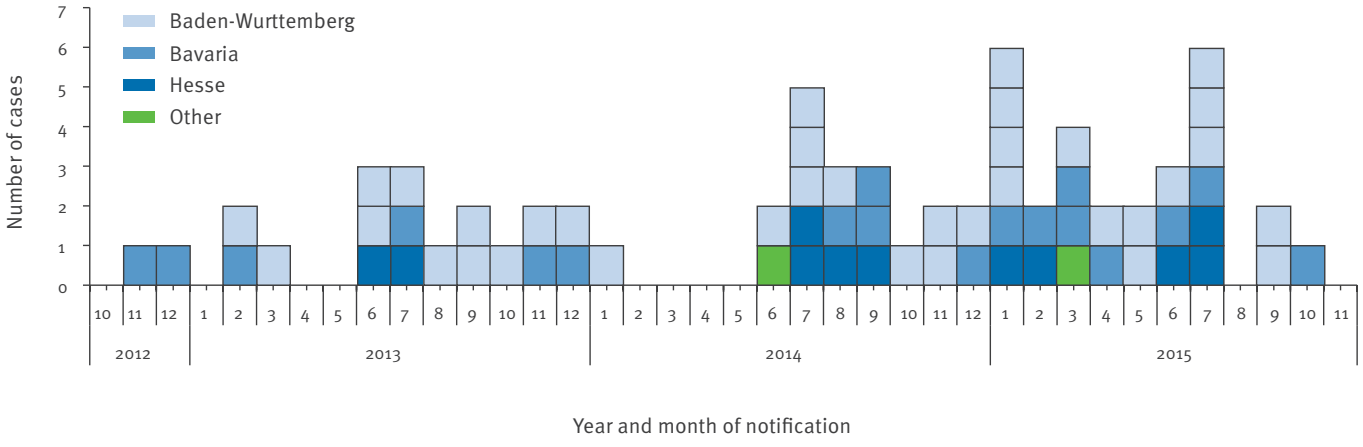


PFGE: pulsed-field gel electrophoresis.

After the evaluation scheme in [1]. Panel A: Sequence-based clonal relationship stratified for pulsed-field pattern designation to PFGE type 13a/54, a similar PFGE type with one band difference in ApaI and other similar PFGE types). Panel B: Stratified for the origin (food-borne case) of isolates. Each circle represents an allelic profile based on sequence analysis of 1,701 target genes. The numbers on the connecting lines illustrate the numbers of target genes with differing alleles. The different groups of strains are distinguished by the colours of the circles. Closely related genotypes (>10 allele difference) are shaded in grey and designated cluster type.

Figure 2

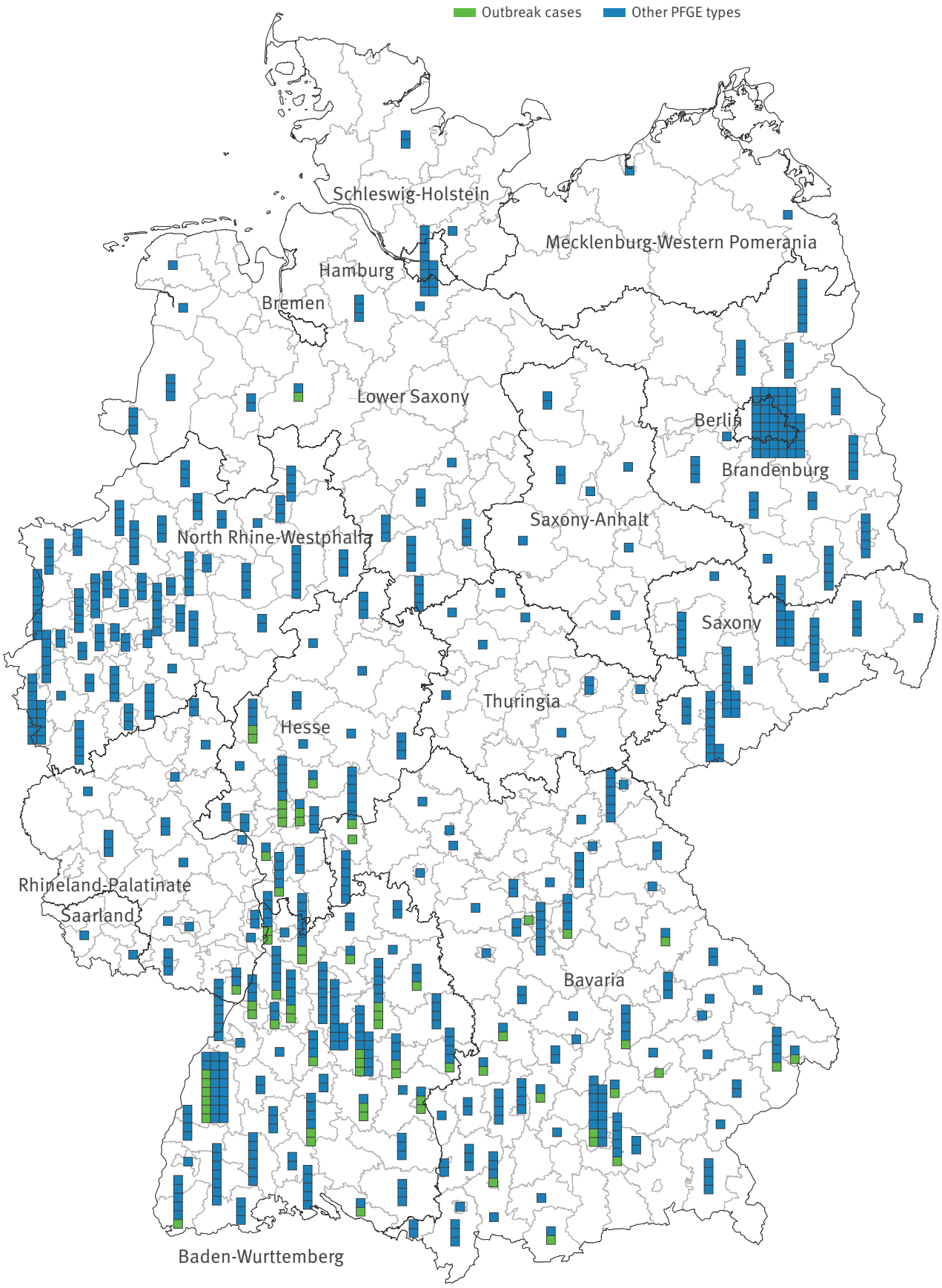
Temporal distribution of listeriosis outbreak cases (28 possible and 38 confirmed) with PFGE pattern 13a/54 and available notification date, Germany, 2012–15 (n = 66)



PFGE: pulsed-field gel electrophoresis.

Figure 3

Spatial distribution of listeriosis cases with known PFGE typing results on district level, Germany, 2012–15 (n = 838)



PFGE: pulsed-field gel electrophoresis.

In green the 66 outbreak-related cases (possible and confirmed). In blue cases with other PFGE types (n=772).

2013, but most cases have occurred since June 2014 (compared with a total of 609 invasive listeriosis cases in Germany in 2014). In 2015, this has so far been the most frequently occurring PFGE pattern among all *Listeria* isolates in molecular surveillance.

The geographical distribution was largely confined to the states of Baden-Wuerttemberg, Bavaria and Hesse, although PFGE typing is also frequently applied for isolates from the north of Germany (Figure 3). Only one case each was reported from Rhineland-Palatinate and Lower Saxony.

Four of the 66 cases were pregnancy-associated. Among 62 not pregnancy-associated outbreak patients 32 were men. The outbreak affected 38 senior citizens (≥ 70 years), 23 younger adults (18–69 years) and one two-year-old child. They did not differ from other listeriosis surveillance cases not related to the outbreak (n = 1,699) with respect to age (p = 0.628) and sex (p = 0.433). Of the 62 cases, 44 suffered from fever ≥ 38.5 °C, 16 had meningitis, 16 had septicaemia and for 15, other listeriosis-related symptoms were reported. Six (not pregnancy-associated) cases died; three of the deaths were confirmed to be due to listeriosis as the major cause.

This outbreak was communicated via the European Epidemic Intelligence Information System (EPIS) platform on 17 July 2015 and updated on 5 November 2015. None of the other participating countries reported cases with the outbreak PFGE pattern or NGS cluster types.

Investigation into the source of infection

Initial screening of food-related *Listeria* isolates in the strain collection of RKI and AGES found a total of six isolates (five from Austria and one from Germany) which had indistinguishable PFGE patterns but belonged to different NGS cluster types (Figure 1). Food consumption histories have been collected from a subset of cases via exploratory interviews by the health authorities since 2013. Furthermore, information on food consumption habits are recorded via collection of patients' grocery receipts [2]. Many patients can have difficulties recalling food consumption because of their age and their disease. Photo documentation of food items regularly purchased by some patients is used for visual support during interviews with other patients. Epidemiological studies were conducted in cooperation with regional and local health departments, considering incubation periods published by Goulet et al. [3].

Regarding the source of the causative food vehicle, the results showed a heterogeneous picture. Until now we have not observed cases with an epidemiological link to an institution (e.g. hospital infection). Preliminary results largely exclude fish and cheese products as a possible source but this has to be complemented by systematic screening of *Listeria* isolates collected from food. Based on sequencing results, a PCR protocol aiming to detect CT1248 was developed for screening of isolates and published on the KL website [4].

Background

L. monocytogenes, the causative agent of listeriosis is mostly caused by the consumption of contaminated food. The majority of infections are mild if they occur in younger, immunocompetent individuals except pregnant women. Infection during pregnancy can lead to miscarriage, stillbirth and serious health problems for the newborn. Invasive listeriosis can cause severe septicaemia, meningoencephalitis and a wide variety of focal infections. It is usually limited to the elderly and those with compromised immune systems or severe underlying medical conditions. Because of the severity of certain clinical manifestations (infections of the central nervous system, septicaemia and abortion), the high case-fatality rate of up to 30% and the long incubation time, human listeriosis is of major public health concern. A recent nationwide case–control study in Germany among sporadic disease cases detected cold cooked sausages, packaged cheese and pre-sliced cheese as risk foods [5]. Medical conditions associated with listeriosis are immunosuppressive therapy, immunocompromising disease and gastric acid suppression [5].

Public health assessment

When considering confirmed as well as possible cases, this is the largest outbreak of listeriosis described in Germany to date [6]. Considering underascertainment, under-reporting and the considerable proportion of isolates that are not typed, the size of the visible outbreak of invasive listeriosis is certainly underestimated. Furthermore, mild and non-invasive gastrointestinal cases, which can make up a significant proportion of disease cases, are not under surveillance in Germany. Until now, the cluster type CT1248 is confined to this outbreak and investigation via EPIS did not generate feedback on isolates with a related sequence in participating countries. Listeriosis cases have become more frequent over the past years in Germany [7] and elsewhere in Europe [8]. Investigations of listeriosis outbreaks are difficult due to the multitude of possible food vehicles including a broad range of ready-to-eat foods.

PFGE is suitable for screening but cannot confirm outbreak isolates, whereas NGS appears highly discriminatory and superior for the allocation of cases to the outbreak. The geographical limitation to southern Germany and the size of the outbreak area with a population of 27 million inhabitants suggest *Listeria*-contaminated food in a supra-regional supermarket grocery chain as the vehicle of infection. Although the number of new cases has decreased since August 2015, new outbreak cases are still being reported. We must therefore assume that the source of infection is still active and further cases are possible. Further epidemiological studies, laboratory investigations and

trace-back of food items are needed and ongoing to narrow down the source of infection.

Diagnostic laboratories are requested to send any *Listeria* isolates to one of the typing centres. The use of NGS is desirable as routine for all *Listeria* isolates collected for typing.

Acknowledgements

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Conflict of interest

None declared.

Authors' contributions

Wrote the manuscript: HW; performed epidemiological analysis: HW, SV; supervised outbreak: FA, ET, KS; regional surveillance: EA, DL, AH, KS; performed laboratory investigation: RP, AP; ET, PH, MB; performed phylogenetic analyses: WR, SH; all authors revised the manuscript.

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Tula hantavirus infection in a hospitalised patient, France, June 2015

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We report an infection with Tula virus in June 2015, leading to hospitalisation, in a patient living approximately 60 km east of Paris with no previous remarkable medical history. Clinical symptoms were limited to a fever syndrome with severe headache. The main laboratory findings included thrombocytopenia and elevated transaminase levels. Based on S (small) gene sequence analysis, the strain affecting the patient was closely related to strains detected in Central Europe, especially to a south-east German strain.

Case report

In June 2015, man in his mid-thirties presented to hospital, three days after the appearance of symptoms (day 3) including sudden fever onset, diffuse pain including back pain, headache and weakness. His previous lifetime medical history was unremarkable with no reported alcohol dependence. His body temperature was 39.6 °C and he reported a severe headache. Physical examination did not reveal any further abnormalities. Blood pressure, and heart and respiratory rate measures were normal. Blood test results however revealed thrombocytopenia, leucopenia, and elevated transaminase and C-reactive protein values (Table).

Results of a chest X-ray and magnetic resonance imaging of the brain found no abnormality. However, abdominal ultrasound demonstrated moderate enlargement of the liver and spleen (lengths 144 mm and 128 mm respectively). The patient was hospitalised and symptomatic treatment was carried out. Serological investigations were requested, to test for cytomegalovirus, Epstein–Barr virus, hantavirus, viral hepatitis, human immunodeficiency virus and parvovirus B19 infection. A microscopic haematuria was observed on day 6 (20,000 red blood cells/mL) but renal function remained unaltered (Table). Symptoms disappeared during the hospitalisation. Blood parameters returned to normal, in particular liver parameters and platelet count (Table). The patient was discharged on day 16.

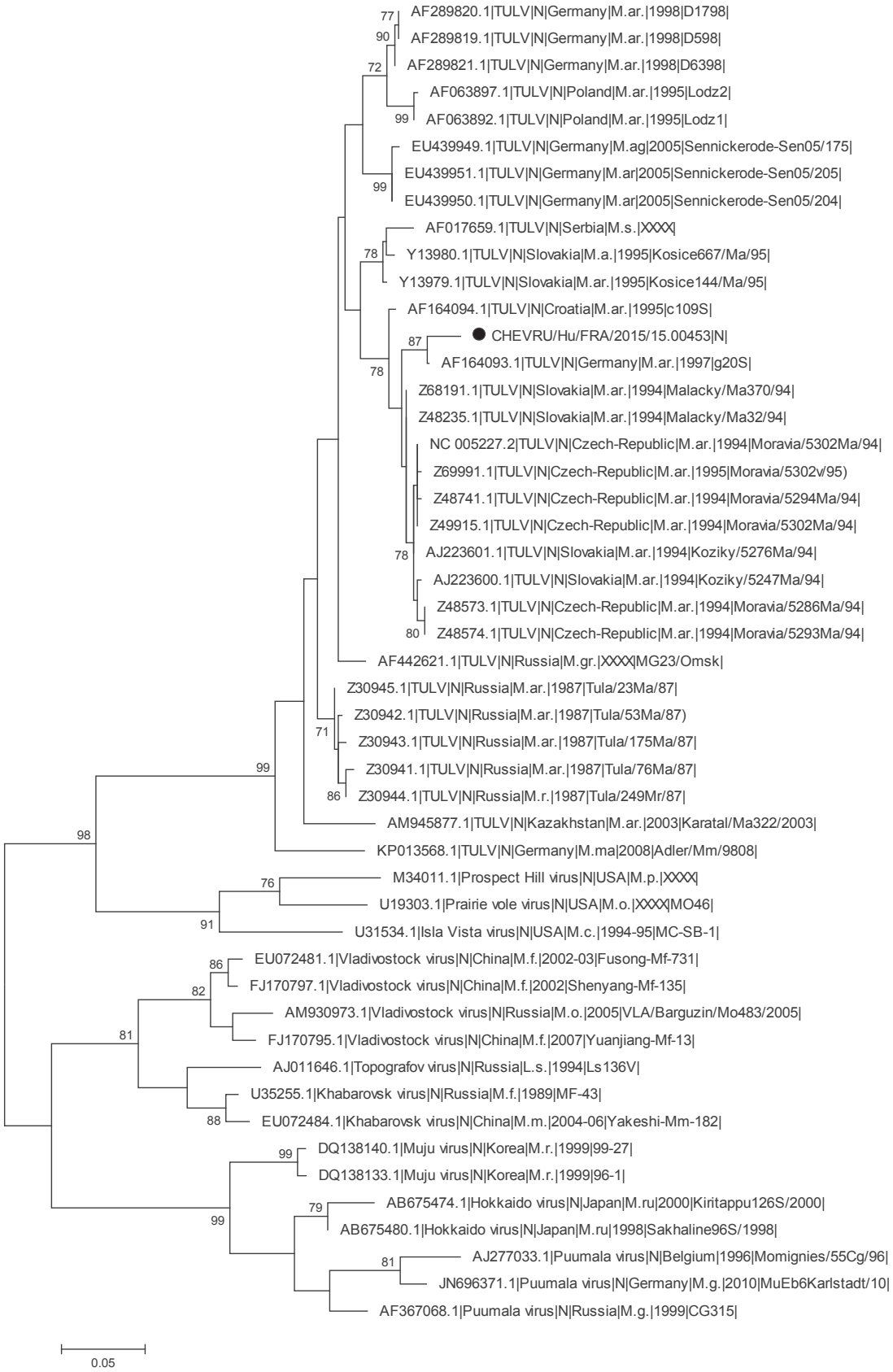
Aetiological investigation

Serological tests were negative, except for tests for the detection of IgM and IgG against hantaviruses (Hantavirus Pool 1 'Eurasia' IgG and Hantavirus Pool 1 'Eurasia' IgM; Euroimmun), including a mixture of purified recombinant nucleocapsid proteins from Hantaan, Dobrava, and Puumala virus (PUUV). These tests were positive on a serum sample collected on day 4 (ratios 1.8 and 4.7 for IgM and IgG respectively, both above the cut-off value of 1.1). As usual in France for surveillance purposes, the sample with positive results was then transferred to the National Reference Centre for Hantavirus. The acute hantavirus infection was serologically confirmed using PUUV native antigen in enzyme-linked immunosorbent assays and immunofluorescence assay, the results being negative using Seoul virus (SEOV) native antigen (both antigens are routinely used). The serum sample was subsequently tested for the presence of hantavirus RNA. The assay was negative using a real-time reverse transcription-polymerase chain reaction (RT-PCR) targeting part of the small (S) genome segment of PUUV, but positive using a pan-hantavirus nested RT-PCR targeting part of the large (L) segment, and a Arvicolinae-borne hantavirus nested RT-PCR targeting part of the S segment, PUUV being used as positive control [1-3].

Amplicons were sequenced and an analysis by basic local alignment search tool indicated that both sequences were very similar to those of Tula virus (TULV) strains, especially to that of the south-east German rodent strain GER/152/Arv (GenBank accession numbers: HQ728459 and HQ697350). Compared to this strain, the patient strain had 89.5% and 90.2% respective nucleotide (nt) sequence identities to the partial

Figure

Phylogenetic analysis of the Tula hantavirus strain found in an infected patient in France, June 2015



The phylogenetic analysis is based on the entire nucleotide (nt) coding sequence of the small (S) genome segment. Sequences from strains of Tula virus and other Arvicolinae-borne hantaviruses are included in the phylogenetic tree and the French Tula virus strain CHEVRU/Hu/FRA/2015/15.00453 retrieved in this study is indicated by a full circle. Bootstrap percentages ≥ 70%, from 500 re-samplings are indicated at each node. The scale bar indicates nt substitutions per site. Sequences were aligned by Muscle, and the tree was constructed using molecular evolutionary genetics analysis (MEGA) version 5.1 with the maximum likelihood method. According to the best fit substitution model proposed, analyses were performed applying the Tamura Nei model using a gamma distribution (+G) with five rate categories.

Table

Haematological and biochemical findings of a Tula hantavirus-infected patient, France, June 2015

Parameters measured on blood specimen	Unit	Norm	Day of sampling[a]					
			Day 3	Day 6	Day 9	Day 11	Day 16	Day 25
White cells	10^9/L	4–10	2.1	6.4	4.3	5.4	4.5	4.6
Platelets	10^9/L	150–450	100	31	88	177	300	254
Haemoglobin	g/dL	13–17	15.7	16.5	14.0	14.9	14,5	13.8
C-reactive protein	mg/L	‹5	17	19	4	ND	ND	ND
Aspartate aminotransferase	IU/L	10–50	114	174	106	188	55	43
Alanine transaminase	IU/L	10–50	163	232	223	322	162	78
Gamma-glutamyltransferase	IU/L	8–61	112	273	228	236	153	121
Prothrombin ratio	%	70–100	88	97	ND	ND	ND	ND
Creatinine	µmol/L	62–106	93	72	81	ND	80	80

IU: international unit; ND: not done.

[a] The sampling day refers to the number of days after symptom onset.

L (n=347 nt) and S segments (n=307 nt). This corresponded, at the amino acid (aa) level, to 99.1% (n=115) and 100% (n=102) aa identity (partial L sequence deposited in GenBank database under accession number: KU297981).

The complete S coding DNA sequence (CDS) (GenBank accession number: KT946591) was recovered via three nested RT-PCRs using primers reported elsewhere [4], producing three overlapping amplicons. The aa sequence (n=429 aa) was similar to those of TULV strains reported in GenBank (divergence 0.2 to 4.9%), and presented highest similarity at the nt and aa levels with the sequence of the rodent Bavarian German strain g20 (GenBank accession number: AF164093). Using molecular evolutionary genetics analysis (MEGA) version 5.1 [5], a phylogenetic analysis based on the S segment coding domain sequence confirmed that the strain – named CHEVRU/Hu/FRA/2015/15.00453 – belonged to the TULV species, and was most closely related to the g20 south-east German strain (Figure).

Sequence comparison was also performed with a reduction of the S CDS dataset to 297 nt (positions 865–1,161 according to the numbering of our sequence) in order to include the only two TULV partial sequences reported from France and detected in *Microtus arvalis* [6]. Divergence at the aa level was 4.0% with these two sequences (compared to only 1.0% with the g20 sequence). The phylogenetic analysis was also performed with this dataset. The French human and animal strains were not closely related but the statistical support was low (data not shown).

Background

Five zoonotic hantaviruses have been described in Europe: Dobrava-Belgrade (DOBV), PUUV, Saaremaa, SEOV and TULV. Among these, PUUV and DOBV are responsible for most human infections, causing mild to severe haemorrhagic fever with renal syndrome [7-9]. The pathogenic potential of TULV in humans is not well known. Although, this virus was found in rodent samples from numerous European countries (including France) after its first identification in 1994 from *Microtus* spp. rodents sampled in 1987 in Tula (Russia), it has only been reported once in humans, from an immunocompromised patient [7-11].

Epidemiological investigation

The investigation was limited to an interview of the patient. The patient lived in a small rural village, surrounded by flat open fields of corn, wheat and sugar beet, in the west part of the Seine-et-Marne department (ca 60 km east of Paris). He was working as an aircraft engine technician. During the six weeks before disease onset, he had often thrown away, barehanded, voles (unidentified species) taken back home by his pet cat. He reported during that period one bite by a live vole. Other potential sources of contamination were not reported.

Discussion

TULV infection in humans without symptoms has been serologically documented [12]. However, evidence of disease in patients is rare with only three such cases being reported (see [7,10] for review). Among these, one, which occurred after a wild rodent bite remained controversial, as clinical symptoms were more compatible with rat-bite fever and late seroconversion suggested that although TULV infection may have occurred, it was perhaps not responsible for the symptoms [13]. From the three reported symptomatic cases, TULV was detected in only one, which was immunocompromised. The molecular evidence of TULV infection in our patient confirms the pathogenic potential of TULV, as this lead to hospitalisation. Furthermore, we mainly observed a fever syndrome with an alteration of the liver function, whereas the two previous non-controversial cases reported, both exhibited a renal and pulmonary syndrome [10,14]. Reported cases are too rare to draw any conclusions about the main tropism of TULV.

Routine hantavirus diagnosis in France is based on commercial serological assays that do not allow discrimination between different hantavirus infections, and consequently diagnosed infections are mostly attributed to PUUV, the main prevalent hantavirus in Europe. Using serological and molecular diagnostic assays as confirmation tests, we recently confirmed virologically for the first time in Europe a human SEOV infection [15]. The diagnostic of this TULV and SEOV infection indicate that molecular diagnostics of hantavirus should be promoted in order to discriminate between hantaviruses involved in human diseases.

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Conflict of interest

None declared.

Authors' contributions

Samir Herti and Nourredine Boukezia took care of the patient. Monique Debruyne performed hantavirus serological analysis. Damien Carli and Jean-Marc Reynes performed the molecular detection and analysis of the Tula virus strain. Jean-Marc Reynes and Samir Herti wrote the manuscript. All co-authors reviewed the manuscript.

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Research article

Assessment of the MSF triage system, separating patients into different wards pending Ebola virus laboratory confirmation, Kailahun, Sierra Leone, July to September 2014

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Prevention of nosocomial Ebola virus (EBOV) infection among patients admitted to an Ebola management centre (EMC) is paramount. Current Médecins Sans Frontières (MSF) guidelines recommend classifying admitted patients at triage into suspect and highly-suspect categories pending laboratory confirmation. We investigated the performance of the MSF triage system to separate patients with subsequent EBOV-positive laboratory test (true-positive admissions) from patients who were initially admitted on clinical grounds but subsequently tested EBOV-negative (false-positive admissions). We calculated standard diagnostic test statistics for triage allocation into suspect or highly-suspect wards (index test) and subsequent positive or negative laboratory results (reference test) among 433 patients admitted into the MSF EMC Kailahun, Sierra Leone, between 1 July and 30 September 2014. 254 (59%) of admissions were classified as highly-suspect, the remaining 179 (41%) as suspect. 276 (64%) were true-positive admissions, leaving 157 (36.3%) false-positive admissions exposed to the risk of nosocomial EBOV infection. The positive predictive value for receiving a positive laboratory result after being allocated to the highly-suspect ward was 76%. The corresponding negative predictive value was 54%. Sensitivity and specificity were 70% and 61%, respectively. Results for accurate patient classification were unconvincing. The current triage system should be changed. Whenever possible, patients should be accommodated in single compartments pending laboratory confirmation. Furthermore, the initial triage step on whether or not to admit a patient in the first place must be improved. What is ultimately needed is a point-of-care EBOV diagnostic test that is reliable, accurate, robust, mobile, affordable, easy to use outside strict biosafety protocols, providing results with quick turnaround time.

Introduction

The current Ebola virus disease (EVD) epidemic in West Africa is unprecedented in history [1]. After the outbreak was officially confirmed in Guéckedou, Guinea, on 23 March 2014 [2] and subsequently developed into a major epidemic with widespread infection in most parts of Guinea, Liberia, Sierra Leone [3], the World Health Organization (WHO) declared the situation a 'Public Health Emergency of International Concern' on 8 August 2014 [4]. By that time, Doctors Without Borders / Médecins Sans Frontières (MSF) was already running six Ebola management centres (EMC) in the these most-affected countries – including one in Kailahun district, Sierra Leone [5].

Ebola virus (EBOV) transmission occurs between humans through contact with body fluids from persons diseased with or who died from EVD [6]. Typical symptoms are sudden onset of fever and a variety of non-specific symptoms such as fatigue, headache, myalgia/arthralgia or nausea within an incubation period of two to 21 days [7,8]. Infectiousness succeeds onset of clinical symptoms and increases with symptom severity [9]. While the reproductive number of Ebola virus (EBOV) is considerably smaller than that of other more common infectious agents, it is highly contagious in case of direct physical contact [10,11]. Infection is confirmed by laboratory testing, most often by quantitative reverse-transcriptase PCR (qRT-PCR) from venous whole blood samples [12].

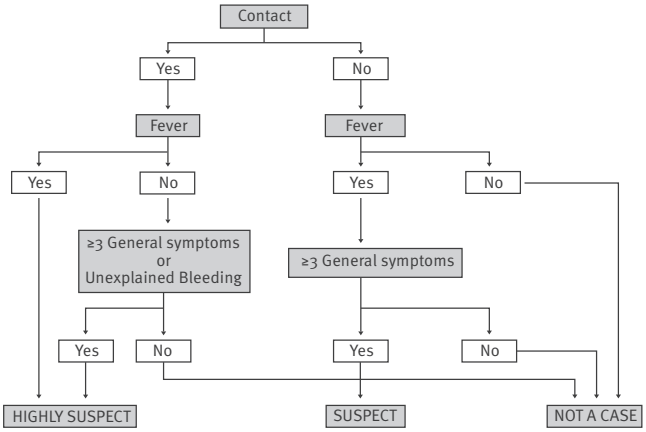
Figure 1

Map of the Médecins Sans Frontières Ebola management centre, Kailahun, Sierra Leone, 1 July–30 September 2014

Source: adapted from Sterk E. Filovirus haemorrhagic fever guideline. Médecins Sans Frontières; 2008.

Figure 2

Médecins Sans Frontières triage algorithm for separating admitted patients into suspect or highly-suspect wards as used at the Ebola management centre Kailahun, Sierra Leone, 1 July–30 September 2014



Source: adapted from Sterk E. Filovirus Haemorrhagic Fever Guideline. Médecins Sans Frontières; 2008.

In the absence of curative treatment, quick and strict isolation of symptomatic persons in EMCs is the main intervention to prevent new infections [13,14]. Admission into an EMC depends on clinical and epidemiological criteria until EBOV infection status is laboratory confirmed. A number of case definitions have been developed for different settings of the current outbreak in West Africa [15-17]. Correct admission of EVD patients is difficult even for experienced medical staff due to non-specificity of symptoms and numerous other diseases with similar early symptoms prevalent in the region such as Lassa haemoragic fever or malaria.

Nosocomial infections among false-positive admissions between the time of admission and laboratory EBOV confirmation is a matter of great concern in the management of an EMC [18,19]. As a basic preventive measure, it is good practice to physically separate patients who are admitted based on clinical symptoms awaiting laboratory confirmation from patients who are laboratory-confirmed EVD cases [20]. Provided that laboratory capacity is available on site, this takes a few hours for patients with symptom onset more than 72 hours before admission. Although the PCR used for laboratory confirmation is highly sensitive, patients with symptom onset less than 72 hours before admission can test negative due to low viraemia during the early stage of disease [21-23]. These patients have to be re-tested at minimum 72 hours after symptom onset and are hence required to stay admitted for up to three days until their final infection status can be established [22].

To further reduce the risk of nosocomial EBOV transmission during this period among patients who turn out to be EBOV-negative, MSF classifies patients at admission into suspect and highly-suspect categories. Suspect and highly-suspect patients are kept in separate wards until final laboratory results are available, after which they are either transferred to the confirmed ward or discharged as not a case. The classification into suspect and highly suspect is based on a standardised algorithm using the patient's reported contact history and a combination of clinical symptoms [24].

It is not known to what extent this triage system serves to differentiate between patients who subsequently test EBOV-positive by PCR (true-positive admissions) and patients subsequently testing EBOV-negative (false-positive admissions). Such information is crucial to decide whether such a refined three-pronged triage process justifies the ressource-intensive maintenance of separate wards for suspect and highly-suspect patients in an EMC.

We aimed to investigate how well triage at admission into suspect and highly-suspect patients can separate between true-positive and false-positive admissions.

Methods

Setting

Kailahun district has an estimated population of 360,000 and is located in the Eastern Province of Sierra Leone bordering Guinea and Liberia [25]. Its capital and largest city is the town of Kailahun, located ca 80 km from Guéckedou, Guinea where the first EVD case in West Africa was recorded on 25 March 2014 [26]. Kailahun district has been the epicentre since the beginning of the EVD epidemic in Sierra Leone with intense transmission occurring at all levels of society [27].

MSF activities in Kailahun started in June 2014 with the erection of an EMC [5]. Initial bed capacity was 50 and increased to 80 in July due to high case load. The management of this particular EMC has already been described in detail elsewhere [28]. Its setup follows the standard MSF EMC layout with separate wards for suspect, highly-suspect, and confirmed cases (Figure 1).

Admission, triage and laboratory testing

Records from all patients who fulfilled the MSF EVD case definition criteria for admission and were hence admitted into the MSF EMC in Kailahun between 1 July and 30 September 2014 were used in this analysis. During the time of analysis the triage system in the MSF EMC in Kailahun was three-pronged with suspect, highly suspect and not a case as outcomes as per MSF guidelines [24]. All patients fulfilling the criteria for either suspect, highly suspect, or confirmed EVD case were admitted (Table 1 and Table 2). Patients who did not qualify for admission were cleared to leave the EMC as soon as possible. No detailed medical or epidemiological information was kept from these patients due to high work load.

Table 1

Triage criteria at Médecins Sans Frontières Ebola management centre, Kailahun, Sierra Leone, 1 July–30 September 2014

Criteria[a]	Sets of criteria to be fulfilled for different wards				
	Suspect	Highly suspect	Highly suspect	Highly suspect	Confirmed
Positive contact history	–	X	X	X	–
Fever	X	X	–	–	–
≥ 3 General symptoms	X	–	X	–	–
Unexplained bleeding	–	–	–	X	–
Positive laboratory EBOV test result[b]	–	–	–	–	X

EBOV: Ebola virus.

[a] See Table 2 for definitions.

[b] For referral patients.

Patients fulfilling the admission criteria were allocated into the suspect ward if they presented with fever (axillary temperature ≥ 37.5 °C) plus at least three of the following general symptoms: abdominal pain, diarrhoea, difficulties breathing, difficulties swallowing, general muscular or articular pain, headache, hiccups, intense fatigue, nausea/loss of appetite, or vomiting. Patient with a positive contact history plus fever; or with a positive contact history plus at least three general symptoms; or with a positive contact history plus unexplained bleeding, were allocated into the highly-suspect ward (Table 1 and Figure 2). Patients in the suspect and highly-suspect wards were not allowed to mingle, and toilets and hand washing points were separate for each ward.

A peripheral venous blood sample was drawn for PCR testing from all admitted patients and tested for presence of Zaire EBOV on qRT-PCR assays for RNA-dependent RNA polymerase (L) and nucleoprotein (NP) target genes [29] using RNA Master Hydrolysis reagents on a Lightcycler Nano platform (Roche Diagnostics, Laval QC, Canada). Cycle threshold (CT) values below 40 were considered EBOV positive. Patients whose test returned positive were transferred into the confirmed ward. Patients with a negative PCR result were discharged immediately if their onset of symptoms was more than 72 hours prior. For patients with a negative result and symptom onset less than 72 hours prior, a second sample was drawn at least 72 hours after the reported time of symptom onset [22]. A field laboratory was operating on site, which was able to provide same-day results for samples taken during morning hours. However, since most admissions occurred during the afternoon and evening times, many admitted patients had to stay overnight in either the suspect or highly-suspect ward until a blood sample was taken and analysed the following day.

Data source and analysis

Demographic, epidemiological and clinical information of all admissions was routinely collected during triage in paper-based registers. From this, operationally relevant data were entered on a daily basis into the MS Excel-based project database, which was used for this analysis: patient age (in years), sex (male, female), date of symptom onset, date of admission, triage ward allocation (suspect, highly suspect), laboratory test result (positive, negative and CT value from PCR testing at admission), treatment outcome (discharged as not a case, discharged cured, death, transferred out), and date of outcome.

Percentages and medians were calculated to describe patient characteristics at admission and during the course of treatment. Overall sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (PLR) and negative likelihood ratio (NLR) were calculated for the triage decision into suspect or highly-suspect ward (index test) with laboratory PCR result as gold standard (reference test). PPVs and NPVs are dependent on the pre-test probability, with increasing PPV and decreasing NPV the higher the pre-test probability ceteri paribus [30]. In our situation, the pre-test probability for at the classification into suspect or highly suspect was defined by the overall proportion of true-positive admissions (patients with subsequent laboratory-confirmed positive test result) during the initial triage decision to admit or not to admit a patient. Therefore, PPV and NPV were also calculated for different weekly rates of true-positive admissions: equal or less than 50%, 51 to 70%, and more than 70%. Software package STATA v.11 (Stata Corporation, Texas 77845, US) was used for the statistical analysis.

Ethics

This research fulfilled the MSF Ethics Review Board (Geneva, Switzerland) criteria for exemption from full ethics review. This study was conducted as part of a formal project agreement with the Government of Sierra Leone and approved by the health authorities of Kailahun district.

Results

Records from 433 patients admitted between 1 July and 30 September 2014 were included in the analysis. 244 (57%) of these patients were male, median age was 28

Table 2

Definitions of the admission and triage criteria at Médecins Sans Frontières Ebola management centre Kailahun, Sierra Leone, 1 July–30 September 2014

Criteria	Definition
Fever	Sudden onset rise of axillary temperature›37.5 °C.
Contact history	Sharing the same bed, household or meals, or touching the same objects as a suspected, probable or confirmed EVD case within the last 21 days.
	Caring for a suspected, probable or confirmed EVD case including touching body fluids within the last 21 days.
	Participating in funeral practices with direct contact of the corpse or objects used during funeral of a suspected, probable or confirmed EVD case within the last 21 days.
General symptoms	Headache
	Vomiting
	Nausea
	Loss of appetite
	Diarrhoea
	Intense fatigue
	Abdominal pain
	General muscular or articular pain
	Difficulties swallowing
	Difficulties breathing
	Hiccups

EVD: Ebola virus disease; EBOV: Ebola virus.

years (interquartile range (IQR): 19–40), and median duration between symptom onset and admission was four days (IQR: 2–7) (Table 3A). The median duration of hospitalisation varied between one, four and 15 days for patients discharged as not a case, dead and cured, respectively (Table 3C). The case fatality ratio among laboratory-confirmed positive patients with available clinical outcome was 51% (131/255). Sixteen patients died before their positive laboratory result became available. All of them had been allocated into the highly-suspect ward.

Of the 433 admitted patients, 254 (59%) including 128 men and 126 women were triaged into the highly-suspect ward. The remaining 179 (41%) admissions were considered suspect and comprised 116 men and 63 women. The vast majority of laboratory results were obtained at the same or the following day of admission (median: 1 day; IQR: 1–1).

Overall, 276 (64%) of the admitted patients, including 136 men, had a subsequent positive laboratory result (true-positive admissions), leaving 157 (36%) with subsequent negative laboratory result (false-positive admissions) exposed to the risk of nosocomial EBOV infection (Table 3B).

The PPV for receiving a subsequent positive laboratory test result after being allocated into the highly-suspect ward was 76% (95% confidence interval (CI): 70–81). The corresponding NPV, i.e. receiving a negative laboratory test result for the suspect ward, was 54% (95% CI: 46–61). Sensitivity, specificity, PLR and NLP were 70%, 61%, 2% and less than 1%, respectively (Table 4).

Among the 157 false-positive admissions, 96 (61%) patients were allocated into the suspect ward and thus would from this triage system have been less exposed to infected patients. Of these 96 patients, 71 were male with median age of 25 years (IQR: 19–41), and 25 were female with median age of 30 (IQR: 25–40). The test results were available on the same day of admission for 26 of these patients (27%), the next day for 61 (63%), two days after for six (6%) and subsequent to three days for one (1%). Two patients (2%) had missing values for the admission-to-result duration.

In contrast, 61 (39%) false-positive admissions were allocated to the highly-suspect ward and were thus exposed to a potentially increased EBOV-contaminated surrounding in that ward while awaiting their laboratory test result. Of these 61 patients, 37 were male with median age of 31 years (IQR: 23.5–41), and 24 were female with median age of 26 years (IQR: 14–40). Most patients received their test results within the first day after admission, with 17 (28%) getting results on the same day, 32 (52%) the day after, six (10%) on the second day, and four (7%) subsequent to three days. Data were missing for two (3%) regarding admission-to-result duration.

For patients admitted during weeks with a true-positive admission rate (i.e. pre-test probability) of≤50%, 51–70% and›70%, the PPVs were 60%, 72% and 85%, respectively; the corresponding NPVs were 64%, 45% and 46% (Table 5).

The overall median CT value of the admission PCR result was 24 (IQR: 21–32). There was no substantial difference in median CT values between patients triaged into the suspect and the highly-suspect ward: 25 (IQR: 25–32) and 24 (IQR: 21–32), respectively (p-value from Wilcoxon rank-sum test: 0.222).

Discussion

To our knowledge, this was the first assessment of a three-pronged triage system in an EMC with EVD patients being classified as suspect or highly suspect upon admission until laboratory confirmation.

The overall proportion of laboratory-confirmed EVD cases among admitted patients (true-positive admissions) at the EMC in Kailahun of 64% (n=276/433) was substantially higher than observed during a study in Conakry, Guinea, (46%, n=37/80) [31] and similar to the six month average seen in Liberia (57%, n=2,941/5,132) [32]. However, this proportion alone is not an good indicator for triage quality since it is

Table 3

Characteristics of patients admitted, triaged, and treated at the Médecins Sans Frontières Ebola management centre Kailahun, Sierra Leone, 1 July–30 September 2014 (n=433)

Characteristics of patients	N (%)[a]
At admission	
Sex	
Male	244 (56)
Female	189 (44)
Age (years)	
<18	93 (21)
18–37	206 (48)
38–57	100 (23)
≥58	27 (6)
Missing values	7 (2)
Median (IQR; range)	28 (19–40; 1–80)
Duration between symptom onset and admission (days)	
0–3	169 (39)
4–7	144 (33)
>7	68 (16)
Missing values	52 (12)
Median (IQR; range)	4 (2–7; 0–27)
During triage	
Ward triage	
Suspect	179 (41)
Highly suspect	254 (59)
Laboratory result	
Negative	157 (36)
Positive	276 (64)
Duration between admission and laboratory result (days)	
0	70 (16)
1	331 (76)
2	18 (4)
3	7 (2)
Missing values	7 (2)
Median (IQR; range)	1 (1–1; 0–3)
During treatment	
Outcome	
Not a case	150 (35)
Cured	124 (29)
Dead	131 (30)
Transferred out	4 (1)
Missing values	24 (6)
Duration between admission and clinical outcome by type of outcome	
Not a case (median, IQR, range)	1 (1–2; 0–7)
Cured (median, IQR, range)	15 (10.5–19; 4–35)
Dead (median, IQR, range)	4 (2–6; 0–31)
Transferred out (median, IQR, range)	–[b]
Missing values	21 (5)
Overall (median, IQR, range)	4 (2–10; 0–35)

IQR: interquartile range.

[a] Unless otherwise specified in row headings, percentages are shown in the column and are based on the column total for the subsection in question.

[b] No observations.

Table 4

Overall test statistics for ward triage into suspect or highly suspect (index test) and Ebola virus positive or negative laboratory result (reference test), Médecins Sans Frontières Ebola management centre Kailahun, Sierra Leone, 1 July–30 September 2014 (n=433 patients)

Test statistics	% (95% CI)
Positive predictive value	76.0 (70.2–81.1)
Negative predictive value	53.6 (46.0–61.1)
Sensitivity	69.9 (64.1–75.3)
Specificity	61.1 (53.1–68.8)
Positive likelihood ratio	1.8 (1.5–2.2)
Negative likelihood ratio	0.5 (0.4–0.6)

CI: confidence interval; EBOV: Ebola virus.

Correct classifications: 193 among 254 highly-suspect patients (76%) tested EBOV positive. 96 among 179 suspect patients (54%) tested EBOV negative. False classification: 61 among 254 highly-suspect patients (24%) tested EBOV negative. 83 among 179 suspect patients (46%) tested EBOV positive.

subject to many factors unrelated to triage such as access and acceptability of the EMC, community perception of the nature and presentation of EVD, survival bias, EVD incidence in the source population, stage of the epidemic etc. Also, too rigid admission criteria are not desirable from a public health point of view since a true-positive admission ratio that approaches 100% increases the likelihood that a substantial proportion of patients with EVD are not recognised at triage and sent back into their community infecting others.

Our findings reveal that 157 (36%) of patients were admitted into the EMC Kailahun on false-positive clinical grounds. These patients were hence exposed to the risk of nosocomial EBOV infection in the EMC until they received their laboratory result. This risk was reduced in Kailahun thanks to a laboratory on site that was able to provide PCR results within one day or less for the vast majority of patients. However, this was not the case for many treatment settings during most parts of the current outbreak due to insufficient laboratory capacity, which led to substantial delays in EBOV status confirmation for many patients in other centres when caseloads were high [33].

The classification of true-positive admissions into the highly-suspect ward and of false-positive admissions into the suspect ward by the triage system applied in the EMC Kailahun showed mixed results. Considering that this was an additional triage step among patients who already fitted the EVD case definition criteria for admission, we expected a relatively high PPV (i.e. proportion of patients allocated into the highly-suspect ward who had a subsequent positive laboratory test) and a relatively lower NPV (i.e. proportion of patients allocated into the suspect ward that had a subsequent negative laboratory test). This was confirmed by an overall PPV of 76% and a corresponding overall NPV of 54% (Table 4). The ratio of the PLR (1.8) and NLR (0.5)

Table 5

Predictive values by weekly true-positive admission rate (pre-test probability) Médecins Sans Frontières Ebola management centre Kailahun, Sierra Leone, 1 July–30 September 2014 (n=433 patients)

Pre-test probability (%)	True-positive admissions classified as 'highly suspect'	True-negative admissions classifications classified as 'suspect'	Positive predictive value % (95% CI)	Negative predictive value % (95% CI)
≤50 (n=135)	33/55	51/80	60.0 (45.9–73.0)	63.7 (52.2–74.2)
>50 –≤70 (n=121)	52/72	22/49	72.2 (60.4–82.1)	44.9 (30.7–59.8)
>70 (n=177)	108/127	23/50	85.0 (77.6–90.7)	46.0 (31.8–60.7)
Overall	193/254	96/179	76.0 (70.2–81.1)	53.6 (46.0–61.1)

CI: confidence interval.

was 3.6 (95% CI: 2.4–5.5), which suggests that correct ward allocation was very unlikely due to chance.

The proportion of patients in the suspect ward that turned out to be EBOV positive was 46% (83/179). Under the assumption that this translated into a reduced risk of nosocomial infection compared with the overall EBOV positivity proportion of 64% (n=276/433), a total of 96 (61%) among the false-positive admissions allocated into the suspect ward were exposed to a less risky environment thanks to this additional triage step. However, this in turn also implied that 61 (39%) of the false-positive admissions allocated in the highly-suspect ward, where an elevated EBOV-positivity surrounding of 76% (n=193/254) was recorded, were exposed to a more risky environment. However, cycle threshold values, a proxy for viral load in blood, from admission test results did not differ between wards, suggesting that EBOV positive patients in either ward were equally infectious.

As to be expected, PPV and NPV varied reciprocally for different true-positive admission rates (i.e. pre-test probabilities). The PPV of ward allocation was 60% during weeks with true-positive admission rates of 50% or less, and increased substantially to 85% during weeks with more than 70% true-positive admission rates. The corresponding NPV decreased from 64% during weeks with low true-positive admission rates to 46% when weekly true-positive admission rates were above 70% (Table 5).

Triage of EVD patients is an immensely difficult yet crucial task, in particular at times when the caseload exceeds capacities as occurred in the EMC Kailahun during the time of analysis. It requires substantial experience, which is problematic to obtain with high staff turnover. MSF tried to address this problem by developing a clear and standardised triage algorithm for patient classification. Also, triage at the EMC Kailahun was always done in pairs of at least one national staff together with one international staff to overcome cultural and linguistic barriers as much as possible.

Physical barriers, however, remained. Any clinical assessment could only be done by distance of minimum two metres across a double fence. No additional diagnostic methods other than a thermometer could be used. Also, many EVD patients at admission showed signs of confusion or exhaustion, or were otherwise clinically too unwell to describe their symptoms or contact history in detail. Furthermore, patients were often scared to disclose behaviour that, due to intense health promotion activities, had become proscribed, such as body washing at funerals or physical contact with persons showing EVD symptoms. Also, due to the high caseload it was not always possible to assure privacy during triage. This might have further limited the quality of information provided by patients during the triage process.

Timely isolation is paramount in order to break chains of transmission during an EVD outbreak. The sooner an infected person gets isolated after symptom onset the smaller the chance of infecting others. In this study, the median time span between symptom onset and admission was four days (IQR: 2–7). This delay was most likely a driving factor for the continuous transmission as observed in Kailahun district, and substantial efforts were made to reduce it. However, the earlier an infected person presents at the EMC, the less pronounced and specific are the symptoms, which in turn further complicates correct patient triage at admission.

The construction and maintenance of two separate wards for patients awaiting laboratory confirmation poses a substantial burden on the logistics, the water and sanitation, and the infection control team of an EMC. Duplicate infrastructure and more staff and supply are required. More entries into the high risk zone by healthcare workers are needed to assure adequate patient care in the separate wards, which increases the risk of EBOV exposure incidents for staff. Balancing these factors against the ambivalent findings of this analysis calls the justification of the three-pronged MSF triage system in its current form into question.

Ideally, admitted patients should be accommodated in single compartments before laboratory confirmation to minimise nosocomial EBOV transmission in an EMC. This, however, was not possible in Kailahun due to high case load at that time. Alternatively, instead of using a

rather sophisticated algorithm requiring detailed contact and clinical information, a simplified classification into liquid producing patients (i.e. patients with bleeding, diarrhoea or vomiting) and non-liquid producing patients might be advisable. This would be easier to apply for healthcare workers and would make triage quicker, while focussing on the probability of transmitting EBOV infection among patients rather than on the probability of an individual patient testing EBOV-positive. However, such a triage system would warrant further research before being implemented.

This research was subject to a number of limitations. Most importantly, the actual incidence and prevention of nosocomial infections among patients could not be assessed. Thus it remains unclear whether awaiting laboratory confirmation in an EMC as a false-positive admission actually results in any nosocomial EBOV infections, and whether an environment of 46% EBOV-positivity as observed in the suspect ward indeed reduces such a risk compared with 76% EBOV-positivity as observed in the highly-suspect ward. During the first nine weeks of operations, we recorded 15 readmitted patients. Among these readmitted patients, nine tested positive. These were patients who were tested negative during a first admission in the EMC, were discharged, and tested positive when they were admitted a second time, within 21 days of their initial admission. In-depth case investigations revealed one or more other high-risk exposure events in the community for all of these patients [18]. Though the exact source of infection could not be established with certainty, the total absence of readmissions without community-related high-risk exposure events in the 21 days before their second admission suggests that the risk of nosocomial infection from the EMC Kailahun was not very high.

In this study it was not possible to comprehensively evaluate the initial triage step, i.e. the decision to admit a patient or not. For this, clinical, epidemiological and laboratory information of patients turned away at triage would have been necessary. Such information was not collected in Kailahun due to high workload.

Due to high work load and demanding working conditions during the overwhelming emergency situation when these data were collected, only the most operationally relevant information was entered into the electronic study database. Patient symptoms were not among them. Therefore, we could not identify key symptoms associated with having a positive laboratory result.

Only one laboratory test result at admission was recorded per patient. Patients with symptom onset less than 72 hours before admission who initially tested negative with a second test taken more than 72 hours after symptom onset which was positive had only had their second (positive) result recorded. Thus, it was not possible to investigate differences in ward allocation among this subgroup of patients.

In addition, no data on staff, logistics, finance and supply were available to estimate the burden of maintaining separate wards. This would have been necessary for a comprehensive evaluation of different EMC setups for patients awaiting laboratory confirmation.

Conclusions

This first assessment of the MSF EVD triage system into suspect and highly-suspect wards showed unconvincing results for the accurate classification of laboratory-confirmed positive and negative admissions.

Instead, we recommend accommodating patients in single compartments pending laboratory confirmation whenever possible. Wherever this is not possible, a simplified separation into liquid and non-liquid producing patients should be considered and evaluated concurrently. At the same time, it is paramount to further improve the initial triage step on whether or not to admit a patient in the first place.

What is ultimately needed is a reliable, accurate, robust, mobile, affordable and easy to use point-of-care test with high throughput capacity and quick turnaround time [34]. First field validations of protein-based rapid tests showed promising results [35,36], and other innovations such as GeneXpert for EBOV diagnostics and capillary blood testing indicate progress is being made, although much work still needs to be done to improve triage of EVD patients [37-39]. Further development of such devices should be encouraged and prioritised.

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Conflict of interest

None declared.

Authors' contributions

Florian Vogt conceptualised and designed this research, led the analysis and interpretation of data, and wrote the first draft of the manuscript. Florian Vogt, Gabriel Fitzpatrick, Gabriela Patten and Kathryn Stinson were involved in the data collection. Gabriel Fitzpatrick, Gabriela Patten, Rafael van den Bergh, Luigi Pandolfi, James Squire, Tom Decroo, Hilde Declerck and Michel Van Herp contributed to the interpretation of data. All co-authors revised the draft manuscript critically for important intellectual content. All authors approved the final version of the manuscript.

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Letter to the editor: Responding to a call for action - where are we now?

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To the editor: In their recent editorial [1] Catchpole and Coulombier pointed out the urgent need of reliable information on infectious disease occurrence among refugees and newly arrived migrants in the European Union (EU), in order to ensure that public health interventions targeting this vulnerable population are relevant, proportionate and appropriately targeted. This call for action comes after the European Centre for Disease Prevention and Control (ECDC) published an analysis of the burden of infectious diseases among migrant populations based on EU surveillance data [2]. This report highlighted limitations in the data and differences in reporting between countries. In 2015, with the increase in the number of people migrating into the EU, the ECDC published numerous additional documents (expert opinion/rapid risk assessments) on the topic of migrant and refugee health [3]. To guide emergency response, information on epidemic prone diseases among newly arrived migrants has been collected in some EU countries for several years through aggregated syndromic surveillance [4]. These data, however, cannot be imported into case-based national and EU surveillance systems.

The recently concluded Monitoring Migrant Health project, funded by ECDC, aimed at gathering evidence to design an EU monitoring framework for migrant health and infectious diseases. We conducted systematic reviews to identify 1) the factors associated with the risk of contracting an infectious disease among migrants, and 2) the main biases that affect the accuracy of migrant health surveillance in the EU. Based on the evidence of the first review, we formulated a multidimensional monitoring framework comprising four domains: migration characteristics, behavioural, socioeconomic and demographic factors. The migration characteristics are those for which we have less information: we should be able to distinguish migrant legal status (e.g. refugee status), migration trajectory (country of origin/travel route) and time since arrival. To date we can rely only on two variables in the European Surveillance System (TESSy) database: 'country of birth' and 'nationality'. Unfortunately, the completeness of surveillance data collected on these migrant-specific variables is either very poor or absent in TESSy [2]. Furthermore, these variables cannot accurately identify subgroups of migrant populations such as refugees and newly arrived migrants [5].

The review on the determinants of infectious disease surveillance accuracy with regards to migrant health, showed three main sources of bias in measuring the occurrence of disease. Firstly, behavioural factors and legal, cultural, logistical barriers, in society and health services, have been found to reduce the probability of a diagnosis in migrants, favouring under-reporting. The second bias was linked to increased screening for asymptomatic infections and increased attention to infectious diseases among migrants who are considered a vulnerable population group. Taking also into account that most EU countries have screening programmes in place targeting newly arrived migrants [6], this increases the probability of diagnosis. The third bias we found was the systematic underestimation of the denominator that favours an overestimation of disease occurrence in certain migrant population subgroups. The few studies we found that tried to compare under-reporting in migrant and native populations, observed a higher probability of reporting for infectious diseases, particularly tuberculosis, in migrants.

Migration is a long-term phenomenon, recognised as one of the key components of population change in Europe. The migrant population within the EU is extremely diverse. We propose to integrate a multidimensional approach to case-based national and EU surveillance, including migration characteristics, to help better cater for the health needs of this population. We

also found evidence that some of the information we have on infectious disease occurrence might be biased, mostly in the direction of overestimating the excess risk for migrants. We need to be aware that this situation could favour misconceptions, ungrounded threat perceptions and mislead public health decisions.

Authors' contributions

All the authors contributed to the work of the ECDC Monitoring Migrant Health Project described in this contribution. Flavia Riccardo and Paolo Giorgi Rossi drafted this letter. All authors were actively involved in the design and revision of the manuscript and approved the final version.

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Call for applications for EPIET and EUPHEM fellows

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Applications are invited for fellow positions in the European Programme for Intervention Epidemiology Training (EPIET). The two-year programme has two paths: the EPIET epidemiology path and EPIET public health microbiology path (EUPHEM).

The programme is managed by the European Centre for Disease Prevention and Control (ECDC).

Closing date for the applications is 10 January 2016. The programme will start on 12 September 2016.

The EPIET epidemiology path provides training and practical experience in intervention epidemiology at the national and regional centres for surveillance and control of communicable diseases in the European Union (EU) and European Economic Area (EEA). The programme is aimed at EU/EEA medical practitioners, public-health nurses, microbiologists, veterinarians and other health professionals with previous experience in public health.

The EPIET public health microbiology path, EUPHEM, focuses on developing a network of public health microbiologists with the purpose to strengthen communicable disease surveillance and control through an integrated laboratory-field epidemiology network for outbreak detection, investigation and response. The programme is aimed at microbiologists, veterinarians, biomedical scientists, medical doctors or biologists with demonstrated experience in microbiology.

For more information and the application forms see here: http://ecdc.europa.eu/en/aboutus/jobs/Pages/fellowships.aspx