RAPID RISK ASSESSMENT

Monkeypox cases in the UK imported by travellers returning from Nigeria, 2018

21 September 2018

Conclusions

In September 2018, the United Kingdom (UK) notified two separated monkeypox cases with recent travel history to Nigeria. These are the first cases of monkeypox in humans reported in the European Union (EU). Both cases were symptomatic while travelling by air to the UK. As of 17 September 2018, no additional cases have been detected in the EU (EU). The notification of imported cases in Europe is not unexpected due to the circulation of monkeypox virus in West and Central Africa. The risk of new introductions of monkeypox to Europe depends on the extent of the circulation of the virus in Nigeria and in other countries of West and Central Africa. Overall, the likelihood of monkeypox importation in Europe remains very low, but new travel-related cases in the European Union/European Economic Area (EU/EEA) Member States cannot be excluded. Hence, public health professionals should follow the development of the epidemiological situation in countries with monkeypox circulation and be aware of the risk of potential monkeypox case importation (more information is available through the weekly ECDC Communicable disease threats reports).

With regards to this event, the epidemiological link with Nigeria has been identified through the travel history in both cases, therefore West African monkeypox clade is expected to be the aetiological agent. The risk for spread in the EU/EEA remains very low due to the moderate transmissibility of the disease reported to date, its distinctive clinical picture – although physicians should be aware of the similarities with and differences from varicella and other human poxvirus infections – the available laboratory capacity in Europe for rapid diagnostics and capacities for appropriate management of cases and their contacts in EU/EEA countries.

The individual risk of infection through contact with a monkeypox patient depends on the nature and duration of the contact. Family members, close contacts (e.g. immediate neighbour on aircraft), or persons who have provided care to patients, including health care workers (HCWs) who have not applied preventive measures, have a moderate risk for infection. In the community, the risk of transmission is considered negligible.

No cases of monkeypox virus transmission through substances of human origin (SoHO) have been documented. However, reported virus transmission from mother to child during pregnancy and through an

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invasive bite or scratch from an ill animal suggest that transmission via SoHO is theoretically possible. There are no data on the beginning of viraemia during the incubation period or in possible asymptomatic cases. No chronic carriage of the virus has been reported. Thus, the risk of monkeypox virus transmission through SoHO is difficult to assess.

Options for response

Prevention and control in healthcare settings

HCWs should be informed and trained to recognize signs and symptoms of monkeypox.

HCWs caring for a suspected or laboratory confirmed case of monkeypox are advised to implement standard contact and droplet infection control precautions and consider the following:

- Seek advice from an infectious disease specialist to evaluate the likelihood of monkeypox infection of the suspected case.
- Apply routine infection control standard precautions. Hand hygiene is a major component of standard precautions and one of the most effective methods to prevent transmission of pathogens associated with health care.
- Apply contact and droplet precautions. HCWs caring for patients should use
  - a disposal gown
  - disposable gloves
  - respiratory protection (FFP3 filter mask or N-95 particulate filter respirator in case of extended contact), and;
  - eye protection (face shield or goggles) for all interactions that may involve contact with the patient or potentially contaminated areas in the patient's environment.
- Patients should be placed in a single-patient room.
- HCWs should have their exposure evaluated, their vaccination status against smallpox virus verified and the benefit/risk ratio of offering the smallpox vaccination prophylaxis assessed.

Contact tracing and precautionary measures

In case of identification of a monkeypox case, EU/EEA Member States should consider the following options for risk and control management:

- Trace all contacts of a monkeypox-confirmed case.
- All identified contacts should be instructed about monkeypox symptoms and self-monitor their temperature daily for 21 days after last exposure. If developing symptoms during this period, contacts should self-isolate at home while calling healthcare services to report their symptoms and indicate their exposure. In general, symptomatic contacts should be isolated during their investigation.
- For passengers in an aircraft sitting in the immediate vicinity of the cases (within a radius of at least two metrers), an exposure assessment by competent health authorities should be carried-out and monitoring implemented accordingly.
- Close family contacts would benefit from an exposure assessment, being checked for smallpox vaccination status and evaluated for receiving prophylactic vaccination (smallpox vaccine) in line with relevant national/international recommendations, keeping in consideration the benefit/risk ratio of the vaccine and the fact that vaccines against smallpox are not licensed for prophylaxis of monkeypox.

Advice to travellers going to affected countries

- Reduce risk of animal-to-human transmission (avoid direct contact with rodents and primates, limit direct exposure to blood and meat, cook meat thoroughly and use gloves and protective clothing when handling sick animals or animal tissues, and during slaughtering procedures).
- Reduce risk of human-to-human transmission (avoid close physical contact with people who have or are suspected to have monkeypox, avoid exposure to contaminated material, use gloves and protective equipment when taking care of sick people and wash hands regularly).

Source and date of request

Internal decision at the ECDC Round Table meeting, 13 September 2018.

Public health issue

The risks assessed in this document are of the introduction and further spread of monkeypox in the EU/EEA, infection with regards to different settings (e.g. healthcare, community, etc.) and transmission through SoHO.

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All experts have submitted declarations of interest and a review of these declarations did not reveal any conflict of interest.

Disease background information

Monkeypox is a zoonotic viral disease caused by the monkeypox virus belonging to the *Orthopoxvirus* genus of the *Poxviridae* family, which also includes smallpox, vaccinia, cowpox, camelpox, ectromelia (mousepox) and other viruses [2]. At least five members of the *Orthopoxvirus* genus cause infection in humans: variola, vaccinia, cowpox, camelpox and monkeypox viruses [3,4].

Monkeypox has been reported in the tropical rainforest regions of Central and West Africa, after its first recognition in 1970 as a human disease during the investigation of a suspected smallpox case in the Democratic Republic of the Congo (DRC). In the past decade, cases of human monkeypox were reported in multiple countries in Central Africa, but mostly in the DRC, which is considered endemic, with more than 1 000 suspected cases per year since 2005. Human cases are less frequently reported in Central African Republic and in the Republic of the Congo, with sporadic cases reported between 2015 and 2017 [2]. In West Africa, only sporadic cases between 2014 and 2017 were notified in Liberia and Sierra Leone [2]. However, Nigeria reported a large multistate outbreak in 2017 to 2018 (see specific section on monkeypox in Nigeria below).

After smallpox eradication in 1980 and consequent to the cessation of smallpox vaccination, monkeypox emerged as the most prevalent orthopoxvirus infection in humans [2,5]. In recent years, the number of reported monkeypox cases has increased and the virus' geographical range has expanded. The number of monkeypox cases is likely underestimated due to limited specific surveillance and laboratory capacity in forested areas of West and Central Africa.

In May 2003, the Centers for Disease Control (CDC) reported monkeypox cases from six federal states in the central part of the US. Patients developed fever and rash after close contact with pet mammals, predominantly rodents. A total number of 81 cases were identified, with 40% laboratory-confirmed. No human-to-human transmission was identified and none resulted in death. Epidemic intelligence revealed the importation of small mammals from Ghana to Texas as the probable source of the introduction of the virus into the US. The spread of the virus between federal states was connected to infected prairie dogs that were co-housed with rodents of African origin [6].

The monkeypox virus is transmitted to humans through a bite or direct contact with an infected animal's blood, body fluids or cutaneous/mucosal lesions [2]. In nature, many animal species were found infected with monkeypox virus, including rope and tree species of squirrels, Gambian giant rats, striped mice, dormice and primates [7]. Rodents like Gambian giant rats (*Cricetomys gambianus*) and squirrels are suspected to be the natural reservoirs of the virus [8].

The virus can be transmitted by respiratory droplets during direct and prolonged face-to-face contact. In addition, monkeypox virus can be transmitted by direct contact with body fluids of an infected person or with virus-contaminated objects, such as bedding or clothing [5,7].

The incubation period is usually 6 to 16 days, but can range from 5 to 21 days [7]. The illness typically lasts for two to four weeks. It is characterised by smallpox-like signs and symptoms, sometimes milder than smallpox [9]. Symptomatology begins with fever accompanied by fatigue and headache. Within three days from the onset of the first symptoms, a maculopapular rash rapidly develops with lesions often present on the palms of the hands and soles of the feet, followed by the spreading to other parts of the body. The lesions progress to the stage of

macules, papules, vesicles, pustules, crusts and scab before falling off [10]. The lesions can be extremely itchy and secondary bacterial infection may occur if scratching occurs. The lesions can cause scarring. Prior to and concomitant with the rash, lymphadenopathy is observed in many patients, which is usually not observed in smallpox or varicella [5,11].

The case fatality ratio (CFR) ranges from 1% to 10% in monkeypox outbreaks [7]. The major disease sequelae are represented by disfiguring scars and permanent corneal lesions [11]. Two different clades of the virus have been identified: the Congo Basin and the West African. The two clades are geographically separated. To date, limited human-to-human transmission and milder disease are observed in the West African clade [5,9,12,13].

Considering varicella as the most relevant differential diagnosis, electron microscopy was traditionally used in the past to distinguish herpesviruses from orthopoxviruses. Today, the detection of the monkeypox virus DNA-genome from suspected skin lesions by real-time polymerase chain reaction (Real-Time PCR) is well established in several laboratories in Europe. Scabs, swabs and aspirated lesion fluid are preferably used for PCR over blood due to limited duration of viremia. Results from these specimens show the best correlation with both infectivity and the clinical course of infection. Recent Real-Time PCR approaches can discriminate not only monkeypox virus from other orthopoxviruses but also the two monkeypox virus clades described above. Serology has limited value due to the immunological cross-reactivity between human-pathogenic orthopoxviruses. However, for contact investigations, IgM and IgG detection by immunofluorescence assays is available in some laboratories. Immunohistochemistry can be used to identify antigens in biopsy samples and to exclude or identify other suspicious agents.

Diagnostic procedures and manipulation of specimens suspected to contain monkeypox virus should be performed in BSL-2 facilities, putting in place BSL-3 work practices (especially for the personnel not vaccinated for smallpox within the past 10 years) [14]. Specimen manipulations should be carried out in a certified class II biosafety cabinet (BSC) [14].

Monkeypox diagnostics are offered by 17 laboratories in 12 EU/EEA countries: Denmark, Finland, France (2), Germany (4), Hungary, Ireland, Italy, Poland, Slovenia, Sweden, the Netherlands (2), and the UK. An overview of the availability and type of diagnostics for monkeypox can be found in the EVD-LabNet Directory [15].

Treatment is symptomatic and supportive, including prevention and treatment of secondary bacterial infections. There is no specific vaccine or treatment available for monkeypox virus infection [7]. Some antivirals (cidofovir and brincidofovir) have shown activity against poxviruses *in vitro* and in animal studies and have been used on a research basis to treat severe smallpox vaccine-associated adverse events. Vaccinia-immune globulin has also been used in this context [5,16]. In specific situations, the use of these products can be considered [16]. Tecovirimat, the only drug with an indication for the treatment of smallpox approved by the U.S. Food and Drug Administration (FDA) [17], can represent an option in the treatment of patients infected by monkeypox virus.

To reduce animal-to-human transmission in an area with active monkeypox virus circulation, it is recommended to avoid contact with animal reservoirs as well as any materials that have been in contact with a potentially sick animal.

In healthcare settings, prevention of transmission is based on appropriate respiratory isolation (contact and droplets precautions) and standard infection control precautions during care of symptomatic suspected and confirmed monkeypox patients [7].

Previous vaccinations against smallpox can confer cross-protection against monkeypox as the two viruses are closely related. Studies carried out in the 1980s showed 85% effectiveness of the smallpox vaccine against monkeypox[5]. Furthermore, it is thought that early post-exposure vaccination may prevent the disease or make its course less severe [16]. Following the worldwide eradication of smallpox, the vaccine is not available to the general public, but vaccine stockpiles are maintained by several countries and WHO [18].

WHO suggests that national health authorities should consider immunisation against smallpox for healthcare workers and those treating or exposed to patients with monkeypox or their samples [7,19,20]. Smallpox vaccines manufactured using older technologies should not be given to people with compromised immune systems [7,18].

Additional information can be found in the following links:

- WHO fact sheet on monkeypox [7]
- CDC resources on monkeypox [21]: infection control at hospital [1], infection control at home [22], and smallpox vaccine guidance [20]
- Monkeypox: information for primary care published by Public Health England (PHE), 11 September 2018 [23]
- Monkeypox: Guidance for environmental cleaning and decontamination published by PHE, 11 September 2018 [24].

Event background information

In September 2018, the UK reported through the European Union Early Warning and Response System (EWRS), two imported cases of monkeypox in travellers coming from Nigeria. There is no epidemiological link between the two patients and according to epidemiological investigations conducted by Public Health England both cases are believed to have contracted the infection in Nigeria.

The first case was notified on 8 September 2018 after travelling to the UK on 2 September from Abuja, Nigeria by airplane. The case was symptomatic on the flight. Contact tracing and monitoring of potential contacts is ongoing. As of 17 September 2018, all the contacts have so far been asymptomatic. The case initially stayed at a naval base in Cornwall UK prior to admittance to the expert infectious disease unit at the Royal Free Hospital in London once the diagnosis of monkeypox was laboratory-confirmed.

The second case was notified on 11 September 2018. On 4 September 2018, the case arrived in the UK by airplane from Lagos, Nigeria via Paris, France to Manchester. The affected individual case was symptomatic on the flight. Contact tracing of potential contacts is ongoing both in the UK and France. As of 17 September 2018, all the contacts have been asymptomatic. The case is being treated in a high-consequence infectious disease facility at the Royal Liverpool Hospital [25]. While in Nigeria, potential exposures may have included bushmeat consumption and contact with an individual with similar skin lesions.

According to PHE, the risk to the public in the country is very low and health authorities are contacting people who may have been in close contact with the individuals in order to provide information and health advice. As a precautionary measure, contact tracing of close contacts of the cases, including flight passengers, airport staff, healthcare workers, is currently under way [25].

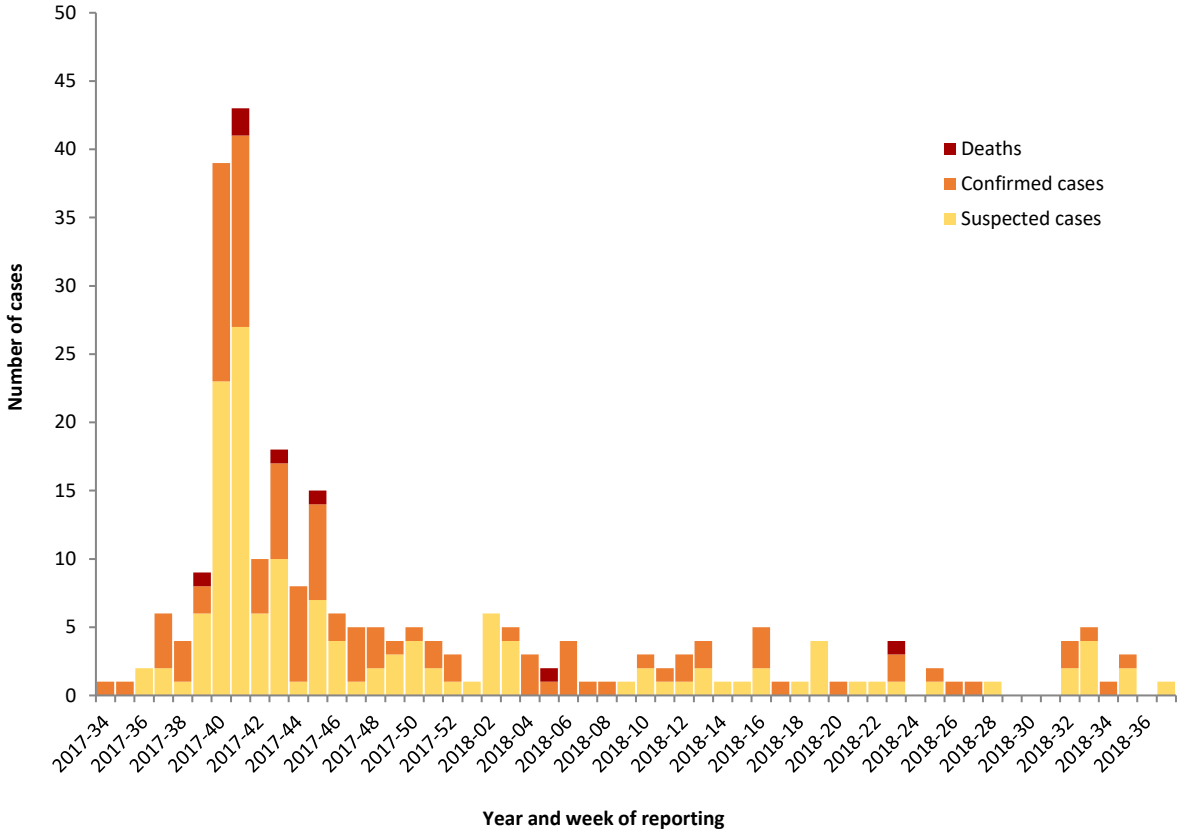
The UK has decided to offer HCWs pre-exposure prophylaxis with a third generation non-replicating smallpox vaccine (Imvanex, Bavarian Nordic). Close contacts are being offered post-exposure prophylaxis with the same vaccine. The vaccine has been acquired and offered to appropriate contacts and HCWs.

Situation in Nigeria in 2017 to 2018

According to the Nigerian Centre for Disease Control (NCDC), 269 cases of monkeypox have been reported from 26 of the 36 states between September 2017 and 15 September 2018 [26]. Among the suspected cases, 115 were confirmed in 17 states. Seven deaths in confirmed cases were recorded since the start of the outbreak, four of which were among immunosuppressed patients. A few family clusters were identified during this outbreak, but the majority of patients had no known person-to-person contact or apparent epidemiological linkage, suggesting spillover events into the human population from multiple wildlife reservoir sources, which is corroborated by genetic analysis [9,27]. The West African clade of monkeypox virus was detected in the confirmed cases [9,27,28].

Since the beginning of 2018 and as of 15 September, 76 monkeypox cases, including two deaths, have been reported in 15 states. Of these cases, 37 have been confirmed [26].

Figure 1. Number of monkeypox cases in Nigeria by year and week of reporting from September 2017 and as of 15 September 2018



Source: Nigeria CDC, Situation report as of 15 September 2018 [26].

NCDC has been working with PHE, the public health departments in the affected states and other partners in Nigeria to investigate the cases recently identified in the UK [29].

Situation in the rest of West and Central Africa in 2018

Cameroon: On 30 April 2018, two suspected cases of monkeypox were reported to the Directorate of Control of Epidemic and Pandemic Diseases (DLMEP) by the Njikwa Health District in the Northwest Region of Cameroon bordering Nigeria. On 14 May 2018, one of the suspected cases tested positive for monkeypox virus by PCR. On 15 May 2018, an incident management system was set up at the National Emergency Operations Center. An investigative mission to the Northwest and Southwest Regions from 1 to 8 June 2018, found 21 new suspected cases without active lesions. As of 13 June 2018, a total of 36 suspected cases have been reported from both the Northwest and Southwest Regions [30].

Central African Republic: The outbreak was officially declared on 17 March 2018 in the sub-province of Ippy, Bambari district. Since the beginning of the outbreak, three districts have been affected, namely Bambari, Bangassou and Mbaïki districts. Cumulatively, 40 cases of monkeypox with one death (CFR 2.5%) have been reported from 2 March to 22 August 2018 in the country and 13 cases have been laboratory confirmed out of 23 samples tested. No new cases have been notified in the three districts after the end of the epidemic.

Democratic Republic of the Congo: From weeks 1 to 33, 2018, there have been 2 585 suspected cases of monkeypox, including 42 deaths (CFR 1.6%). Suspected cases have been detected in 14 provinces. Sankuru Province has had a remarkably high number of suspected cases in 2018.

Liberia: Since the beginning of 2018 and as of 19 August, four suspected cases have been reported from Sinoe, Rivercess, Nimba and Maryland Counties [31].

Sierra Leone: In April 2017, an isolated case of monkeypox was confirmed in Pujehun District, Sierra Leone. This is the third known occurrence of monkeypox in the country, with the first reported case in 1970 and the second in 2014 [32].

ECDC risk assessment for the EU

The notification of imported cases in Europe is not unexpected due to the circulation of monkeypox virus in West and Central Africa and the travel volume pattern observed from this region into the EU. According to the International Air Transport Association (IATA) database, over half a million people travelled from Nigeria to the EU Member States in 2017. Among these travellers, the UK has the highest travel volume of passengers from Nigeria (59%), followed by Italy (9%), Germany (7%) and Ireland (6%). France, the Netherlands, Spain and Sweden account for less than 5% each. In total, these eight countries accounted for 93% of the travellers from Nigeria to the EU in 2017 (See Annex 1). In 2017, travellers came from other countries with reported monkeypox virus circulation to the EU Cameroon (215 658), DRC (97 380), Sierra Leone (40 023), Liberia (29 768) and Central African Republic (10 853).

The notification of two imported cases in a short period of time could indicate an enhanced circulation of monkeypox virus in West Africa in 2017 to 2018. This is supported by continuous reports of sporadic cases in Nigeria after the outbreak reported in late 2017 and the notification for the first time of an outbreak in southern Cameroon in 2018.

Risk of introduction and further spread within the EU/EEA

The risk of new introductions of monkeypox to Europe depends on the extent of the circulation of the virus in Nigeria and other countries in West and Central Africa. Cases continue to be reported from several countries, but present information indicates that the peak of the outbreak in Nigeria occurred in October 2017.

Overall, the likelihood of monkeypox importation to Europe remains very low, but new travel-related cases into EU/EEA countries cannot be excluded. Therefore, public health professionals should follow the development of the situation in West and Central Africa and maintain healthcare awareness about the risk of occurrence of potential monkeypox cases among individuals travelling back from affected areas with compatible clinical presentation.

With regard to this event, due to the epidemiological link with Nigeria, the West African clade is expected to be the aetiological agent, pending genomic confirmation. The risk of spread in the EU/EEA is very low due to the moderate transmissibility of the disease reported to date, its distinctive clinical picture – although physicians should be aware of the similarities with and differences from varicella and other poxvirus infections in humans – the available laboratory capacity in Europe for rapid diagnostic and capacities for appropriate management of cases and their contacts in EU/EEA countries.

Risk of infection with regard to different settings for EU/EEA citizens

In the community, the risk of transmission is considered negligible.

The individual risk of infection through contact with a patient depends on the nature and duration of the contact. Close contacts (e.g. immediate neighbour on aircraft, family members with close contact), or persons who have provided care to patients, including HCWs whoo have not applied preventive measures, have a moderate risk for infection. Consequently, HCWs and others caring for patients should implement necessary precautionary measures to reduce the risk of infection.

Risk of transmission through SoHO

No cases of monkeypox virus transmission through SoHO have ever been documented. However, reported virus transmission from mother to child during pregnancy [33] and through an invasive bite or scratch from an ill animal [34] suggest that transmission via SoHO is theoretically possible. There are no data on the beginning of viraemia during the incubation period or in possible asymptomatic cases. No chronic carriage of the virus has been reported. Thus, the risk of monkeypox virus transmission through SoHO is difficult to assess.

Substances of human origin (SoHO) safety authorities should be aware of the possibility that travellers returning from affected areas are at risk of infection. Monkeypox outbreaks are present in malaria-endemic areas in Africa and according to EU Directive 2004/33/EC, asymptomatic blood donors returning from malaria risk areas should defer from blood donation for at least four months [36]. Consequently, this will prevent possible blood donations from monkeypox virus-infected travellers. However, donor deferral for malarial risk is not required when the donation is used exclusively for plasma for fractionation. Multiple pathogen reduction steps used in the fractionation process have been effectively used for the inactivation of vaccinia virus and may also provide safety assurance against the presence of poxviruses like monkeypox virus in plasma-derived medicinal products.

Therefore, the deferral of asymptomatic plasma donors returning from monkeypox-affected areas is not recommended by the authorities.

According to EU directives, cell, tissue and organ donors returning from malaria-endemic areas are only deferred when laboratory screening is positive [36,37]. Therefore, prudent practice would be to defer such donors after returning from an area affected by monkeypox virus for a minimum of 21 days. Based on the incubation period, CDC has recommended that asymptomatic close contacts of infected people or animals be placed under fever surveillance for 21 days [38]. The 21 days would be a minimum deferral from SoHO donation if such contact has occurred.

Disclaimer

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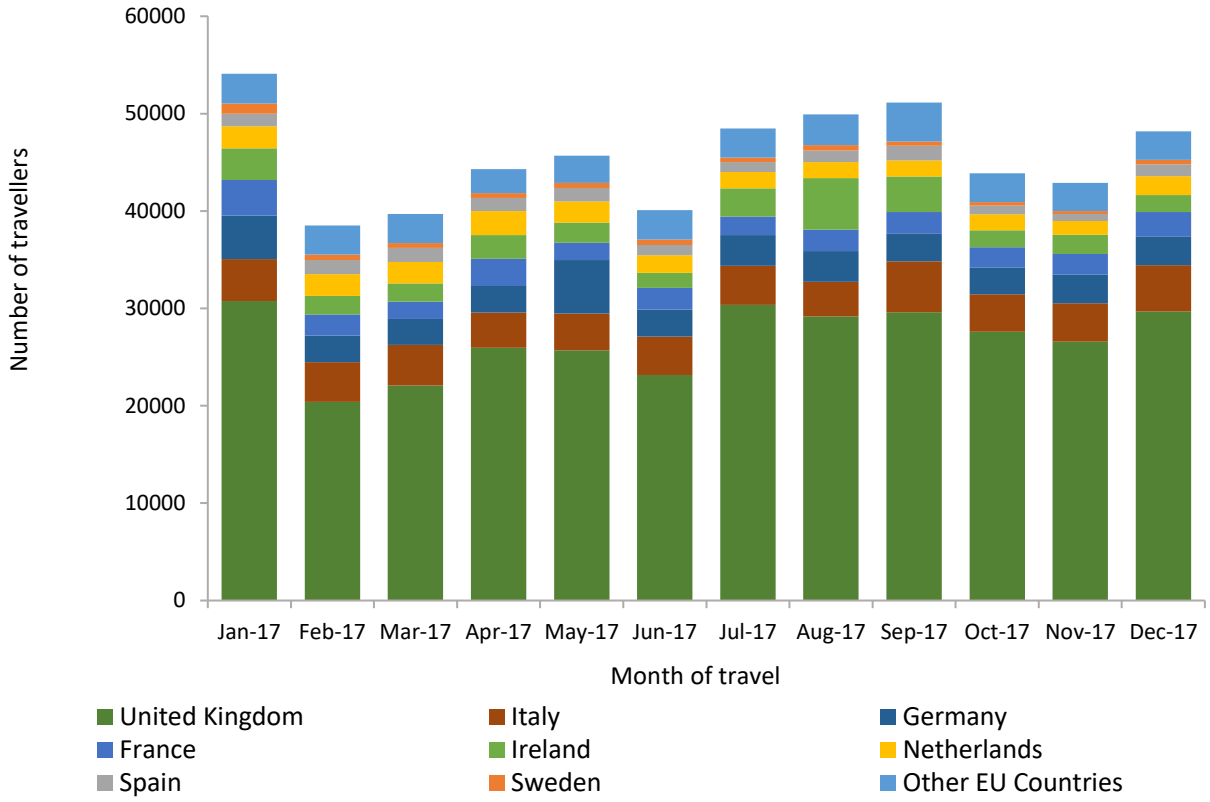
This report was written with the coordination and assistance of an Internal Response Team at the EC DP C. All data published in this risk assessment are correct to the best of our knowledge at the time of publication. Maps and figures published do not represent a statement on the part of ECDC or its partners on the legal or border status of the countries and territories shown.

Annex 1. Number of travellers from Nigeria to the EU in 2017 by month of travel

According to the International Air Transport Association (IATA) database, over half a million people travelled from Nigeria to EU countries in 2017. Among the travellers, 59% travelled to the UK, 9% travelled to Italy, 7% to Germany, 5% to France, 6% to Ireland, 4% to Netherlands, 3% to Spain and 1% to Sweden. These seven countries accounted for 93% of the travellers from Nigeria to the EU in 2017 (Figure 2).

Figure 2. Number of travellers from Nigeria to the EU in 2017 by month of travel



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