Gulf Rapid Risk Assessment:
Marburg Virus Disease Outbreak in GCC

16 February 2023

This document has been developed by the Gulf Center for Disease Prevention and Control (GCDC) for the awareness of public health authorities within countries of the Gulf Cooperation Council. The rapid risk assessment provides guidance based on the information available to the Gulf Public Health Emergencies Network as of 16 February 2023.

I. Background

(a) Event detected by Gulf CDC

On 7th of February 2023, nine deaths following undiagnosed hemorrhagic fever linked to funeral ceremony have been reported in the Nsok-Nsomo district, Kie-Ntem province in Equatorial Guinea. The affected individuals experienced mainly fever, fatigue, joint pain and blood-stained vomit and diarrhea and were documented within a short period in two different communities. The information about these cases has been reported by the national health authorities of Equatorial Guinea on February 9 through officials social media channels. On 13th of February 2023, one sample of the 8 tested samples has been confirmed positive for Marburg virus disease (MVD) at the regional reference lab of Institut Pasteur (Senegal).

(b) Hazard (emerging disease)

The Marburg virus (MARV) is a zoonotic emerging pathogen belonging to the Filoviridae family, that includes also Ebolavirus. The clinical manifestations of MVD are similar to Ebolavirus disease (EVD) with a typical sudden onset of fever, chills, diarrhea (that can be bloody), and vomiting. Other possible signs and symptoms include anorexia, severe headache, myasthenia; hemorrhagic signs and symptoms are considered rare in the early stages. Laboratory findings in patients are similar to those seen in EVD patients and include, among others, leukopenia, thrombocytopenia and increases in serum transaminase levels.

The incubation period ranges from 2 to 21 days (mean 4 to 9 days). The case fatality rate is often high, ranging from 24 to 80 percent. The virus spreads among humans through person-to-person direct contact or contact with contaminated equipment or other material with droplets of bodily fluids (e.g, blood, urine, saliva, sweat, feces, vomit, breast milk, amniotic fluid, and semen) of infected persons (including deceased) with MVD, or sexual intercourse.

There is no approved specific medical treatment for MVD. Case management is based on clinical supportive care as for EVD patients. The same infection prevention and control precautions as for EVD should be used to prevent transmission. There are no approved vaccines for MVD.

The first recognized MVD outbreaks in humans were documented in 1967 at two separates sites in Europe as a result of infection from monkeys imported from Uganda for research purposes. Since then, all known human infections have occurred in Africa.

Marburg outbreaks are rare, but have a high case fatality rate; there have been 13 major Marburg virus outbreaks reported since 1967 (*see table 1*). The MVD outbreak in Angola (2004-2005) remains the largest event documented with more than 250 confirmed cases and an important nosocomial component in terms of spread. The last cases of MVD have been identified in Ghana 2022: a small family cluster with three cases and two associated deaths.

Table 1. History of Marburg Outbreaks (1967-2022)

Year	Location	Cases
1967	Germany, Yugoslavia	31 cases, 7 deaths
1975	South Africa	3 cases, 1 death
1980	Kenya	2 cases, 1 death
1987	Kenya	1 fatal case
1998-2000	Democratic Republic of Congo	154 cases, 128 deaths
2005	Angola	252 cases, 227 deaths
2007	Uganda	4 cases, 2 deaths
2008	Netherlands, USA	2 cases among tourists from the Netherlands(fatal) and USA after a trip to Uganda
2012	Uganda	15 cases, 4 deaths
2014	Uganda	1 fatal case
2017	Uganda	4 cases, 3 deaths
2021	Republic of Guinea	2 cases
2022	Ghana	3 cases, 2 deaths

More detailed information on the historical outbreaks in table 1 is available in *Annex 1.*

II. Situation Update

The investigations of the deaths of undiagnosed cases with haemorrhagic fever began on 7th of February 2023. The deaths have been reported to have occurred between 7 January and 7 February 2023. The initial samples collected were sent to the Institut Pasteur reference laboratory in Senegal, where one of the 8 tested specimens confirmed Marburg virus. As of 13 of

February, 16 suspected symptomatic cases and 9 human deaths have been reported by Equatorial Guinea. Contact tracing, isolation and case management in the community is still ongoing; there are more than 200 contacts being followed up so far. Investigations are ongoing and epidemiological surveillance has been strengthened. One challenge to the response is the unavailability of a licensed vaccine and approved antiviral treatment against Marburg virus.

Cameroonian health authorities have officially announced on February 10 movement restrictions at the borders with Equatorial Guinea in order to avoid the importation of cases. Cameroon is taking proactive measures to contain a possible outbreak, signaling their concern while test results are pending. Among these measures are restrictions on cross-border movement, contact tracing, and epidemiological surveillance

On February 13, several media quoting the national health authorities have reported the identification in Cameroon of two cases of undiagnosed hemorrhagic fever suspected to be due to MVD. The cases, two 16-year-old children, a boy and a girl, have no previous travel history to the affected areas and were identified in Olamze, a district approximately 100km across the border. On February 15, the Minister of Health has reported that Marburg Disease has been ruled out as tests returned negative.

III. Risk assessment

Risk assessed			
Low	Moderate	High	Extreme

The risk of an outbreak of Marburg Virus Disease occurring in the GCC will depend on the risk of importation from the countries reporting the outbreak, as well as the risk of zoonotic spillover from fruit bats. Despite the reports of suspected cases in Cameroon returning negative, Cameroon is still a neighboring country to Equatorial Guinea with fluid population movement. As such, likelihood of importation from Cameroon is also included within this risk assessment.

Likelihood of an outbreak occurring in GCC

Based on the available IATA data, Equatorial Guinea and Cameroon seem to have high local and regional (Africa) connectivity, in addition to connections to Spain and the United States (Annex II). The latest estimated number of air travelers between Equatorial Guinea and Cameroon to each of the six GCC country in January 2023 (table 2) can serve as a proxy for evaluating the connectivity between the countries and the GCC. The relative number of estimated travelers from Cameroon to the GCC is higher than travelers from Equatorial Guinea to the GCC. As this number is very low, and the probability of these travelers being infected is very low as well, the **likelihood of importing cases** of Marburg virus through air travel at this time is considered **rare**.

Table 2. Estimated number of air travellers and infected air travellers from Equatorial Guinea and Cameroon to Gulf countries from January 2023 (BlueDot, 2023)

Destination	Estimated number of air travellers from Equatorial Guinea	Estimated number of air travellers from Cameroon
Saudi Arabia	14	295
Bahrain	3	309
Oman	17	50
Qatar	18	51
Kuwait	6	89
United Arab Emirates	50	2176

Marburg virus has been documented in Egyptian fruit bats (*Rousettus aegyptiacus*) captured in a mine in Uganda where numerous cases had occurred. The wide geographical dispersion of MVD cases in African countries suggests that the virus is present among chronically infected bats throughout sub-Saharan Africa. This has been recently confirmed by the identification of the virus in apparently healthy fruitbats in Sierra Leone, South Africa and Zambia. This species has also been identified in the southern parts of the Arabian Peninsula in Yemen, Saudi Arabia, and Oman (*see figure 1*). Although this species of bats is not migratory it is also possible that other migratory bats could transmit MARV to the bats in GCC and pose a threat of zoonotic spillover. However, there is no data to confirm the presence or lack of MARV in bats in the GCC areas. As such, the likelihood of zoonotic transmission is unknown.

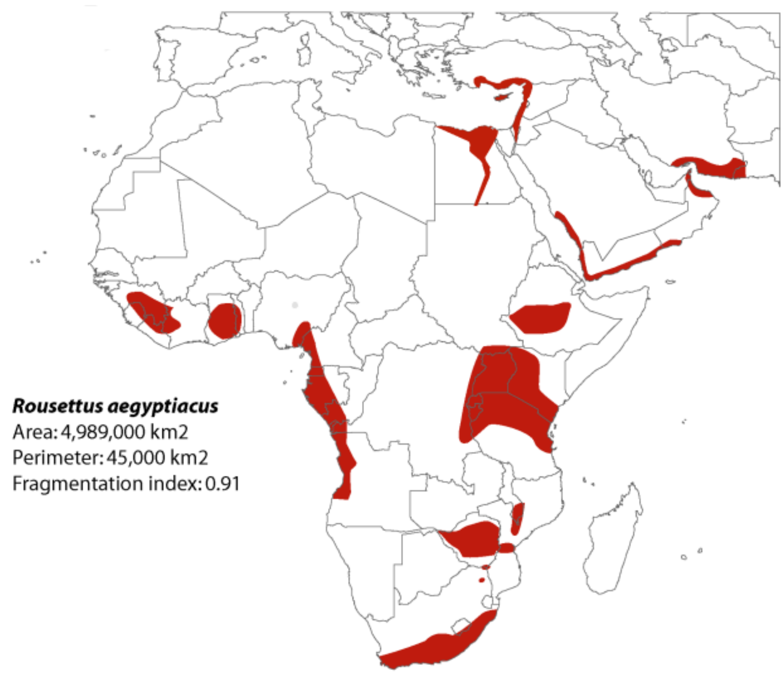


Figure 1. Range maps for *Rousettus aegyptiacus* in which Ebola antibodies have been detected (Guyton and Brook, 2015)

Impact of an outbreak in GCC

With regards to the impact of an outbreak, if one was to occur, its severity could be as high as the previous outbreaks. MARV has been reported to cause outbreaks with high case fatality rates, such as the outbreak in Angola in 2004-2005 (252 cases and 227 deaths). No licensed vaccination (despite availability of experimental formulations) or antivirals exist to date. The unvaccinated Gulf population is highly vulnerable to severe disease and death if infected. GCC countries have high reported capacities for detecting and responding to epidemic prone diseases. MARV transmission has previously occurred in healthcare settings with poor infection prevention and control (IPC) measures. The GCC countries all have high IPC standards. However, Marburg virus disease has not been detected in the GCC countries previously, as such, there may be low familiarity with the disease presentation and its specific control measures. Nevertheless, if an outbreak of Marburg virus disease occurs in the GCC region, it would have **<u>minor</u> impact**.

Overall risk of an outbreak

In light of the factors considered for the rare likelihood and moderate impact, at this time, the risk of an outbreak of Marburg Virus Disease occurring in the GCC is **<u>low</u>**. Nevertheless, the importation of several individual Marburg Virus Disease cases should be considered. Also, it is plausible that the extent of this outbreak could be larger than currently reported, due to the first death occurring on 7 January 2023 (one month before the cluster of deaths has been noted) and incubation period ranging from 2 to 21 days.

IV. Recommendations

GCC countries should consider the following recommended actions for better preparedness, readiness, and response:

- Review and disseminate viral haemorrhagic fever guidance (guidelines, case definitions and investigation forms) to all stakeholders involved in surveillance and contact tracing
- Disseminate Marburg case definition to relevant surveillance and clinician staff and send an alert to clinicians and points of entry (PoE) staff to maintain a high suspicious index for Marburg, following the below case definition:

  Gulf standard case definition for current outbreak

  - **Confirmed case:**
    A suspected case with laboratory confirmation (ELISA, positive IgM antibody, positive PCR or viral isolation)

  - **Suspected case:**
    Any person, alive or dead, suffering or having suffered from a sudden onset of high fever AND

    (1) with a travel history to Kie-Ntem province in Equatorial Guinea in the last 21 days

    OR
    (2) contact in the last 21 days with a suspected, probable or confirmed Marburg case (including direct contact with laboratory specimens)

- Designate at least one hospital/facility with adequate supplies and isolation rooms to provide care for up to 5 potential cases with suspected Marburg. Disseminate the referral procedures to health facilities and PoE
- Ensure the national reference laboratory is equipped to test specimens of suspect Marburg and ensure the necessary arrangements are made for receiving the specimens. Establish stand-by arrangements and ensure agreements are in place with reference laboratories across the GCC and internationally for confirmatory testing and sequencing

- Raising awareness of travellers to Equatorial Guinea (including aircraft personnel) of the risk factors for Marburg virus disease and the protective measures individuals can take to reduce exposure in affected geographic areas
- Raise awareness of healthcare workers, including rapid response teams, on standard and transmission-based infection prevention and control precautions when caring for suspected or confirmed Marburg virus disease (particularly for early recognition and isolation)
- To reduce the risk of zoonotic transmissions, collaborate with the Ministry of Agriculture in investigating serological evidence of Marburg infection, particularly where the bats have previously been identified, and in assessing likelihood of exposure of populations living/working/visiting areas in these areas. Consider providing risk communication materials to tour agencies that visit caves inhabited by fruit bat colonies, in particular in Africa

V. Acknowledgements

- BlueDot insights
- Herve Zeller, subject-matter expert
- Jas Mantero, subject-matter expert

VI. References

Event detected

- https://twitter.com/GuineaSalud/status/1623777563435728896
- https://africacdc.org/news-item/press-release-on-marburg-virus-disease-in-equatorial-guinea/
- https://www.afro.who.int/countries/equatorial-guinea/news/equatorial-guinea-confirms-first-ever-marburg-virus-disease-outbreak
- https://www.minsante.cm/site/?q=en/content/press-release
- https://www.reuters.com/world/africa/cameroon-restricts-movement-along-equatorial-guinea-border-after-several-2023-02-10/

Disease background

- Kortepeter MG, Bausch DG, Bray M. Basic clinical and laboratory features of filoviralhemorrhagic fever. J Infect Dis 2011; 204 Suppl 3:S810.
- https://www.cdc.gov/vhf/marburg/pdf/factsheet.pdf
- Glaze ER, Roy MJ, Dalrymple LW, Lanning LL. A Comparison of the Pathogenesis of Marburg Virus Disease in Humans and Nonhuman Primates and Evaluation of the Suitability of These Animal Models for Predicting Clinical Efficacy under the 'Animal Rule'. Comp Med 2015; 65:241.

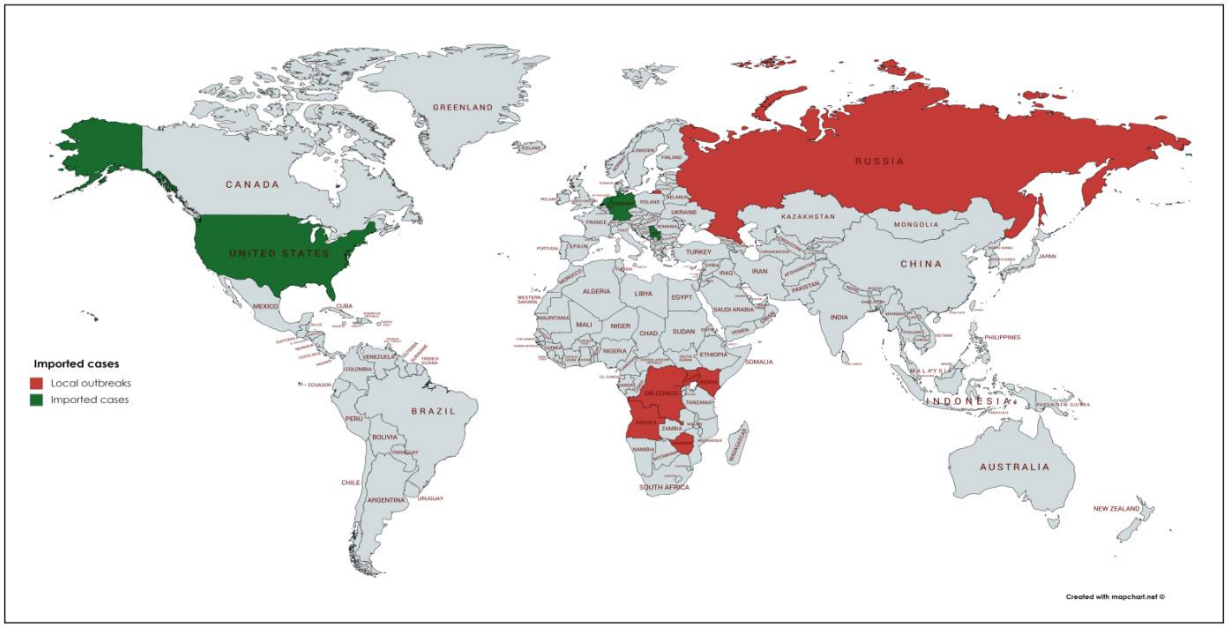
- Bausch DG, Nichol ST, Muyembe-Tamfum JJ, et al. Marburg hemorrhagic feverassociated with multiple genetic lineages of virus. N Engl J Med 2006; 355:909.
- Amman BR, Bird BH, Bakarr IA, et al. Isolation of Angola-like Marburg virus fromEgyptian rousette bats from West Africa. Nat Commun 2020; 11:510
- Pawęska JT, Storm N, Markotter W, et al. Shedding of Marburg Virus in NaturallyInfected Egyptian Rousette Bats, South Africa, 2017. Emerg Infect Dis 2020; 26:3051.
- Kajihara M, Hang'ombe BM, Changula K, et al. Marburgvirus in Egyptian Fruit Bats,Zambia. Emerg Infect Dis 2019; 25:1577.
- Guyton, J.A. and Brook, C.E., 2015. African bats: Conservation in the time of Ebola. Therya, 6(1), pp.69-88.

Previous outbreaks

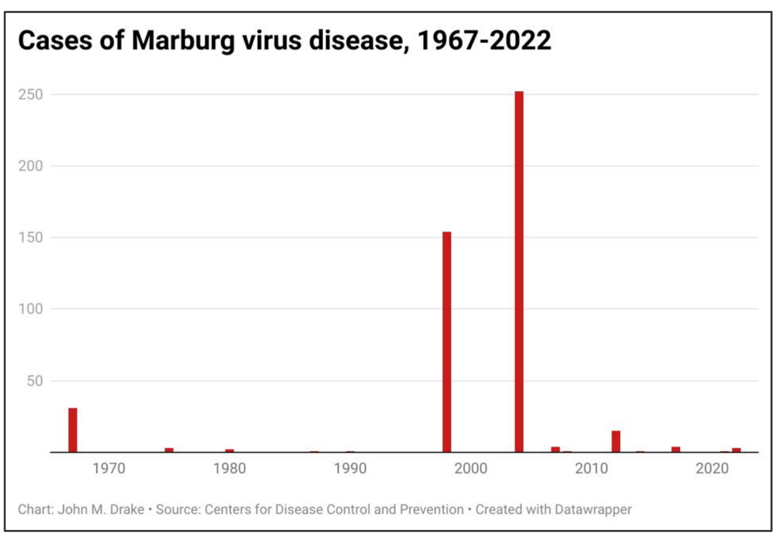
- Martini GA. Marburg virus disease. Postgrad Med J 1973; 49:542.
- Ristanović ES, Kokoškov NS, Crozier I, et al. A Forgotten Episode of Marburg VirusDisease: Belgrade, Yugoslavia, 1967. Microbiol Mol Biol Rev 2020; 84. .
- Gear JS, Cassel GA, Gear AJ, et al. Outbreake of Marburg virus disease in Johannesburg. Br Med J 1975; 4:489.
- Smith DH, Johnson BK, Isaacson M, Swanapoel R, Johnson KM, Killey M, Bagshawe A, Siongok T, Keruga WK. Marburg-virus disease in Kenya. Lancet. 1982 Apr 10;1(8276):816-20. doi: 10.1016/s0140-6736(82)91871-2. PMID: 6122054.
- Johnson ED, Johnson BK, Silverstein D, Tukei P, Geisbert TW, Sanchez AN, Jahrling PB. Characterization of a new Marburg virus isolated from a 1987 fatal case in Kenya. Arch Virol Suppl. 1996;11:101-14. doi: 10.1007/978-3-7091-7482-1_10. PMID: 8800792.
- Bausch DG, Nichol ST, Muyembe-Tamfum JJ, et al. Marburg hemorrhagic fever associated with multiple genetic lineages of virus. N Engl J Med 2006; 355:909.
- Towner JS, Khristova ML, Sealy TK, et al. Marburgvirus genomics and association with a large hemorrhagic fever outbreak in Angola. J Virol 2006; 80:6497.
- Jeffs B, Roddy P, Weatherill D, et al. The Medecins Sans Frontieres intervention in theMarburg hemorrhagic fever epidemic, Uige, Angola, 2005. I. Lessons learned in thehospital. J Infect Dis 2007; 196 Suppl 2:S154.
- Roddy P, Weatherill D, Jeffs B, et al. The Medecins Sans Frontieres intervention in theMarburg hemorrhagic fever epidemic, Uige, Angola, 2005. II. lessons learned in thecommunity. J Infect Dis 2007; 196 Suppl 2:S162. 19.
- Ligon BL. Outbreak of Marburg hemorrhagic fever in Angola: a review of the history of the disease and its biological aspects. Semin Pediatr Infect Dis. 2005 Jul;16(3):219-24. doi: 10.1053/j.spid.2005.05.001. PMID: 16044395; PMCID: PMC7130051
- Adjemian J, Farnon EC, Tschioko F, et al. Outbreak of Marburg hemorrhagic fever among miners in Kamwenge and Ibanda Districts, Uganda, 2007. J Infect Dis 2011; 204 Suppl 3:S796.
- Timen A, Koopmans MP, Vossen AC, et al. Response to imported case of Marburg hemorrhagic fever, the Netherland. Emerg Infect Dis 2009; 15:1171. 21.
- Centers for Disease Control and Prevention (CDC). Imported case of Marburg hemorrhagic fever - Colorado, 2008. MMWR Morb Mortal Wkly Rep 2009; 58:1377.
- Knust B, Schafer IJ, Wamala J, et al. Multidistrict Outbreak of Marburg Virus Disease-Uganda, 2012. J Infect Dis 2015; 212 Suppl 2:S119.
- Nyakarahuka L, Ojwang J, Tumusiime A, Balinandi S, Whitmer S, Kyazze S, Kasozi S, Wetaka M, Makumbi I, Dahlke M, Borchert J, Lutwama J, Ströher U, Rollin PE, Nichol ST, Shoemaker TR. Isolated Case of Marburg Virus Disease, Kampala, Uganda, 2014. Emerg Infect Dis. 2017 Jun;23(6):1001-1004. doi: 10.3201/eid2306.170047. PMID: 28518032; PMCID: PMC5443453.

- Nyakarahuka L, Shoemaker TR, Balinandi S, et al. Marburg virus disease outbreak inKween District Uganda, 2017: Epidemiological and laboratory findings. PLoS Negl TropDis 2019; 13:e0007257.
- Wasswa H. Uganda grapples with new Marburg disease outbreak. BMJ 2017; 359:j5252.
- https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON409
- https://www.cdc.gov/vhf/marburg/outbreaks/chronology.html
- https://www.infezmed.it/media/journal/Vol_28_3_2020_6.pdf

Annex 1. History of MVD Outbreaks



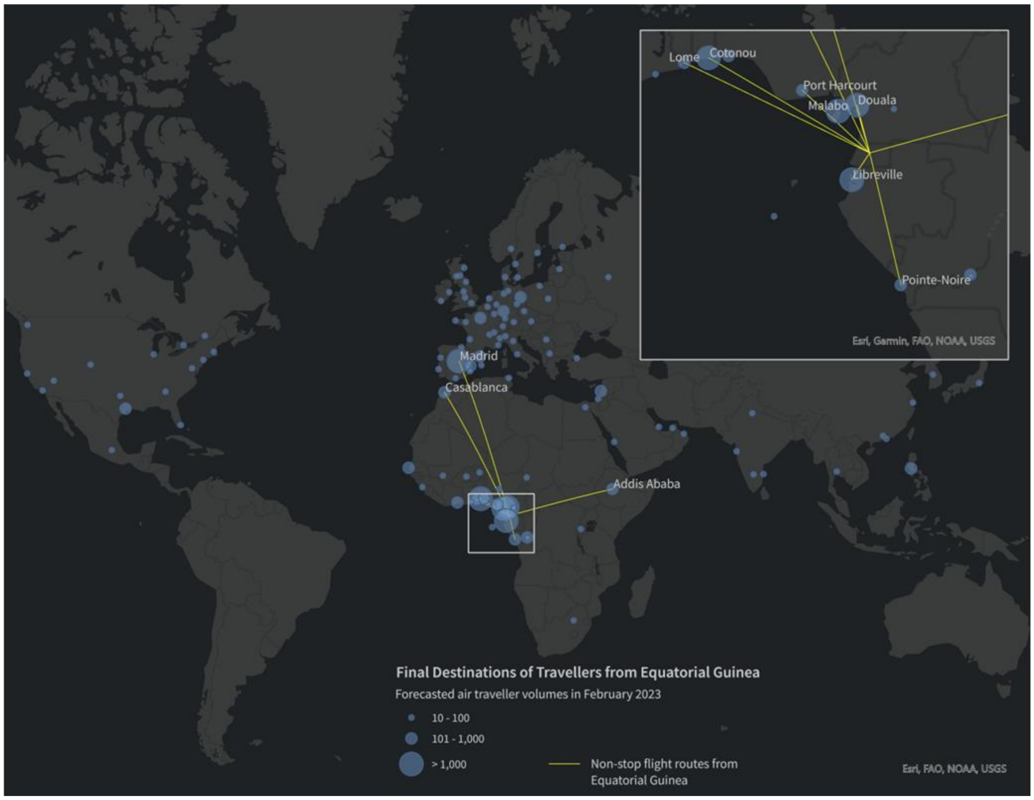
Asad, A., Aamir, A., Qureshi, N.E., Bhimani, S., Jatoi, N.N., Batra, S., Ochani, R.K., Abbasi, M.K., Tariq, M.A. and Diwan, M.N., 2020. Past and current advances in Marburg virus disease: a review. *Infez Med*, *28*(3), pp.332-345.



https://www.forbes.com/sites/johndrake/2023/02/14/what-you-need-to-know-about-the-outbreak-of-marburg-hemorrhagic-fever-in-equatorial-guinea-and-cameroon/?sh=4fb28c8e5122

Annex II: Forecasted flight volumes internationally from Equatorial Guinea and Cameroon

Forecasted flight volumes from Equatorial Guinea and Cameroon to countries globally for the next 30 days (BlueDot)



The risks of local and regional dispersion are significant, but the risks of broader international spread is currently low.

- Population mobility via air travel is primarily regional
- One notable exception is Spain, which receives the highest volume of international travellers and has non-stop flights into Madrid
- The United States receives the second highest volume of travellers from Equatorial Guinea outside of Africa (after Spain)

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