RAPID RISK ASSESSMENT

Outbreak of Ebola virus disease in West Africa

Ninth update, 30 January 2015

New developments since the eighth update

Since December 2013, and as of 29 January 2015, 22 136 cases of Ebola virus disease (EVD), including 8 833 deaths, have been reported by the World Health Organization (WHO) in nine reporting countries (Guinea, Liberia, Mali, Nigeria, Senegal, Sierra Leone, Spain, the United Kingdom, and the USA).

Guinea, Liberia and Sierra Leone are described as countries with widespread and intense transmission. The remaining six countries have all been declared as countries with an initial case or cases, or with localised transmission. Five of them (Mali, Nigeria, Senegal, Spain and the USA), previously declared as affected, are now Ebola-free. The UK has not been declared affected.

On 18 January 2015, the government of Mali and WHO declared the country Ebola-free, 42 days after the last patient tested negative on 6 December 2014 [1]. In the second half of January 2015, WHO reported a significant drop in weekly cases and the end of the spread of the disease in all three currently affected countries. The most visible advancement is in Liberia.

Regarding the Ebola outbreak in West Africa, the International Health Regulation (IHR) Emergency Committee unanimously concluded on 20 January 2015 that the event continues to constitute a Public Health Emergency of International Concern (PHEIC).

As the epidemic of Ebola in West Africa is slowing down and cases are clearly declining in all three countries, the local and international response and support efforts should be strengthened in order to maintain the momentum and keep the downward trend towards zero cases.

The risks posed to Europe are lower than previously assessed as the number of cases in West Africa decreases each week. However, EU/EEA citizens traveling to affected countries, especially healthcare workers, are still at risk of being infected, so the recommended risk reduction measures for EU/EEA citizens remain unchanged.

Main conclusions

The significant drop of EVD cases in West Africa can only continue if control efforts are maintained. The situation in the three most affected countries varies considerably: some areas are experiencing small outbreaks, and the situation is not yet under control. A resurgence of cases and the epidemic remains a possibility. There is also a

Erratum. On 9 February 2015, a correction was made to page 6 concerning the number of medical evacuations to Europe: 13 was corrected to 12 and nine corrected to ten (with the addition of one in Spain).

Suggested citation: European Centre for Disease Prevention and Control. Outbreak of Ebola virus disease in West Africa. Ninth update, 30 January, 2015. Stockholm: ECDC; 2015.

possibility that the epidemic continues at a low intensity due to incomplete contact tracing and the inadequate management of new infections. All public health measures should be continued or enhanced in order to mitigate the remaining risk of exposure. Surveillance activities and effective contact tracing should be strengthened in order to achieve zero cases. In this respect, the Ebola outbreak continues to be a Public Health Emergency of International Concern (PHEIC). The IHR Emergency Committee also reviewed and confirmed all previously issued recommendations.

The risk of EVD spreading between affected countries and into the countries sharing borders with Guinea, Liberia and Sierra Leone is still present due to the frequent movement of people and insufficient Ebola surveillance in the border areas[2].

It is expected that the treatment centres and other response or technical bodies will eventually reduce their activity levels and lay off staff in response to the downward trend of the epidemic. This would lead to additional domestic and international travel, including trips by healthcare workers returning from affected areas to their home countries in the EU.

This will not necessarily result in an increased number of imported cases because the risk of exposure in the community is now lower, and the exit control measures at the airports in the affected countries seem to be reasonably effective.

It is likely that the need for repatriations and medical evacuations will decrease as the epidemic continues to decline and fewer international staff are engaged in the response efforts. However, continued vigilance is essential in order to ensure that re-entry standards do not lapse: returnees with high body temperature need to be tested in order to determine the cause of their fever, which could be caused by, for example, Lassa or dengue fever, malaria, or influenza. In this context it is important to keep in mind that the affected countries are at high risk for malaria [3], and that the influenza season has started in the EU [4].

The risk of EVD being imported into the EU or the risk of transmission occurring within the EU remains low or very low due to the range of risk reduction measures that have been put in place by the Member States and the affected countries.

Source and date of request

Internal decision, 22 January 2015.

Public health issue

Assessment of the risk of importation of Ebola virus to the EU and its potential transmission in the wake of the epidemic of Ebola virus disease in West Africa which currently affects Guinea, Liberia and Sierra Leone.

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 [5]. Detailed information about the Ebola virus and the epidemiology of EVD can be found in a series of ECDC publications available on the ECDC website [5-12].

Consulted experts

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Epidemiological update

On 29 January 2015, WHO has reported 22 136 confirmed, probable, and suspected cases of Ebola virus disease, with 8 833 deaths, in three affected countries (Guinea, Liberia and Sierra Leone) and five previously affected countries (Mali, Nigeria, Senegal, Spain and the United States of America).

On 18 January 2015, the Government of Mali and WHO declared the country Ebola-free, 42 days after the last patient tested negative on 6 December 2014 [1].

According to the latest WHO Situation Report, case numbers are declining in Guinea, Liberia, and Sierra Leone, with a halving time of 1.4 weeks in Guinea, 2.0 weeks Liberia, and 2.7 weeks in Sierra Leone. A combined 99 confirmed cases were reported from the three countries in the week ending 25 January 2015: 30 in Guinea, 65 in Sierra Leone and four in Liberia. The most recent WHO Ebola Situational Report, which refers to a stratified

analysis of cumulative confirmed and probable cases, indicates that the number of cases in males and females is similar. Compared with children under 15 years of age, people between 15 and 44 years of age are approximately three times more likely to be affected. People 45 years of age and older are almost four times as likely to be affected as children.

Distribution of cases

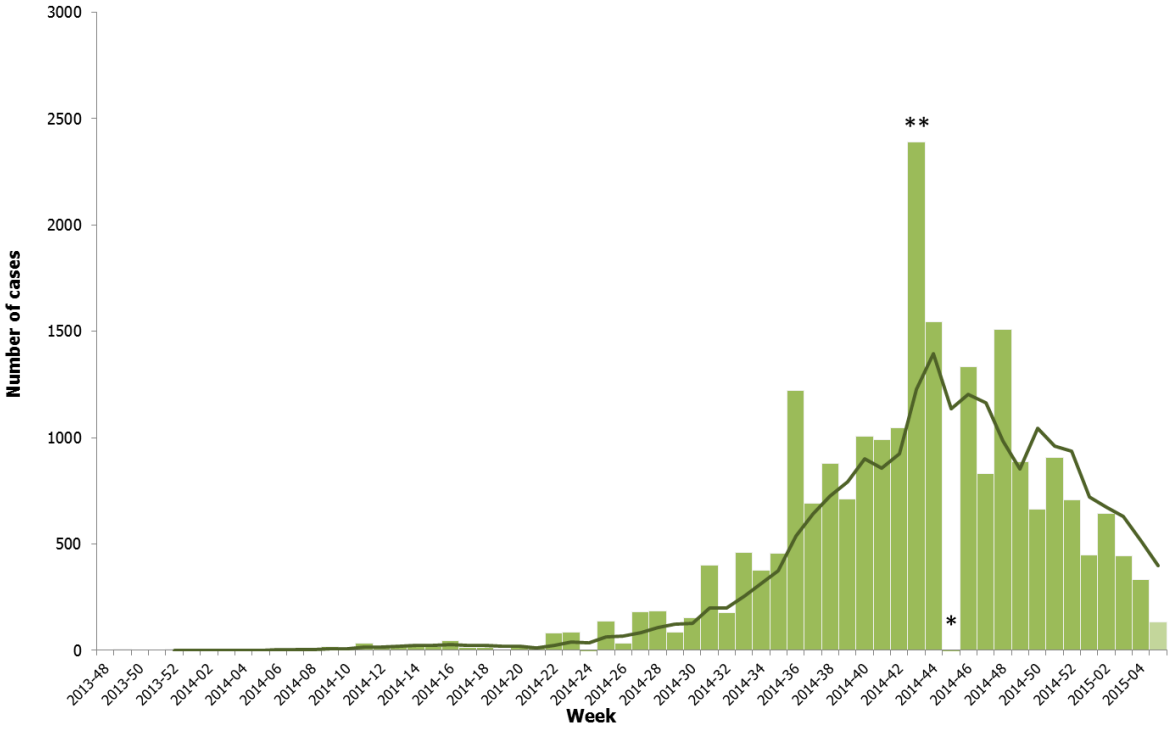
Countries with widespread and intense transmission

- Guinea: 2 921 cases and 1 911 deaths (as of 26 January 2015)
- Liberia: 8 643 cases and 3 700 deaths (as of 26 January 2015)
- Sierra Leone: 10 537 cases and 3 199 deaths (as of 25 January 2015).

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

- United Kingdom: one confirmed case on 29 December 2014
- United States: four cases including one death. The last case tested negative on 11 November 2014 in New York
- Mali: eight cases, six deaths. According to WHO, Mali was declared Ebola-free on 18 January 2015
- Nigeria, Senegal and Spain were declared free of EVD after reporting cases related to the epidemic in West Africa.

Figure 1. Distribution of cases of EVD, by week of reporting: Guinea, Sierra Leone, Liberia, Nigeria, Senegal and Mali, weeks 48/2013 to 5/2015, as of 27 January 2015



** In week 45/2014, WHO carried out a retrospective correction in the data which resulted in 299 fewer cases and a negative value for new cases in week 45 (not plotted) [13].*
*** 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 which resulted in 3 792 additional cases. These cases have actually occurred throughout the entire epidemic period.*
The green trendline is 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) [14].

Situation in the affected West African countries

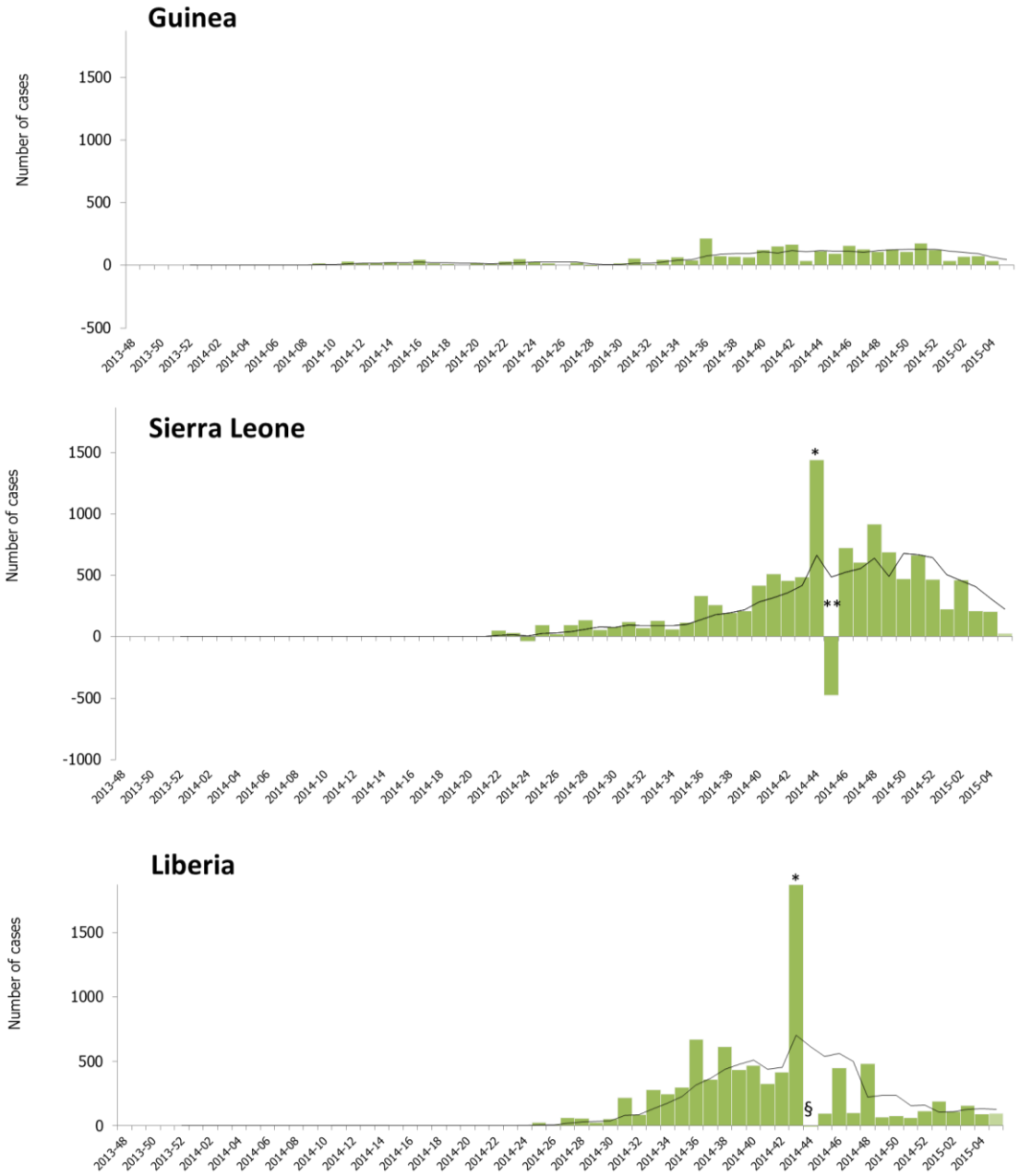
According to WHO, case incidence continues to fall in all transmission-intense countries, all of which have sufficient capacity to isolate and treat patients (more than two treatment beds for every confirmed, probable and suspected case reported). The planned number of beds in each country has been reduced in line with the falling case numbers.

Between 89% and 99% of registered contacts are being monitored in the three countries with intense transmission, though the number of contacts traced per EVD case remains lower than expected in many districts. Since the beginning of 2015, around 50% of newly confirmed cases in Guinea and Liberia have been associated with known contacts; equivalent data are not yet available for Sierra Leone.

The cumulative case–fatality rate in the three transmission-intense countries among hospitalised patients is between 54 and 62%.

According to WHO, as an indication of community engagement, 71% of the districts in Guinea and 100% of districts in Sierra Leone have a list of key religious leaders who promote safe and dignified burials. No data are available for Liberia [15].

Figure 2. Distribution of cases of EVD, by week of reporting: Guinea, Liberia and Sierra Leone, as of week 5/2015



** The marked increase in the number of cases reported in Sierra Leone (week 44) and Liberia (week 43) is the result of 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 2014 for Guinea and Sierra Leone and 31 October 2014 for Liberia [13].
*** In week 45/2014, WHO reported 476 fewer cases than the week before in Sierra Leone because of retrospective corrections.*
§ 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 04/2015)

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

Healthcare workers

Up to 25 January 2015, 834 healthcare workers (HCWs) were known to have been infected with EVD, 495 of whom have died. Please note that this number is lower than the one previously reported by WHO (18 January 2015).

Distribution of cases among HCWs: 162 in Guinea, 371 in Liberia, 283 in Sierra Leone, two in Mali, 11 infected in Nigeria, one infected in Spain while treating an EVD-positive patient, one in the UK who became infected in Sierra Leone, and three in the USA (one infected in Guinea and two infected during the care of a patient in Texas).

Table 1. Number of Ebola cases and deaths among healthcare workers, as of 28 January 2014

Country	Healthcare workers: cases	Healthcare workers: deaths
Guinea	162	88
Liberia	371	179
Mali	2	2
Nigeria	11	5
Sierra Leone	283	221
Spain	1	0
United Kingdom	1	0
United States	3	0
Total	**834**	**495**

Source: Data are based on official information reported by ministries of health [15]

Situation outside West Africa

United Kingdom

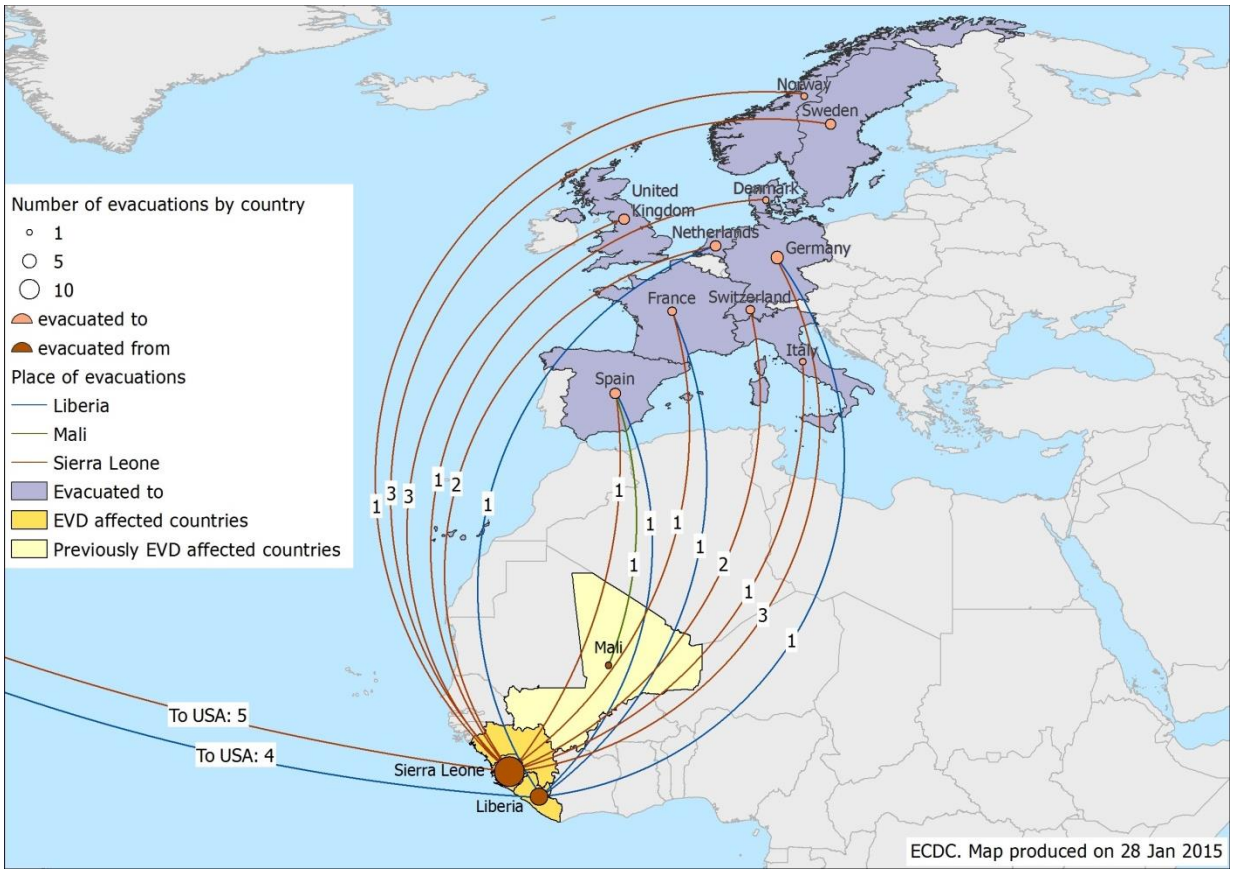
One case was reported in Scotland in a patient who travelled from Sierra Leone via Casablanca and London and arrived in Glasgow late on 28 December 2014. Media report that the Scottish nurse was discharged from hospital on 24 January 2015, after being declared free of the virus [16]. Public Health England (PHE) has completed contact tracing of the case. No high-risk contacts have been identified.

Medical evacuations and repatriations from EVD-affected and previously affected countries

Thirty-two individuals have been evacuated or repatriated from EVD-affected countries. As of 28 January, there have been 12 medical evacuations of confirmed EVD-infected patients to Europe (three to Germany, two to Spain, two to France, one to the UK, one to Norway, one to Italy, one to the Netherlands and one to Switzerland). Ten persons exposed to Ebola who then tested negative have been repatriated to Europe (two to Sweden, two to the UK, two to the Netherlands, one to Denmark, one to Germany, one to Spain and one to Switzerland).

According to media reports (25 January 2015), a Red Cross aid worker who was exposed to EVD in Sierra Leone has been medically evacuated to Sweden. The woman did not present any symptoms and was discharged. Results of the tests are still pending [17].

Figure 4. Medical evacuations and repatriations from EVD-affected and previously affected countries, as of 28 January 2015



ECDC threat assessment

In the second half of January 2015, WHO reported a significant decrease in new EVD number of cases in the three most affected countries as well as a halt of the geographical spread of the disease. The largest decrease has been reported in Liberia [18-20].

The situation in the three most affected countries varies considerably, with new cases continuing to be reported and the epidemic not yet fully under control. A resurgence of cases remains possible until all contacts of every case have been monitored for 21 days. A single undetected case can spark a new transmission chain [52]. Failing to achieve zero cases could result in continued low intensity human-to-human transmission with recurrent flare-up outbreaks. As new cases are decreasing, contact-tracing and active case finding efforts must be stepped up to ensure control. This is also the right moment to shift resources from case management to early detection of cases, rapid diagnosis, contact tracing, and building trust in the local communities.

The IHR Emergency Committee recently reviewed the Ebola outbreak and concluded that it still is a Public Health Emergency of International Concern (PHEIC) and that the current temporary recommendations should remain in effect.

The risk of EVD spreading to the countries which share borders with Guinea, Liberia and Sierra Leone is still present because of the frequent movement of people and insufficient Ebola surveillance in the border areas [2].

The current outbreak still requires a concerted international effort to improve healthcare services and infection control measures, ensure the supply of protective equipment in treatment facilities, and strengthen capacities for epidemiological surveillance and laboratory diagnosis. In the most affected countries, other sectors are suffering, notably the economic sector and food security, which makes this crisis an international and complex health emergency requiring a large-scale multi-sectorial response [21,22].

Risk of exposure to EVD for EU citizens and travellers in affected West African countries

Exposure in the community

- As stated in earlier risk assessments [23], the risk of infection through daily interaction in the community is low if visitors and long-term residents adhere to the recommended precautions. The declining number of new EVD cases over the past weeks has further reduced the already low probability of exposure to Ebola-infected persons. People who visit friends and relatives in the affected countries are at higher risk because they are likely to have more and closer contacts in the community and participate in activities known to be associated with the transmission of the Ebola.

Exposure in healthcare settings

- The risk of exposure to EVD in healthcare facilities is still present. The level of risk is related to how well infection control measures are implemented and the nature of the care required. The risk is neither limited to centres dedicated to the care of EVD patients nor is it limited to geographical areas with ongoing transmission.
- The risk of exposure to Ebola viruses is obviously higher for HCWs and volunteers who provide assistance in settings where infection control measures are not fully or incorrectly 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 personal protective equipment [24].

Risk of importation to the EU

The risk of EVD being imported into the EU and the risk of transmission occurring within the EU following an importation remains low or very low because of the range of risk reduction measures that have been put in place by Member States and affected countries.

If the downward trend in Guinea, Liberia and Sierra Leone continues, the likelihood of EVD-infected individuals arriving in the EU is expected to decrease. However, as long as the epidemic continues, it cannot be ruled out that EVD-infected people arrive in the EU by direct or indirect flights from affected countries or on board freighters or passenger ships.

Screening travellers at the point of departure cannot prevent asymptomatic infected people from boarding a plane, who could then develop symptoms while travelling or after arrival.

Almost all EU/EEA countries have issued temporary travel advice against non-essential travel to EVD-affected countries. However, a substantial number of EU professionals are involved in the international response to the Ebola outbreak [25].

As the number of EVD patients falls, it is expected that the number international healthcare workers required for case management will also decrease. A gradual scaling-down of Ebola treatment centres has been announced, and it is expected that the number of healthcare workers returning to the EU will increase in the coming weeks.

International travel to the affected countries is expected to increase over time, which in turn implies an increase in the number of returning travellers. This will not necessarily result in an increased risk of importation of EVD cases to the EU because of the falling number of new EVD cases in the affected countries. It is likely that the need for repatriations and medical evacuations will decrease as the epidemic continues to decline and less international staff is engaged in the response. The probability that a person who has returned from the affected countries and develops fever within 21 days has EVD is small. Investigations must include causes other than EVD to determine the cause of the fever, which could be caused by, for example, Lassa or dengue fever, malaria, or influenza. In this context it is important to keep in mind that the affected countries are at high risk for malaria [3], and that the influenza season has started in the EU [4].

Previously, ECDC considered the risk of importation to Europe via routes used by undocumented migrants from West Africa who arrive at the southern coast of the Mediterranean as a remote possibility. As the epidemic slows down, this possibility also diminishes.

Several other risks are also reduced but cannot be excluded, e.g. travel and transportation risk; risks related to biosafety and transmission through substances of human origin; the risk of Ebola virus transmission in the EU following importation, repatriation and medical evacuation; and the risks from infected individuals seeking medical care in the EU/EEA.

Options for risk reduction

The risk reduction measures for individual protection and the options for mitigating the risk of importation and spread in the EU recommended in previous risk assessments remain valid [23].

Reduction of the risk of infection in West Africa

To reduce the risks of EVD infection, non-essential travel to the affected areas should be avoided. WHO does not recommend any travel or trade restrictions to the affected countries [26].

Visitors and residents in EVD-affected areas should strictly follow precautionary measures:

- 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 bush meat.
- Wash hands regularly, using soap or antiseptics.

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

- 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.
- Identify appropriate in-country healthcare resources prior to travelling.
- Ensure that your travel insurance covers medical evacuation in the event of illness or accident in order to limit exposure to local health facilities.

Following the declaration of the Public Health Event of International Concern (PHEIC) on 8 August 2014, WHO recommended the following measures:

- 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. Exit screening would not detect an incubating passenger who has not yet developed fever [27].
- 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.

Screening of travellers

Some EU Member States implemented entry screening to complement the exit screening protocols in place in the affected countries. Complementing exit screening with entry screening may be considered:

- when there are doubts about the efficiency of exit screening;
- to detect any individual who develops a 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.

Complementing temperature screening with a 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 who had high-risk exposure so they can be monitored or quarantined.

Travel restrictions and passenger screening on arrival at sea ports, airports or ground crossings in non-affected countries that do not share borders with affected countries is currently not recommended by WHO [27].

Healthcare settings

To reduce the risk of transmission in the EU following importation of Ebola virus, the following options are available:

- Implementation of infection control measures for EVD during the treatment of cases. Transmission to healthcare workers can be prevented by the strict application of infection control measures as recommended by WHO. According to WHO guidelines [24], the following measures are essential for the safe medical care of EVD patients:
  - Isolation rooms with dedicated bathroom
  - Availability of personal protective equipment
  - Personnel adequately trained to use the equipment
  - HCWs returning from affected areas have a different probability of exposure than general travellers. They should be given pertinent information upon their return. In addition, they should undergo an individual

exposure assessment as early as possible. ECDC published a document on the public health management of HCWs returning from Ebola-affected areas [28].

- 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 medevac an infected or exposed person from an Ebola-affected country to an EU Member State [29].

Public health measures

- Contact tracing and contact management of contacts of a case. ECDC has produced a document for the management of those who had contact with EVD cases [30].
- Raising awareness and sensitising healthcare workers in the EU about EVD, and supporting them with resources that will help them identify and manage potential EVD patients.
- Additional information and communication to travellers departing from EVD-affected countries.
- 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).

Options for information and communication

In order to minimise the time between onset of symptoms and isolation and diagnosis, people who return from Ebola-affected areas should be informed 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).

In addition, healthcare providers in the EU should be informed of and sensitised 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 [24,31].

Healthcare providers and support staff should be provided with training before caring for EVD patients (e.g. stress management). ECDC has developed guidance for supporting healthcare providers and public health authorities in the EU to identify and manage potential EVD patients.

Advice and information by ECDC is available through the following publications:

- Assessing and planning medical evacuation by air to the EU for patients with Ebola virus disease and people exposed to Ebola virus [32]
- Case definitions for Ebola patients in the EU [33]
- Algorithm for the laboratory diagnosis of Ebola virus disease [34]
- Contact management algorithm [35]
- Public health management of healthcare workers returning from Ebola-affected areas [28]
- Public health management of persons having had contact with Ebola virus disease cases in the EU – update [30]
- Options for preparing for gatherings in the EU in the context of the current outbreak of EVD in West Africa [36]

Supporting information

Disease background information

Infections with African Ebola viruses cause a severe disease in humans called Ebola virus disease. There are five species of the genus *Ebolavirus* (Filoviridae family): *Zaire ebolavirus, Sudan ebolavirus, Reston ebolavirus, Taï Forest ebolavirus* and *Bundibugyo ebolavirus* [37,38]. The current outbreak in West Africa is caused by *Zaire ebolavirus*.

Further background information can be found in the previous risk assessment [23].

The seroprevalence of IgG antibodies to *Zaire ebolavirus in* 1997 in a region of Gabon where multiple epidemics of EBO haemorrhagic fever had previously occurred was 1.0% [39]. Another study on asymptomatic replicative infections in close contacts of symptomatic EVD patients during the outbreak in 1996 in Gabon reported that out of 24 asymptomatic individuals, 11 (46%) had developed IgM and IgG response to Ebola antigens with signs of a strong inflammatory response [40,41]. The results in these and other studies depend heavily on the sensitivity and specificity of the diagnostic tests used.

It is unknown what proportion of close contacts in the current outbreak has gone through an asymptomatic infection, and what proportion of the population has acquired protective immunity without clinical disease. Further studies during and after the current outbreak can increase our understanding these aspects. To which extent this aspect has affected the epidemiology of the outbreak is unknown. The existence of asymptomatic infections should also be considered in the design of clinical vaccine trials [42].

Event background information

Chronology of events – key dates

23 January 2015: EVD vaccine developed by GSK ships to Liberia for phase-3 trial expected to start in February 2015 [43] .

21 January 2015: WHO publishes a statement following the fourth meeting of the IHR Emergency Committee stating that the event continues to constitute a Public Health Emergency of International Concern (PHEIC) [44].

18 January 2015: The government of Mali and WHO declare Mali free of Ebola virus transmission [1].

29 December 2014: Scotland reports the first imported case of EVD to the UK that is not a medical evacuation. The case is a healthcare worker who returned after volunteering at an Ebola treatment centre in Sierra Leone. According to WHO, all possible contacts of the case have been investigated and no high risk contacts have been identified.

2 December 2014: WHO declares Spain Ebola-free because 42 days have passed since the confirmed case tested negative.

25 November 2014: WHO confirms two additional cases of EVD in Bamako, Mali. Both infected persons were close contacts of previously identified EVD-infected patients.

17 November 2014: WHO reports two additional cases in Bamako, Mali. All cases were linked to an imported EVD case from Guinea on 25 October.

12 November 2014: WHO reports four additional cases in Bamako, Mali, that are not linked to the case reported on 23 October. Two are probable cases from Guinea, one admitted to a clinic in Bamako on 25 October, the other one a visitor of this patient (both died). The two other cases are confirmed cases in HCWs. One died on 11 November [45].

1 November 2014: A UN worker is medically evacuated from Sierra Leone to France upon request from WHO [46].

28 October 2014: WHO publishes a press release regarding the approval of an Ebola vaccine trial at Lausanne University Hospital in Switzerland. The trial, supported by WHO, is the latest in a series of trials that are conducted in Mali, the UK and the USA [47].

23 October 2014: The US Centers for Disease Control and Prevention report 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 [48].

23 October 2014: The Ministry of Health in Mali reports that a two-year-old girl who recently arrived from Guinea tested positive for Ebola. This is the first confirmed case of Ebola virus infection in Mali [49].

20 October 2014: WHO officially declares Nigeria free of Ebola virus transmission [50].

17 October 2014: WHO officially declares Senegal free of Ebola virus transmission [51].

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

10 October: In the USA, a healthcare worker at Texas Health Presbyterian Hospital who cared for the first imported EVD patient tests positive for Ebola [52].

6 October 2014: The Spanish authorities report 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 complete the 21-day follow-up period without developing disease. No local transmission of EVD reported in Senegal.

30 September 2014: The US Centres for Disease Control and Prevention announce 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 forecasts 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 [53]. The same study estimates 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 recognises the EVD outbreak as a 'threat to international peace and security' and unanimously adopts a resolution on the establishment of an UN-wide initiative which focuses assets of all relevant UN agencies to tackle the crisis [54].

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

8 August 2014: WHO declares the Ebola outbreak in West Africa a Public Health Event of International Concern (PHEIC) [55]. On 23 October, WHO reconfirms that the outbreak continues to constitute a Public Health Event of International Concern.

End of July 2014: A symptomatic case travels by air to Lagos, Nigeria, where he infects a number of HCWs and airport contacts before his condition is recognised as EVD.

May 2014: Sierra Leone and Liberia report the first cases [56,57]. 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 notifies WHO about a rapidly evolving outbreak of Ebola viral disease (EVD) [58]. 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 [59-61]. The first cases were reported from south-eastern Guinea and the capital Conakry.

Treatment and vaccine development

No drug for the treatment of EVD, or vaccine preventing the development of EVD, has been authorised in the EU. The use of whole blood or plasma from EVD survivors, as recommended by WHO in September 2014 [23,62], does not require an EU authorisation and is the responsibility of the national competent authorities for blood and blood components. In addition, early supportive clinical treatment and management are essential and can improve the chances of recovery [31,63].

Potential new Ebola therapies and vaccines were reviewed during four WHO meetings with relevant stakeholders, starting in September 2014 [64]. Further, the European Medicines Agency (EMA) is reviewing available information on Ebola treatments and vaccines currently under development in order to support fast-track authorisation [65].

Convalescent whole blood or plasma

The rationale behind treatment with convalescent whole blood or plasma is the presence of antiviral neutralising antibodies. A smaller study, conducted in the Democratic Republic of the Congo in 1995 involving eight patients, suggested a positive impact of convalescent whole blood on the survival of EVD patients [66]. In September 2014, WHO published interim guidance for national health authorities and blood transfusion services on the use of convalescent whole blood or plasma collected from recovered EVD patients for transfusion to infected individuals [62]. Most patients treated for EVD in Europe or the US during 2014 have received convalescent plasma from an EVD survivor.

Formal clinical trials assessing the impact of convalescent plasma on the clinical outcome of EVD in affected adult patients (offered to individuals > 18 years of age) have been initiated in Guinea (Centre National de Transfusion Sanguine de Conakry, Hôpital National Donka, Conakry) in collaboration with the Belgian Institute of Tropical Medicine [67], and in Liberia (ELWA hospital in Monrovia) in collaboration with Clinical Research Management, Inc.

[68]. Convalescent plasma in the trials is tested for relevant infectious disease markers and pathogen-inactivated by psoralen/UV technology (Cerus INTERCEPT) in order to substantially reduce the risk of any transfusion-transmitted infection.

The availability of convalescent plasma from survivors in the EU/EEA is monitored by the European Blood Alliance. At current, the availability is low. A treatment protocol is under development.

Ebola antivirals

A number of candidate antiviral treatments have shown promise in non-human primate models. Several potential drugs have been used in experimental treatments of individual EVD cases, e.g. brincidofovir (Chimerix, USA), favipiravir (Toyama Chemicals, Japan and MediVector Inc., USA), TKM-Ebola (Tekmira pharmaceutical Corporation, Canada) and ZMapp (Mapp Biopharmaceutical Inc., USA). These several experimental drugs were often used in combination with convalescent plasma from EVD survivors, which makes evaluation of the clinical impact difficult [69].

Clinical trials assessing the efficacy in affected patients in Africa have either just started (as in the case of favipiravir [70]), or are about to begin (brincidofovir, amiodarone and ZMapp) [71]. The Institut National de la Santé Et de la Recherche Médicale, France, is sponsoring a study [72] on favipiravir (offered to individuals older than one year of age) in three centres in Guinea (MSF Ebola treatment centre in Gueckedou, French Red Cross Ebola care centre in Macenta, and ALIMA Ebola care centre in Nzerekore). Chimerix is sponsoring a clinical trial assessing the efficacy of brincidofovir (offered to individuals older than two months) in the US. Finally, the Emergency NGO Onlus will conduct a trial in a hospital located in Freetown, Sierra Leone, using Amiodarone [73], an anti-arrhythmic drug. The US-based Biomedical Advanced Research and Development Authority (BARDA) announced last week that a clinical trial with 100–150 volunteers will be conducted in Liberia and the United States (http://www.phe.gov/about/barda/Pages/default.aspx).

Ebola vaccines

Three vaccine candidates in advanced stages of development are being studied in clinical trials focusing on healthy adults:

Vaccine candidates	Producers
Chimpanzee adenovirus 3 expressing *Zaire Ebolavirus* glycoprotein (cAd3-EBO Z)	GSK
Recombinant vesicular stomatis virus expressing *Zaire Ebolavirus* glycoprotein (rVSV-ZEBOV)	Newlink/Merck
Adenovirus 26 expressing *Zaire Ebolavirus* glycoprotein + multivalent modified vaccinia virus Ankara containing *Zaire Ebolavirus* glycoprotein to be used in a heterologous prime-boost strategy (Ad26.ZEBOV + multivalent MVA-ebola virus)	Crucell Holland and Bavarian Nordic

For the vaccine candidate cAd3-EBO Z, phase-1 trials have been initiated in Switzerland, the UK, the US, and Mali. First results assessing the cAd3-EBO Z vaccine candidate in the US show that this vaccine candidate was well-tolerated and produced antibody and cell-mediated immune responses in a dose-response manner in all 20 participating healthy adults (18–59 years of age) [74]. The first 300 doses were shipped 23 January 2015 to Liberia for use in a phase-3 trial planned to enrol 30 000 and expected to start in February 2015 [43] . In parallel, phase-2 safety trials will be conducted in several West African countries not affected by Ebola: Cameroon, Ghana, Mali, Nigeria and Senegal. A prime-boost strategy is also being evaluated in the UK, using the cAd3-EBO Z candidate as a primer and the MVA-BN Filo as a booster to assess extent of the immune response [75].

The vaccine candidate rVSV–ZEBOV is currently being tested in phase-1 trials in Germany, Switzerland, the UK, the US and Kenya, with the goal of assessing immunogenicity and safety. At one of the trial sites, the University Hospital of Geneva, investigators temporarily suspended the trial (total enrolment: 59 volunteers as of 11 December 2014) after the identification of four cases of mild joint pain (in the hands and feet) 10 to 15 days after receiving the injection [76]. The trial was resumed on 5 January 2015, but with a lower vaccine dose.

A further phase-1 trial was initiated on 6 January 2015 in the UK, testing prime-boost regimens using MVABN-Filo and Ad26.ZEBOV.

It is unlikely that vaccine efficacy data will be available before fast-track authorisations of the vaccines by regulatory agencies. If the vaccines are proven safe and immunogenic in phase-1 and 2 trials, vaccines could be available in the coming months for priority use in healthcare workers. However, it should be noted that if the vaccines are rolled out early, they will have undergone one limited testing in humans, and post-authorisation monitoring of safety and effectiveness will be important.

Study designs for the phase-3 vaccine trials to be conducted in West Africa have been the subject of intense ethical and methodological discussions by expert groups convened by WHO and held with the participation of all relevant governmental bodies in the involved African countries [77].

The WHO Director General has established a Strategic Advisory Group of Experts (SAGE) Working Group on Ebola Vaccines and Vaccination [78]. SAGE will be asked to give its Ebola vaccine recommendations based on the best scientific evidence and public health policy, but the final decision on offering vaccines in West Africa lies with the ministries of health in each of the affected countries. It is at this time difficult to estimate when vaccines will become available for general use [79].

Finally, ECDC has set up an extranet to support the Ebola Clinical Network [80]. The aim of this network for EVD Reference Treatment Centres in EU/EEA Member States is to share experiences and update technical information (e.g. protocols, methods, materials and approaches regarding the treatment of EVD patients, infection prevention and control procedures, EVD training).

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