



RAPID RISK ASSESSMENT

Outbreak of Ebola virus disease in West Africa

Eighth update, 18 November 2014

New developments since seventh update

Since December 2013, and as of 17 November 2014, 14 415 cases of Ebola virus disease (EVD), including 5 177 deaths, have been reported by the World Health Organization (WHO) in eight reporting countries (Guinea, Liberia, Mali, Nigeria, Senegal, and Sierra Leone in West Africa, and Spain and the USA).

In Mali, after the report of a first case in Kayes imported from Guinea on 23 October, WHO reported five additional cases in Bamako that are not linked to the first case. These five additional cases are four confirmed cases and one probable. Four of these cases died. All these new cases are associated with a 70-year-old male case from Guinea who was admitted to a clinic in Bamako on 25 October and died on 27 October. Among the four confirmed cases in Bamako, two are healthcare workers who cared for the imported case. No information is available at the moment on the other two confirmed cases.

This update to the rapid risk assessment includes recent epidemiological data and the latest on treatment and vaccine development. The main conclusions and the risks posed to Europe remain unchanged. The options for risk reduction are the same with the addition of a summary of exposure assessment guidance and options for measures for returning healthcare workers. This is drawn from an ECDC technical report on the topic published on 10 November 2014.

Main conclusions and options for risk reduction

The evolving epidemic of EVD over the past weeks maintains the likelihood that EU residents and travellers to the EVD-affected countries will be exposed to infected or ill persons. The risk of infection for residents and visitors in the affected countries through exposure in the community is considered low if they adhere to the recommended precautions. Residents and visitors to the affected areas run a risk of exposure to EVD in healthcare facilities. The level of this risk is related to how well the infection control measures are being implemented in these settings and the nature of the care required.

As the epidemic is still evolving and more staff are deployed in the affected countries to support the epidemic control, the risk of importation of EVD cases to the EU is increasing. The risk of Ebola virus spreading from an EVD patient who arrives in the EU as result of a planned medical evacuation is considered to be low when appropriate measures are strictly adhered to, but cannot be excluded in exceptional circumstances. The transmission to a healthcare worker in Spain illustrates the connection between the epidemic in West Africa and the risk for the EU, and further stresses the need to control the epidemic in West Africa.

If a symptomatic case of EVD presents in an EU Member State, secondary transmission to caregivers in the family and in healthcare facilities cannot be excluded. This may happen in particular at an early stage of the disease, when patients are not yet very contagious but unprotected contacts are occurring, and at a late stage of the

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disease, after EVD is confirmed, when patients may experience very high viral loads and severe loss of bodily fluids, and undergo contamination-prone invasive procedure in intensive care units.

The options for risk reduction are:

- To reduce the risk of infection in West Africa the following options are available: avoid non-essential travel to the affected areas and strictly follow the EVD prevention measures in communities. As there is an increased risk of infection in healthcare facilities, visitors to the EVD-affected countries should identify appropriate in-country healthcare resources prior to travelling.
- To reduce the risk of importation to the EU, the WHO recommendations related to the declaration of a Public Health Event of International Concern (PHEIC) should be applied, in particular effective exit screening. Screening cannot detect infected cases still incubating and not yet presenting with symptoms.
- Based on the evidence of the validity of methods currently available for entry screening at major points of entry, and the likely prevalence of screening-detectable cases among those who have undergone exit screening, the added value of entry screening, if exit screening is being conducted effectively, is likely to be very small, and the resource implications considerable. In the absence of an evaluation of the performance of exit screening, entry screening remains an option to be considered.
- To reduce the risk of transmission within the EU following importation of Ebola virus, the following options are available:
 - epidemic control based on interruption of transmission by infection control measures and implementation of isolation and treatment of patients, and monitoring and contact tracing of contacts
 - raising awareness and sensitising healthcare providers in the EU about EVD, and supporting them with
 resources that will help them identify and manage potential EVD patients
 - enhancing information and communication to travellers departing from EVD-affected countries.
- Transmission to healthcare workers can be prevented by the strict application of infection control measures as recommended by WHO. However, even when infection control measures are thoroughly applied, transmission to healthcare workers can still exceptionally occur. Infection of a healthcare worker may result from a breach in the strict application of the infection control measures, when caring for an infectious patient, when involved in waste management or when removing personal protective equipment (PPE).

Tools that need to be considered for the optimisation of the safe management of patients include regularly repeated hands-on training in the use of PPE, the performance of simulation exercises, continuous supervision and monitoring of both the care of the patient and the putting on and removal of PPE and working in pairs (buddy system). The transfer of the patient to a specialised high level isolation unit is an option that may be considered, taking into account availability, feasibility and the safety of transfer.

Source and date of request

Internal decision, 12 November 2014.

Public health issue

To update the assessment of the risk of importation and transmission of Ebola virus in the EU associated with the epidemic of Ebola virus disease in West Africa currently affecting Guinea, Liberia, Mali, Sierra Leone, Spain and the United States of America. We have added evidence on the risks of transmission and on hospital infection control, since three healthcare workers (HCWs) having cared for EVD patients outside of West Africa have become infected.

This assessment does not cover the ongoing EVD epidemic in the Democratic Republic of Congo.

The current EVD outbreak was first assessed in an ECDC rapid risk assessment entitled 'Outbreak of Ebola haemorrhagic fever in Guinea', dated 23 March 2014 [1]. Detailed information about the Ebola virus and the epidemiology of EVD can be found in a series of ECDC publications that are available on the ECDC website [1-8].

Consulted experts

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Disease background information

Infections with Ebola viruses originating from Africa cause a severe disease in humans called Ebola virus disease. There are five species of the genus Ebolavirus (Filoviridae family): Zaïre ebolavirus, Sudan ebolavirus, Reston ebolavirus, Taï Forest ebolavirus and Bundibugyo ebolavirus [9,10]. The current outbreak in West Africa is caused by Zaire ebolavirus. A concurrent EVD outbreak was declared on 26 August 2014 in the Democratic Republic of Congo (DRC). The two outbreaks are not connected [11].

Ebola viruses are biosafety level-4 pathogens (BSL-4; risk group 4) and require special containment measures and barrier protection, particularly for HCWs. The viruses can survive in liquid or dried material for many days [12]. They are inactivated by gamma irradiation, heating for 60 minutes at 60 °C or boiling for five minutes, and are sensitive to sodium hypochlorite (bleach) and other disinfectants [13,14]. Freezing or refrigeration will not inactivate Ebola viruses [15,16].

The incubation period (the period between infection and first symptoms) is usually four to ten days but can be as short as two days and as long as 21 days. The case-fatality ratio for Zaire ebolavirus infections is estimated to be between 44% and 90% [17].

Ebola viruses are highly transmissible by direct contact with infected blood, secretions, tissues, organs and other bodily fluids from dead or living infected persons [18]. Transmission via inanimate objects contaminated with infected bodily fluids (fomites) is possible [19]. The principal mode of transmission in human outbreaks is personto-person transmission through direct contact with a symptomatic or dead EVD case (Table 1). Airborne transmission has not been documented [20].

The probability of transmission is considered low in the early phase of human disease (i.e. the prodromal phase) [17]. Risk of transmission may increase with transition to later stages of the disease. During an Ebola outbreak in DRC, the most important risk factor was direct physical contact with an infected sick person. The risk was higher with exposure to bodily fluids during the late stages of the disease [21]. Ebola virus is shed in a wide variety of bodily fluids during the acute period of illness [22,23]. A marked difference in viral load, especially early in the course of disease, was previously observed with Zaire ebolavirus between survivors and non-survivors with high levels of viraemia associated with poor outcomes [22].

Burial ceremonies and handling of dead bodies play an important role in transmission [24]. Ebola virus genome has been detected in semen up to 91 days after onset of disease [25], and replicative Ebola virus has been detected in semen 41 days after onset of disease [18,26].

Table 1. Risk levels of transmission of Ebola viruses according to type of contact with an infected patient

Level of risk	Type of contact
Low risk	 Casual contact with a feverish but ambulant and self-caring patient, e.g. sharing a seating area or public transportation; receptionist tasks.
High risk	 Close face-to-face contact (e.g. within one metre) without appropriate personal protective equipment (including eye protection) with a probable or confirmed case who is coughing, vomiting, bleeding, or who has diarrhoea; or has had unprotected sexual contact with a case up to three months after recovery. Direct contact with any material soiled by bodily fluids from a probable or confirmed case. Percutaneous injury (e.g. with needle) or mucosal exposure to bodily fluids, tissues or laboratory specimens of a probable or confirmed case. Participation in funeral rites with direct exposure to human remains in or from an affected area without appropriate personal protective equipment. Direct contact with bushmeat or bats, rodents, primates, living or dead in/from affected areas.

Publications since the onset of this outbreak have provided additional information about the clinical presentation of EVD case series in Conakry (Guinea) and Kenema (Sierra Leone) [27-29]. Common symptoms for all the EVD patients, in all locations, were fever and weakness. In almost half of the cases, the symptoms were accompanied by gastro-intestinal symptoms (diarrhoea, nauseas, vomiting). During hospitalisation, the frequency of haemorrhagic signs or bleedings varied across studies with 2% in Sierra Leone (n=43 EVD cases) and 26% and 51% in case series in Conakry (n=90 and n=37 respectively).

Treatment and vaccine development

In September 2014, WHO published interim guidance for national health authorities and blood transfusion services on 'Use of convalescent whole blood or plasma collected from patients recovered from EVD for transfusion, as an empirical treatment during outbreaks [30,31]. The rationale behind treatment with convalescent whole blood or plasma is the presence of antiviral neutralising antibodies. The interim guidance contains recommendations on the collection of whole blood or plasma from EVD survivors, screening of donors for infectious agents such as HIV, hepatitis B, hepatitis C, syphilis and other infectious agents, storage, and administration of ABO and RhD matched units for transfusion in confirmed EVD patients, preferably in its early stages. Availability of convalescent plasma from survivors in the EU/EEA is monitored by the European Blood Alliance but is currently very scarce.

No other antiviral treatments or vaccines are presently authorised for EVD. However, early supportive clinical treatment and management are essential and can improve the chances of recovery [32,33].

Potential new Ebola therapies and vaccines were reviewed during four WHO meetings organised with relevant stakeholders from early September 2014 and further assessed by scientific reviews [34-36].

A number of candidate treatments have shown promise in non-human primate models, although none of these drugs are licensed for treatment of EVD and their availability is currently limited. Several such potential drugs have in the past months been used in experimental treatment of individual EVD cases, e.g. brincidofovir (Chimerix, US), favipiravir (Toyama Chemicals, Japan and MediVector Inc, US), TKM-Ebola (Tekmira pharmaceutical Corporation, Canada) and ZMapp (Mapp Biopharmaceutical Inc, US). One or several experimental drugs have often been used in combination with convalescent plasma from EVD survivors making evaluation of clinical impact difficult.

The first trials for Ebola treatments will start at West African Médecins Sans Frontières (MSF) sites in December using favipiravir, brincidofovir and convalescent plasma from Ebola survivors [37].

In addition, three vaccine candidates in advanced stages of development have been identified:

- ChAd3-ZEBOV vaccine (GSK)
- rVSV-ZEBOV vaccine (NEWLINK with Public Health Agency Canada)
- Ad26 + MVA with unknown *Ebolavirus* antigen expressed (priming with vaccine from Janssen with booster 2 months later from Bavarian Nordic).

For the two first vaccine candidates, ChAd3 (Chimpanzee Adenovirus 3)-ZEBOV and rVSV (recombinant Vesiculo Stomatis Virus) -ZEBOV, Phase 1 trials have been initiated in Switzerland, the UK, USA and Mali, and are beginning in Gabon, Germany and Kenya with the goal of assessing immunogenicity and safety. First results will be available in the first part of December when phase 2 trials will start. It is unlikely that vaccine efficacy data will be available before a fast-track authorisation of the vaccines. If the vaccines are proven safe in phase 1 and 2 trials, vaccines could be available in the coming months for priority use in HCWs. However, it should be noted that if the vaccines are rolled out early, they will have undergone limited testing in humans, and post-authorisation monitoring of safety and effectiveness will be important. The third vaccine candidate is somewhat behind and will start phase 1 studies in the spring of 2015.

The WHO Director General has initiated a Strategic Advisory Group of Experts (SAGE) Working Group on Ebola Vaccines and Vaccination [38]. SAGE will be asked to give its Ebola vaccine recommendations based on the best scientific evidence and public health policy.

The European Medicines Agency (EMA) has started to review available information on a larger panel of Ebola treatments and vaccines currently under development in order to support fast-track authorisation in the EU/EEA [39].

Finally, ECDC has set up an extranet to support the Ebola Clinical Network [40]. The aim of this network tool is to allow EVD Reference Treatment Centres in EU/EEA Member States, with or without experience of EVD cases to support each other by exchanging experiences and updated technical information as well as sharing, in a confidential manner available protocols, methods and similar materials and approaches regarding the treatment of EVD patients, infection prevention and control procedures, EVD training and finally to ask each other any relevant questions in a secure environment. The extranet carries a clear disclaimer/legal notice on ECDC and Commission liabilities.

Event background information

Chronology of events – key dates

17 November 2014: In Mali, WHO reported two additional cases in Bamako, all these cases are linked to an EVD imported case from Guinea on 25 October.

12 November 2014: In Mali, WHO reported three additional cases in Bamako that are not linked to the case reported on 23 October. Two are probable cases from Guinea, one was admitted in a clinic in Bamako on 25 October and died on 27 October, the second was a visitor of this patient who also died (the date of his death is not available). The two other cases are confirmed cases in HCWs who cared for the patient in the clinic. One died on 11 November [41].

1 November 2014: A UN worker was medically evacuated from Sierra Leone to France upon request from WHO [42].

28 October 2014: WHO published a press release regarding the approval of an Ebola vaccine trial at Lausanne University Hospital in Switzerland. The trial, which is being supported by WHO, is the latest in a series of trials that are ongoing in Mali, UK and the USA [43].

23 October 2014: The US Centers for Disease Control and Prevention (CDC) reported a new case in New York City. The case is a medical aid worker who volunteered in Guinea and recently returned to the United States [44].

The Ministry of Health in Mali reported that a two-year-old girl who recently arrived from Guinea tested positive for Ebola. This was the first confirmed case of Ebola virus infection in Mali [45].

20 October 2014: WHO officially declared Nigeria free of Ebola virus transmission [46].

17 October 2014: WHO officially declared Senegal free of Ebola virus transmission [47].

14 October 2014: In the US, a second healthcare worker at Texas Health Presbyterian Hospital who also provided care for the imported EVD patient tested positive for Ebola.

10 October: In the USA, a healthcare worker at Texas Health Presbyterian Hospital who cared for the first imported EVD patient tested positive for Ebola [48].

6 October 2014: The Spanish authorities reported a confirmed case of EVD in a healthcare worker who cared for the second of two EVD patients that were evacuated to Spain.

3 October 2014: In Senegal, all contacts of the imported EVD case completed the 21-day follow-up period without developing disease. No local transmission of EVD has been reported in Senegal.

30 September 2014: The US Centres for Disease Control and Prevention (CDC) announced the first imported case of EVD in the USA linked to the current outbreak in West Africa.

23 September 2014: A study published by the WHO Ebola response team forecasted more than 20 000 cases (5 740 in Guinea, 9 890 in Liberia, and 5 000 in Sierra Leone) by the beginning of November 2014 [49]. The same study estimated the doubling time of the epidemic at 15.7 days in Guinea, 23.6 days in Liberia, and 30.2 days in Sierra Leone.

18 September 2014: The United Nations Security Council recognised the EVD outbreak as a 'threat to international peace and security' and unanimously adopted a resolution on the establishment of an UN-wide initiative which focuses assets of all relevant UN agencies to tackle the crisis [50].

29 August 2014: The Ministry of Health in Senegal reported a confirmed imported case of EVD in a 21-year-old male native of Guinea.

8 August 2014: WHO declared the Ebola outbreak in West Africa a Public Health Event of International Concern (PHEIC) [51]. On 23 October, WHO re-confirmed that the outbreak continued to constitute a Public Health Event of International Concern.

End of July 2014: A symptomatic case travelled by air to Lagos, Nigeria, where he infected a number of HCWs and airport contacts before his condition was recognised to be EVD.

May 2014: Sierra Leone and Liberia reported the first cases [52,53]. The disease is assumed to have spread from Guinea through the movement of infected people over land borders.

22 March 2014: The Ministry of Health in Guinea notified WHO about a rapidly evolving outbreak of Ebola viral disease (EVD) [54]. The first cases occurred in December 2013. The outbreak is caused by a clade of *Zaïre ebolavirus* that is related but distinct from the viruses that have been isolated from previous outbreaks in central Africa, and clearly distinct from the *Taï Forest ebolavirus* that was isolated in Côte d'Ivoire 1994–1995 [24,55,56]. The first cases were reported from south-eastern Guinea and the capital Conakry.

Epidemiological update

Since December 2013 and as of 17 November 2014, WHO has reported 14 415 confirmed, probable and suspected cases of Ebola virus disease (EVD) in six affected countries (Guinea, Liberia, Mali, Sierra Leone, Spain and the United States of America) and two previously affected countries (Nigeria and Senegal) [57]. There have been 5 177 reported deaths. This is an increase of 1 145 cases and 217 deaths since 4 November 2014. [58,59].

Distribution of cases

Countries with widespread and intense transmission:

- Guinea: 1 919 cases and 1 166 deaths as of 11 November 2014
- Liberia: 6 878 cases and 2 812 deaths as of 10 November 2014
- Sierra Leone: 5 586 cases and 1 187 deaths as of 11 November 2014.

Countries with an initial case or cases, or with localised transmission:

- Mali reported five confirmed and one probable cases, including four deaths [60,61].
- United States: four confirmed cases, including one death.
- Spain: one case, no deaths.
- Nigeria: 20 cases and eight deaths. Nigeria was declared Ebola free on 19 October 2014.
- Senegal: one confirmed imported case. Senegal was declared Ebola free on 17 October 2014.





* In week 45/2014, WHO carried-out retrospective correction in the data resulting in reporting 299 fewer cases resulting in a negative value for new cases in week 45 which is not plotted [62] (See <u>World Health Organization</u>. Ebola response roadmap situation report. 5 November 2014 [Internet]. Geneva: WHO; 2014).

** According to WHO the marked increase in the cumulative total number of cases in week 43 is due to a more comprehensive assessment of patient databases leading to 3 792 additional reported cases. However, these cases have occurred throughout the epidemic period [63]. (See: <u>World Health Organization. Ebola response roadmap situation report. 29 October 2014 [Internet].</u> <u>Geneva: WHO; 2014</u>)

The green line represents the trend based on a five week moving average plotted on the fifth week of the moving average window. The figure includes cases in Nigeria (20), Senegal (1) and Mali (4) [57] (See: <u>World Health Organization</u>. Ebola response roadmap situation report. 14 November 2014 [Internet]. Geneva: WHO; 2014)

Situation in specific West African countries

According to WHO, the weekly incidence appears to be stable at the country level in Guinea. In Sierra Leone, the weekly incidence continues to rise, while in Liberia it appears to be declining. In all three countries, EVD transmission remains persistent and widespread, particularly in the capital cities. All administrative districts in Liberia and Sierra Leone have reported at least one confirmed or probable case of EVD since the start of the epidemic. Cases and deaths continue to be under-reported.

In Mali, after the report of a first case in Kayes imported from Guinea on 23 October, WHO reported five additional cases in Bamako that are not linked to the first case. They are four confirmed cases and one probable. Four of these cases died. These new cases are associated with a 70-year-old male from Guinea who was admitted to a clinic in Bamako on 25 October and died on 27 October. Among the four confirmed cases in Bamako, two are HCWs who cared for the imported case. No information is currently available on the other two confirmed cases.



Figure 2. Distribution of cases of EVD by week of reporting, Guinea, Liberia and Sierra Leone, as of week 46/2014

* The marked increase in the number of cases reported in Sierra Leone (week 44) and Liberia (week 43) results from a more comprehensive assessment of patient databases. The additional 3 792 cases have occurred throughout the epidemic period. Source: Data are based on official information reported by ministries of health up to the end of 2 November for Guinea and Sierra Leone and 31 October for Liberia (See: World Health Organization. Ebola response roadmap situation report. 5 November 2014 [Internet]. Geneva: WHO; 2014).

** In week 45/2014, WHO reported 476 fewer cases than the week before in Sierra Leone due to retrospective corrections.

 ${\it g}$ In week 44/2014, WHO reported zero cases for Liberia.



Figure 3. Distribution of cases of EVD by week of reporting in Guinea, Sierra Leone and Liberia (as of week 45/2014)

Source: Data from ministries of health reports (suspected, probable and confirmed cases).

Situation among healthcare workers in West Africa

As of 12 November 2014, WHO reported, in West Africa, 562 HCWs (HCWs) infected with EVD of whom 321 died. Table 2 details the distribution of cases and deaths among HCWs.

Table 2. Number of Ebola cases and deaths among healthcare workers West Africa, as of 11 November 2014

Country	Healthcare worker cases (% of reported cases)	Healthcare worker deaths (% of reported deaths)
Guinea	92 (4.9)	51 (4.5)
Liberia	329 (4.8)	162 (5.7)
Mali	2 (40.0)	1 (20.0)
Nigeria	11 (55.0)	5 (62.5)
Sierra Leone	128 (2.4)	102 (8.7)
Total	562 (4.0)	321 (6.2)

Source: Data are based on official information reported by Ministries of Health [57,62] (See: World Health Organization. Ebola response roadmap situation report. 12 November 2014 [Internet]. Geneva: WHO; 2014 and World Health Organization. Ebola response roadmap situation report. 5 November 2014 [Internet]. Geneva: WHO; 2014)

Situation outside West Africa

USA

No new EVD cases have been reported since 23 October. The latest reported case concerns a medical aid worker who volunteered in Guinea and recently returned to the United States. He was hospitalised in New York City and was discharged healthy on 11 November 2014.

Spain

No new cases have been reported since 6 October when a healthcare worker was infected while caring for an Ebola-infected patient in Madrid. She recovered and tested negative for EVD on 19 October. A second negative test was obtained on 21 October. All 83 contacts of the HCW have completed a 21-day follow-up. Spain will be declared free of EVD 42 days after the date of the second negative test if no new cases are reported.

Medical evacuations and repatriations from EVD-affected countries

Nineteen individuals have been evacuated or repatriated from the EVD-affected countries (Table 3, Figure 4). As of 17 November, there have been nine medical evacuations of confirmed EVD-infected patients to Europe (three to Germany, two to Spain, two to France, one to the UK and one to Norway). Two persons exposed to Ebola have been repatriated to the Netherlands and tested negative. One individual was evacuated to Switzerland and was not confirmed.

Date of evacuation	Evacuated from	Evacuated to	Profession	Status	Confirmed	Citizenship
02 August 2014	Liberia	Atlanta (USA)	Healthcare worker	Discharged	Yes	USA
05 August 2014	Liberia	Atlanta (USA)	Healthcare worker	Discharged	Yes	USA
06 August 2014	Liberia	Madrid (Spain)	Healthcare worker	Death	Yes	Spain
24 August 2014	Sierra Leone	London (United Kingdom)	Healthcare worker	Discharged	Yes	UK
27 August 2014	Sierra Leone	Hamburg (Germany)	Epidemiologist	Recovered	Yes	Senegal
04 September 2014	Monrovia, Liberia	Omaha (USA)	Physician (obstetrician)	Discharged	Yes	USA
09 September 2014	Kenema, Sierra Leone	Atlanta (USA)	Physician	Discharged	Yes	USA
14 September 2014	Sierra Leone	Leiden (the Netherlands)	Healthcare worker	Discharged	No	the Netherlands
14 September 2014	Sierra Leone	Leiden (the Netherlands)	Healthcare worker	Discharged	No	the Netherlands
19 September 2014	Liberia	Paris (France)	Healthcare worker	Discharged	Yes	France
22 September 2014	Sierra Leone	Madrid (Spain)	Healthcare worker	Death	Yes	Spain
22 September 2014	Sierra Leone	Lausanne (Switzerland)	Healthcare worker	Admitted	Unknown	Non-Swiss
28 September 2014	Sierra Leone	Maryland (USA)	Healthcare worker	Admitted	Unknown	USA
02 October 2014	Sierra Leone	Frankfurt (Germany)	Healthcare worker	Stable	Yes	Uganda
02 October 2014	Liberia	Omaha (USA)	Cameraman	Discharged	Yes	USA
06 October 2014	Sierra Leone	Oslo (Norway)	Healthcare worker	Discharged	Yes	Norway
08 October 2014	Liberia	Leipzig (Germany)	Laboratory worker	Death	Yes	Sudan
01 November 2014	Sierra Leone	Paris (France)	UN worker	Unknown	Yes	Sierra Leone
15 November 2014	Sierra Leone	Nebraska (USA)	Healthcare worker	Death	Yes	USA

Table 3. Medical evacuation and repatriation from EVD-affected countries, as of 12 November 2014





*Numbers displayed over the connection lines are referring to number of medical evacuations.

ECDC. Map produced on 18 Nov 2014

ECDC threat assessment

With more than 14 000 cases and more than 5 000 deaths reported from West Africa by mid-November 2014, the control measures implemented so far have failed to control the epidemic. All evidence and forecasting indicate that the epidemic will continue to increase and spread geographically in affected countries if control efforts remain unchanged.

The clinical course of the disease and the estimated transmissibility of the virus are similar to previous EVD outbreaks. Current knowledge does not indicate that this unprecedented epidemic results from increased pathogenicity of the epidemic strain of *Ebolavirus* [49]. As in earlier EVD outbreaks, transmission seems to be primarily driven by direct contact with EVD cases and dead bodies. There is no convincing evidence that the recommended infection control measures are inappropriate to ensure protection if adhered to strictly by trained staff working in health services with appropriate facilities.

The current outbreak magnitude challenges response activities and requires a large international effort to enhance healthcare services and infection control measures, ensure supply of protective equipment in treatment facilities and strengthen and support capacities for epidemiological surveillance and laboratory diagnosis. Beyond the public health emergency, the current crisis of unprecedented scale is a threat to healthcare systems with an impact on standard medical care for other pathologies. In the most affected countries, others sectors are suffering, notably economic sectors and food security, making this crisis an international and complex health emergency requiring a large-scale multi-sectorial response [64,65].

However, the teams of the international medical humanitarian organisation MSF are witnessing a decline in the number of Ebola patients admitted to case management centres in Liberia for the first time since the beginning of the Ebola epidemic [66-68].

Risk of exposure to EU residents and travellers in West African-affected countries

Exposure in the community

- The risk of infection for EU residents and visitors in the affected countries through exposure in the community is considered low if they adhere to the recommended precautions. The upsurge in the number of new EVD cases over the past weeks, the existence of urban transmission, and the fact that not all chains of transmission are known, increase the likelihood that residents and travellers to the EVD-affected countries will be exposed to infected or ill persons.
- People visiting friends and relatives in the affected countries tend to have more and closer contacts in the • community, and they are more likely to be at risk than other visitors, particularly if they care for sick friends and relatives or participate in burial ceremonies - activities known to be associated with transmission of the Fbola viruses.

Exposure in healthcare settings

- Residents and visitors to the affected areas run a risk of exposure to EVD in healthcare facilities. The level of this risk is related to how well infection control measures are being implemented in these settings and the nature of the care required.
- The risk of exposure in healthcare settings also exists in areas that have not yet reported cases because it can be assumed that not all cases of EVD are immediately detected and reported.
- The infection risk is not limited to hospitals that provide care to known EVD cases because infectious cases may initially seek medical attention at any healthcare provider.
- While the risk is low for a consultation requiring non-invasive tests and prescription of oral drugs to patients who do not have severe symptoms such as profuse diarrhoea or haemorrhage, it may be increased if invasive procedures are required.
- The risk of being exposed to Ebola viruses is obviously higher for HCWs and volunteers who provide assistance in settings where no infection control measures have been implemented. The risk is extremely high for HCWs who carry out invasive medical procedures or provide care to EVD patients without proper infection control measures and PPE [69].

Risk of importation to the EU

General assessment

It is expected that the number of new cases will continue to rise in Guinea, Liberia and Sierra Leone in the coming weeks and possibly months [6]. Therefore, the likelihood of individuals arriving in the EU with potential Ebola virus infection has increased since the previous assessments were made.

People infected with EVD may arrive to the EU by direct or indirect flights from affected countries or on board freighters or passenger ships:

- They may arrive while incubating the disease. These persons do not show symptoms and cannot be detected through screening at points of exit or entry.
- They may arrive sick because they developed symptoms while travelling.

Almost all EU/EEA countries have issued temporary travel advice against non-essential travel to EVD-affected countries. A number of international airlines have stopped or substantially reduced the number of flights to the three most affected countries in West Africa.

A remote possibility is a chain of transmission along the routes used by undocumented migrants who end up on the southern shore of the Mediterranean and attempt to reach Europe by sea. Although the probability of this event is very small, the consequences of an outbreak in a detention centre or on board ship at sea could be dramatic.

The international response continues to be scaled up with the involvement of UN agencies, international organisations, non-governmental and governmental actors [70]. The number of EU citizens involved in the response is expected to increase with the progressive deployment of EU support to outbreak response activities in affected countries. In general, the standards of infection control and personal protection measures must be strictly maintained in order to minimise the exposure of care givers to Ebola virus and the need for repatriation or medical evacuation of HCWs and volunteers. There has been a recent increase in reports of expatriate HCWs being repatriated or medically evacuated from EVD-affected countries following exposure or infection with Ebola virus (Table 3). The need for repatriations and medical evacuations will increase as the epidemic continues to grow and more international staff are engaged in the response. It is likely that the crisis will continue for several months and the probability of unplanned importations (non-medical evacuations) of Ebola virus to the EU will increase over time as the epidemic spreads.

Patients presenting with symptoms and seeking medical attention in the EU

There is a possibility that a person who was exposed to Ebolavirus develops symptoms while on a commercial flight. It is expected that such patients would be detected and reported to a healthcare facility upon arrival in the EU and then be isolated to reduce the risk of further transmission.

Travel and transport risk assessment

A traveller on board an airplane may be already ill or become ill during the flight, showing symptoms compatible with EVD. In this situation, the possibility of transmission to co-passengers and crew should be assessed using the ECDC RAGIDA guidelines [71].

If an investigation concludes that the passenger has symptoms compatible with EVD and was exposed to EVD in the past 21 days, all passengers and crew who report direct contact, as well as all passengers seated one seat away from the sick person, should be monitored for 21 days. In addition, all passengers, crew members and cleaning staff who had direct contact with the suspected case's bodily fluids or potentially contaminated fomites such as contaminated clothing, towels or other utensils, should be investigated and monitored.

Any person who was exposed to Ebola viruses and develops symptoms while on board a freighter/passenger ship sailing to the EU should be declared in a Maritime Declaration of Health form and in accordance with article 37 of the 2005 International Health Regulations [72]. Affected crew members or passengers should be taken care of appropriately in order to prevent further spread of the disease.

Risk related to biosafety

There is a theoretical risk that a biological sample is sent to an EU laboratory for further testing, without proper indication of a possible connection to Ebola virus. Strict compliance with sample shipment regulations and universal precautions in the receiving laboratory should mitigate this risk [73].

Risk of transmission through substances of human origin

According to the EU Blood Directive [74], current geographic deferrals for malaria also exclude residents and travellers from EVD-affected countries from donating blood. An ECDC technical report assessing the risk of Ebola virus transmission through substances of human origin was published on the 6 October 2014. The document offers quidelines on the safety of donations where the potential donors are travellers returning from Ebola-affected countries, people exposed to Ebola virus and patients who have recovered from the disease [75].

Risk of Ebola virus transmission in the EU following importation

The probability of sustained chains of EVD transmission in the EU is low due to the high capacity of Member States to identify suspected cases, perform laboratory testing, isolate and treat EVD patients, and to conduct contact tracing. Recent reports from Spain and the USA indicate, however, that there is no place for complacency about the risks of healthcare-associated transmission unless infection control measures are strictly and assiduously applied and followed.

Repatriation and medical evacuation

The risk of Ebola virus spreading from an EVD patient who arrives in the EU as result of a planned medical evacuation is considered to be low when appropriate measures are strictly adhered to, but cannot be excluded in exceptional circumstances. The risk associated with an asymptomatic person who is repatriated following a low-risk exposure to Ebola virus in the affected area is equally low.

Individuals seeking medical care in the EU

EVD cases may travel during the incubation period and therefore not present with symptoms at the time of departure from affected countries or arrival in the EU. Once in the EU, detection may be delayed when either symptomatic persons are unaware of exposure or deny it, or, when presenting to an EU healthcare facility, clinicians do not suspect EVD.

The infectiousness of EVD patients is low at the early prodromal stages of the disease and increases as the disease progresses and the viral load increases. Infectiousness becomes particularly high when symptoms include the dissemination of infected bodily fluids, e.g. when vomiting, experiencing diarrhoea or bleeding.

The risk of unprotected contact is high during the period from the start of symptoms until the EVD-infected individual seeks medical care. The risk still exists in healthcare settings during the initial ascertainment until precautions to prevent transmission are fully and appropriately implemented [76,77].

Therefore, secondary transmission to caregivers in the family and in healthcare facilities can occur, particularly through exposure to bodily fluids (bleeding, diarrhoea) before an Ebola virus infection is suspected and appropriate infection control measures have been implemented.

The periods most at risk of secondary transmission include early and late stages of the disease:

- early stage of the disease, when patients are not yet very contagious, but unprotected contacts are occurring
- late stage of the disease, after EVD is confirmed, when patients may experience very high viral loads and • severe loss of bodily fluids, and undergo contamination-prone invasive procedure in intensive care units.

Delays in recognition of EVD as the cause of symptomatic disease can result in a significant risk of transmission if infection control measures are not taken during the period between symptom onset and recognition of EVD as the suspected or confirmed cause of disease. Once a case is detected and appropriate Ebola infection control measures are implemented, the risk of transmission becomes very low if those measures are fully adhered to, including assiduous care with respect to the donning and removal of PPE. Interventions aimed at reducing the risk of spread from an imported case in the EU should therefore focus on narrowing the window from onset of symptoms to implementation of effective infection control measures and ensuring that those infection control measures are strictly adhered to.

The case who developed the disease in Dallas, Texas, after arriving from Liberia, reminds us of the possibility of a similar situation occurring in the EU. In this situation, reduction of the risk of EVD secondary transmission to close contacts depends on early detection of suspected cases by healthcare professionals, rapid laboratory confirmation of infection and early isolation of the patient following onset of symptoms.

The investigation in Spain has provided information to further understand how the infection was transmitted to this healthcare worker. There is currently no evidence that the transmission to the healthcare worker may have resulted from a change in the transmissibility of the virus [49]. Therefore, the recommended infection control measures remain appropriate to ensure protection, if strictly applied [78,79].

Following the detection of EVD cases in the EU, the interruption of all chains of human-to-human transmission is of the highest priority. This can be achieved by:

- quickly identifying and isolating suspected EVD cases for confirmation by laboratory diagnosis and supportive treatment in an isolation ward
- identifying all contacts of each EVD case, including HCWs involved the patient's care, monitoring (actively or
 passively depending on risk) their health for the maximum incubation period of 21 days, and offering
 immediate care, isolation and laboratory diagnosis to all contacts that develop symptoms.

Options for risk reduction

The focus of this document is on individual protection and the various options for mitigating the risk of importation and spread in the EU.

Reduction of the risk of infection in West Africa

Avoiding travel to affected areas

The most obvious option to decrease the risk of importation from affected areas is to advise travellers to defer their travel to affected countries or areas until the outbreak is controlled there. Thirty EU/EEA countries have recommended this option for their citizens. Twenty-six countries are currently recommending that non-essential travel should be avoided or postponed, and four advising against all travel in the affected areas. The World Health Organization does not recommend any travel or trade restrictions to countries involved in this outbreak [80].

Preventing infection in communities

Visitors and residents in EVD-affected areas face a low risk of becoming infected in the community if the following precautions are strictly followed:

- avoid contact with symptomatic patients and their bodily fluids
- avoid contact with corpses and/or bodily fluids from deceased patients
- avoid contact with wild animals (including primates, monkeys, forest antelopes, rodents and bats), both alive and dead, and consumption of bushmeat
- wash hands regularly, using soap or antiseptics.

Generic precautions for travelling in West African countries also apply to the prevention of EVD infection:

- wash and peel fruit and vegetables before consumption
- avoid unprotected sexual intercourse
- avoid habitats which might be populated by bats, such as caves, isolated shelters or mining sites.

Avoidance of risk of acquiring infection in healthcare settings

There is an increased risk of exposure and infection in healthcare facilities. Options for prevention and control of this risk include:

- avoid non-essential travel to EVD-affected areas and countries
- identify appropriate in-country healthcare resources in the EVD-affected countries prior to travelling there
- ensure that your travel insurance covers medical evacuation in the event of illness or accident in order to limit exposure to local health facilities.

However, recent events in the affected countries have demonstrated that it may not always be possible to comply with the above precautions and this is the rationale behind many countries' advice against non-essential travel to affected countries.

Reduction of the risk of importation to the EU

Options in affected countries

Following the declaration of the Public Health Event of International Concern (PHEIC) on 8 August 2014, WHO recommended the following measures for affected Member States, which are expected, if implemented efficiently, to reduce the risk for importation to the EU:

- Affected countries are requested to conduct exit screening of all persons at international airports, seaports and major land crossings for unexplained febrile illness consistent with potential Ebola infection.
- There should be no international travel of known Ebola cases or contacts of cases, unless the travel is part of an appropriate medical evacuation. To be fully effective, this measure should restrict asymptomatic contacts of EVD cases from leaving the EVD-affected country on an international flight until the 21-day incubation period has passed. As the ratio of contacts to cases is high, this measure represents a significant logistical challenge. It may also prevent expatriate professionals engaged in outbreak control from leaving the EVD-affected country if they have been exposed to Ebola viruses.

Exit screening could potentially prevent a febrile EVD case from boarding a flight but it would not detect an incubating passenger who has not yet developed fever [81]. Information about exit screening in the affected countries will remain of interest in order to monitor the risk of importation of potential EVD cases to non-affected countries.

Options for EU countries

Screening of travellers

The following section is adapted from the summary of the ECDC document on screening [82].

As the epidemic of Ebola virus disease (EVD) continues to rise in West Africa, there is an increasing possibility that infected individuals will travel to the EU.

Exit screening focuses efforts on those at highest risk, thereby minimising the resources required and maximising the positive predictive value of screening. Affected countries have implemented exit screening, supported by the US Centers for Disease Control and Prevention (CDC). Based on current estimates of prevalence of infection (2 per 10 000 population in the affected countries) and what was observed during the first two months of exit screening in the three affected countries, the predictive positive value of the detection of one individual through screening is extremely low, as no EVD was confirmed in the 77 who were detected out of 36 000 travellers screened.

Entry screening to non-affected countries is being considered, or has been adopted, by a small number of countries, in addition to the ongoing exit screening. Based on the evidence of the validity of methods currently available for entry screening at major points of entry, and the likely prevalence of screening detectable cases among those who have undergone exit screening, the added value of entry screening, if exit screening is being conducted effectively, is likely to be very small, and the resource implications considerable.

Complementing exit screening with entry screening may, however, be considered:

- When there are doubts about the efficiency of exit screening.
- To detect the few who may develop fever between the time of departure and the time of arrival. This could be considered in particular for long-haul flights with multiple connections, extending beyond 12 hours.

The following points need to be considered in order to support decision making by EU public health authorities:

- No information is currently available regarding the quality and performance of the exit screening implemented in the affected countries.
- The use of screening for infectious diseases has not proven to be effective to prevent or delay transmission in past epidemics such as SARS.
- Temperature screening of passengers is able to detect travellers presenting with high fever with an appropriate level of performance when using appropriate equipment operated by trained staff.
- Temperature screening requires protocols and resources to further investigate possibly febrile passengers detected in order to treat them appropriately.
- Screening will result in a significant increase in the request for Ebola testing.
- Even the best temperature screening scheme will:
 - miss up to 20% of the febrile symptomatic EVD cases (sensitivity of the measurement)
 - _ miss travellers concealing their fever
 - miss two-thirds of infected cases, still incubating and not yet presenting with symptoms _
 - detect cases of fever related to many different infectious diseases such as malaria or influenza; it is likely that EVD cases will account for an extremely small proportion of febrile passengers, if any.

- Complementing temperature screening with visual review and a health questionnaire may be considered:
 - to increase the performance of screening relying only on temperature screening
 - to identify possibly contagious travellers missed by temperature screening
 - to identify travellers having had high-risk exposure and enrol them in monitoring schemes or quarantine.

Overall, screening for EVD among travellers may detect a few contagious EVD cases over time. Given that there is no available evidence of the effectiveness of exit screening in the affected countries, entry screening remains an option to be considered, in particular for direct flights, despite its low yield and high investment, to contribute to the prevention of importation of the disease.

Travel restrictions and screening of passengers on arrival (entry screening) at sea ports, airports or ground crossings in non-affected countries that do not share borders with affected countries are not currently recommended by WHO [81].

A specific case may be represented by HCWs returning from affected areas. They have a different probability of exposure than the general traveller. They should be provided with information upon their return. In addition they should undergo an individual exposure assessment as early as possible upon returning. Additional measures can be considered on the basis of the results of the exposure assessment, using the guidance in Table 4.

Table 4. Exposure assessment

Type of exposure	Proposed option(s) for measures
No direct contact with EVD patients or their bodily fluids (e.g. involved in training local HCWs)	Passive monitoring
Appropriately protected contact with bodily fluids of EVD patients (e.g. laboratory worker), fomites (e.g. bed linen) or during clinical activities	Active monitoring
Unprotected, inappropriately protected contact or known breach of protection while caring for an EVD patient, handling bodily fluids of a patient or fomites	Active monitoring Restriction of engagement in clinical activities No travel abroad
Mucosa or parenteral direct contact with bodily fluids of a patient (e.g. pricking a finger with a needle used for a patient or getting bodily fluid projection in the eyes).	Active monitoring Restriction of engagement in clinical activities Restriction of social interactions Restriction of movement

The proposed options in the table above should be modulated according to the individual risk assessment. Healthcare workers need to be informed of the measures they should expect upon returning from affected areas prior to departure. Upon returning from affected areas, all HCWs should be informed of the procedures for their monitoring, following an individual assessment of exposures.

Measures for returning HCWs should be proportionate to their risks, ensure the best possible management in case they become ill, while aiming at protecting public health and in respect of their personal rights. Current evidence on transmission, particularly that it has only been clearly documented in symptomatic patients, suggests that full quarantine of asymptomatic contacts, including HCWs, would be a disproportionate measure, unless there is evidence of non-compliance with recommended measures resulting in a potential risk for public health.

ECDC published a specific document on the public health management of HCWs returning from Ebola-affected areas [79].

Reduction of the risk of transmission within the EU following an importation

The risk of EVD transmission in the EU can be reduced by the early detection of suspected EVD cases imported into the EU and the use of appropriate infection control measures. Interventions aiming to reduce the risk of transmission within the EU include the following options:

Investigation of possible cases

The time window between the onset of first symptoms and the detection by healthcare systems should be minimised. Investigation of individuals who present to healthcare providers with EVD-like symptoms and meet the criteria for 'persons under investigation'^{*} should be swiftly and safely conducted in order to allow timely detection of EVD cases. In addition, investigations should consider other possible aetiologies of febrile illness upon return from tropical areas, with priority given to malaria, even though malaria positivity does not exclude an EVD infection. It is expected that a significant number of people will be tested for EVD in the EU/EEA, but the likelihood of identifying and confirming an EVD case is low (low positive predictive value) and other infections will be identified.

Public health management of persons having had contact with Ebola virus disease cases in the EU

As long as the outbreak in West Africa continues, it can be expected that a person who has travelled from an Ebola-affected area might develop EVD after arriving in the EU. ECDC produced an option document for public health authorities for the management of those having had contact with EVD cases [78].

Contact tracing

After identification and management of confirmed and/or probable EVD case(s) and potential chains of transmission in the EU, effective contact tracing and contact management should reduce the risk of spread of EVD in the EU. The aim is to identify all contacts of each EVD case, assess their level of exposure, actively monitor their health for the maximum incubation period of 21 days, and isolate, diagnose and treat all contacts who develop symptoms.

Medical evacuations

There are increasingly frequent reports about expatriate HCWs being repatriated from EVD-affected countries for monitoring after exposure to Ebola viruses. Such repatriations should be executed as soon as possible after the potential exposure, while the risk of transmission is still minimal should the exposed person turn out to be infected.

A document entitled 'Assessing and planning for medical evacuation flights to Europe for patients with Ebola virus disease and people exposed to Ebola virus' provides decision-makers with additional information when there is a perceived need to evacuate by air an infected or exposed person from an Ebola-affected country to an EU Member State [83]. The decision to evacuate must be based on: the likelihood of the person being infected with Ebola virus; the potential benefits of evacuation for the concerned person/patient; the risks associated with medical evacuation by air for the person/patient; and the risk of transmission to the crew and accompanying medical staff.

It is anticipated that medical evacuation needs will grow over the coming months as the outbreak continues and the number of expatriate HCWs engaged in outbreak control increases.

Healthcare settings

Transmission to HCWs can be prevented by the strict application of infection control measures as recommended by WHO [25]. However, even when infection control measures are thoroughly applied, transmission to HCWs can still exceptionally occur. Infection of a healthcare worker may result from a breach in the strict application of the infection control measures, when caring for an infectious patient, when involved in waste management or when removing PPE.

^{*} European Centre for Diseases Prevention and Control. Ebola virus disease case definition for reporting in the EU. http://ecdc.europa.eu/en/healthtopics/ebola_marburg_fevers/EVDcasedefinition/Pages/default.aspx

The early detection and isolation of a patient with EVD decreases the risk of transmission in the community. However, care in the hospital setting especially when aerosol-generating procedures are performed during the late stages of the disease when patients are highly contagious, implies a risk to healthcare practitioners. Minimising this risk constitutes an essential target.

According to WHO guidelines [69] the following are essential for the safe medical care of EVD patients:

- isolation rooms with dedicated bathroom
- availability of personal protection equipment
- personnel adequately trained to use the equipment.

Tools that need to be considered for the optimisation of the safe management of patients include regularly repeated hands-on training in the use of PPE, the performance of simulation exercises, continuous supervision and monitoring of both the care of the patient and the putting on and removal of PPE, and working in pairs (buddy system). The transfer of the patient to a specialised high-level isolation unit is an option that may be considered, taking into account availability, feasibility and the safety of transfer.

An enhanced occupational health policy with active monitoring of staff who have been involved in the care of EVD patients would ensure the early detection, isolation and treatment of secondary cases among HCWs. Such policies should also consider psychosocial support of HCWs. The possibility of restricting the number of contacts and recording contacts (e.g. contact diary) during the 21 days following the last exposure may be considered, particularly for a case of high-risk exposure.

Information and communication

Raising awareness among returning travellers from affected areas or any person having had a contact with probable or confirmed cases about disease symptoms and appropriate actions (self-isolation and seeking medical care mentioning potential exposure) should be considered to reduce the time between the onset of illness and isolation, in order to reduce the opportunity for further transmission to other persons and the generation of new chains of transmission.

The following are considered:

- Informing travellers departing from EVD-affected countries and travellers arriving in the EU on direct flights from EVD-affected countries about:
 - the possibility of exposure to Ebola while in the affected countries
 - the clinical presentation of the disease and the need to seek immediate medical care if symptoms develop
 - the need to immediately disclose their travel history when seeking medical care, and to preferably do so before arriving at a healthcare facility
 - the need to indicate possible contact with sick individuals or wild animals while in the EVD-affected country
 - how to contact public health authorities for support if infection is suspected (leaflets, phone numbers, telephone hotline).
- Informing and sensitising healthcare providers in the EU about:
 - the possibility of EVD among returning travellers from affected areas
 - the clinical presentation of the disease and the need to inquire about travel history and contacts with family and friends visiting from EVD-affected countries
 - the availability of protocols for the ascertainment of possible cases and procedures for referral to healthcare facilities
 - the imperative need for strict implementation of barrier management, use of personal protective equipment and disinfection procedures, in accordance with specific guidelines and WHO infection control recommendations when providing care to suspected EVD cases [32,69]
 - provide training before caring for EVD patients and support staff during their duties (e.g. stress management).
- Supporting healthcare providers and public health authorities in the EU with resources that will help them to identify and manage potential EVD patients:
 - Assessing and planning medical evacuation by air to the EU for patients with Ebola virus disease and people exposed to Ebola virus [84]
 - Case definitions for Ebola patients in the EU [85]
 - Algorithm for laboratory diagnosis of Ebola virus disease [77]
 - <u>Contact management algorithm</u>
 - Public health management of healthcare workers returning from Ebola-affected areas [79]
 - Public health management of persons having had contact with Ebola virus disease cases in the EU update [78]
 - Options for preparing for gatherings in the EU in the context of the current outbreak of EVD in West Africa
 [86]

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