Ebola and Marburg Virus Infections in Resource-Rich Countries: Implications for Future Outbreaks

Eyal Meltzer[1,2] · Eli Schwartz[1,2]

Abstract

Purpose of Review Ebolavirus and Marburgvirus are Filoviruses that cause an extremely virulent hemorrhagic fever syndrome. Most Ebolavirus (EVD) and Marburgvirus (MVD) disease outbreaks occurred in Africa, usually in remote, rural settings. The aim of this review is to compare collated data on EVD/MVD cases treated in resource-rich countries with data from local outbreak conditions.

Recent Findings A longitudinal view of EVD outbreaks suggest increased recognition of outbreaks the last 30 years , but a declining case fatality rate. This probably reflects improved diagnostics and better recognition of less severe cases. Compared to the data from Africa, cases treated in resource-rich countries fared much better, with a cumulative case fatality rate that was about half that reported from Africa for EVD and about a third that reported for MVD. High rates of secondary cases were reported from Africa among household contacts, often associated with unhygienic funerary practices. In addition, nosocomial transmission had resulted in alarming rates of secondary cases among healthcare workers. Collated information from resource-rich countries suggests that with even in the absence of specific EVD targeted measures, with standard hygiene practices and infection control measures, the secondary case rate was <1% in healthcare workers, with no secondary cases reported from household or community contacts.

Summary EVD/ MVD are severe, life-threatening infections, but very high case fatality rates and secondary case reported from Africa may reflect poverty and lack of adequate medical infrastructure. The risk posed to healthcare workers is significantly mitigated by the universal availability of standard hygiene and infection control measures. No secondary cases were reported among community contacts in high-income countries. Therefore, rigorous infection-control measures may cause delays in the diagnosis and treatment of other important life-threatening infections.

Keywords Ebolavirus · Marburgvirus · Africa · Health personnel · Travelers

The *Filovirideae* are a family of RNA viruses whose main natural reservoir is bats, but which can infect other mammals

including primates (events known as spillovers). Of the six genera constituting this family, *Ebolavirus* and the closely related *Marburgvirus*, which are endemic to Africa, can infect humans, resulting in a severe and frequently fatal viral hemorrhagic syndrome [1]. The genus *Ebolavirus* includes five species, of which the leading human pathogens are *Ebolavirus* Zaire and *Ebolavirus* Sudan; *Marburgvirus* includes a homonymous single species. With the exception of rabies, these infections probably result in the highest case fatality rates reported for any zoonotic/arboviruses.

In February 2023, an outbreak of *Marburgvirus* was reported from Equatorial Guinea; by March 25, there were 29 confirmed/probable cases, of whom 27 have died [2]. Cases have been reported from several districts, suggesting more widespread viral circulation. Concomitantly in March

2023, another outbreak of *Marburgvirus* was reported from Tanzania, with nine confirmed cases, eight of whom died [3]. These outbreaks come shortly after the termination of the latest *Ebolavirus* disease (EVD) outbreak, which was reported from Uganda in September 2022, with 164 cases and 55 fatalities [4]. It is likely that a rapid, community-engaged Ugandan response [5] contributed to the relatively swift resolution of this outbreak. Also, the quick engagement of multiple international partners in the form personal protective equipment (PPE), epidemiological support personnel, diagnostic capacity, et cetera [6•] (in addition to potential vaccines for clinical trials for healthcare workers and exposed persons [7]) assisted in the curtailment of this outbreak.

In all these parameters, the 2022 Uganda EVD outbreak differed from the massive West African EVD outbreak of the previous decade. The West African outbreak was also the first to have resulted in relatively high-number imported cases to several resource-rich countries, including the USA, Spain, and the UK. Furthermore, several secondary cases among healthcare workers were reported there. Compared with autochthonous cases, the total number of EVD cases reported in resource-rich countries was very small; similarly, only a small number of cases of *Marburgvirus* disease (MVD) have been recorded in resource-rich countries, largely in association with laboratory exposures. However, studying these cases can highlight the role played by poverty and lack of medical resources in the outcome and epidemiology of Filoviral infections. The aim of this review is to compare outcome and epidemiological data, mainly the rate of secondary infection of local vs. imported EVD and MVD cases, in particular in the context of West African EVD outbreak, which was by far the largest Filoviral epidemic to date. This information may assist decision-makers in future outbreaks. The data presented was gathered through a MEDLINE search which included the terms Ebolavirus and Marburgvirus, as well as other data sources including international and national sources, including the WHO and the US CDC.

The 2013–2016 West-African EVD Outbreak

In December 2013, in N'Zérékoré Prefecture, Guinea, a child died from "severe diarrhea." However, it was not until nearly four months had elapsed that a laboratory confirmation of EVD Zaire strain was made, allowing cases to multiply unchecked in the interval. The outbreak began in a rural, forested area of Guinea, which was typical of previous EVD outbreaks. What singled out this outbreak was its spread to urban centers, including Guinea's capital Conakry. Here, rapid person-to-person transmission resulted in a massive expansion of case numbers that went from dozens in March 2014 to more than 25,000 within a year. This was coupled with high mobility of cases and resulted the swift spread of EVD to many regions of Guinea as well as to neighboring Sierra Leone and Liberia, with multiple reintroductions between these countries, as well as smaller outbreaks in neighboring Nigeria and Mali [8].

It was only in August 2014 that that a Public Health Emergency of International Concern (PHEIC) was announced by the WHO [9]: a first occurrence for an EVD outbreak. Eventually some 176 international, governmental and non-governmental organizations participated in the response to the epidemic [10], with billions of dollars spent, and thousands of personnel (some 4000 workers from the US CDC alone [11]) involved.

By 2016, when the outbreak was considered over, 28,652 cases were documented, and 11,325 deaths: a number that was an order of magnitude higher than all previous EVD outbreaks combined. The death toll was especially shocking among healthcare workers, with 1455 cases reported (5% of total reported cases), of whom 58% died [12].

The reverberations caused by this enormous public health disaster are not entirely over. *Ebolavirus* can persist in the body for long periods of time. In a follow-up study of 267 male EVD survivors in Liberia, intermittent viral shedding in semen was recorded in 30% of cases, with the longest documented period from acute illness being 40 months [13]. Although recommendations for semen testing in EVD survivors and for safe sex practices until after repeated negative testing have been published by the WHO, surveys of EVD survivors in Liberia suggest that this is infrequently adhered to, even among persons with *Ebolavirus* positive semen [14]; the potential for late sexual transmission with a renewed outbreak is real. In addition, the virus is occasionally not eliminated completely from the body with clinical recovery but can recrudesce long afterwards, and may again create a new chain of transmission [15••]. In 2021, these concerns appeared to be justified, when renewed *Ebolavirus* transmission was recorded in Nzérékoré, Guinea. Sequencing of *Ebolavirus* strains had shown that the virus did nor result from a new spillover event from bats, but was closely related to the original 2014 strain, whose circulation was presumed over 5 years earlier. This suggested that either sexual transmission or disease recrudescence was the probable mechanism [16].

It was inevitable perhaps that EVD cases would eventually be diagnosed and treated in countries outside Africa. Some 10 cases were treated in the USA (including both evacuated healthcare workers and persons who became ill in the USA) [17••]. The total number of EVD cases treated outside Africa is uncertain, but 24 cases were reported by the New York Times be early 2015 [18].
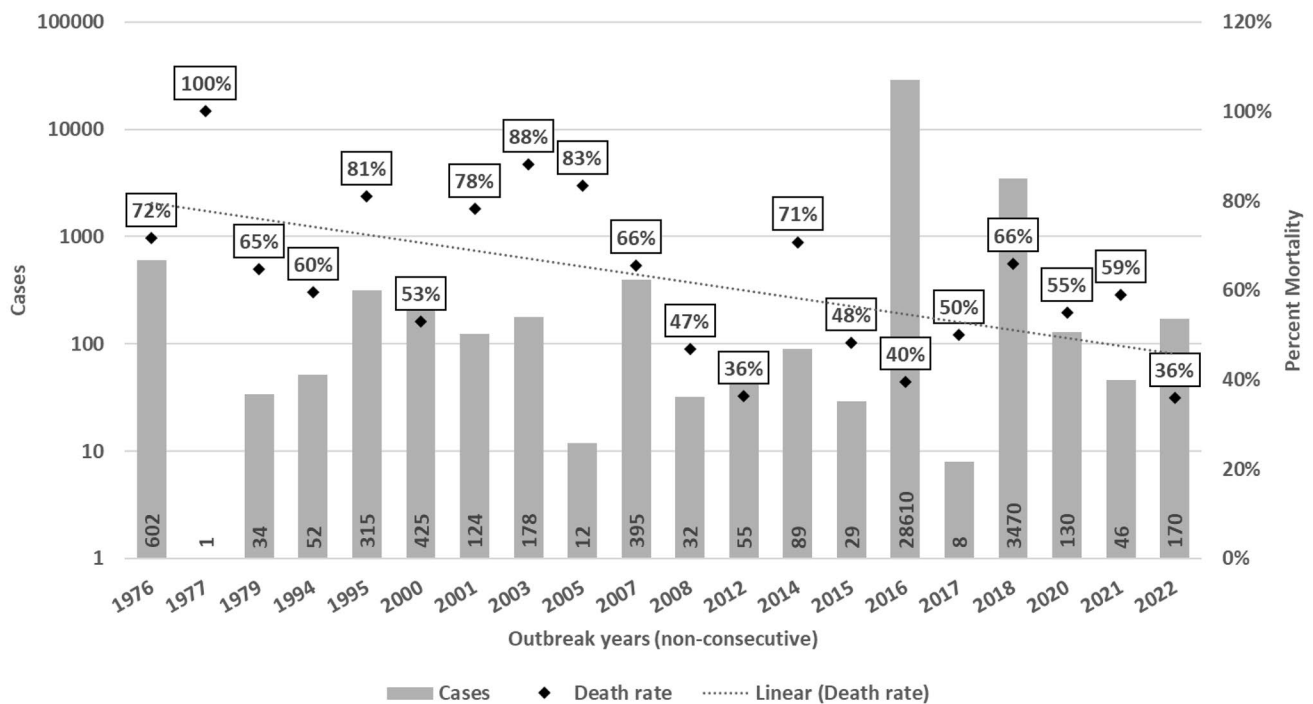
Fig. 1 Ebola viral disease outbreaks: reported numbers and case fatality rates: superscript letter (a): numbers were compiled from EVD reports summarized by the CDC [19]

Case Fatality Rate (CFR): A Comparison of Data on EVD in Resource-Poor and Resource-Rich Countries

From the very first Yambuku outbreak in 1976, extreme case fatality rates were reported for EVD. This has contributed greatly to the fear, panic responses, and stigmatization generated by this infection. EVD is certainly a severe and potentially life-threatening infection; however, the true CFR is uncertain. If one collates all the data on EVD outbreaks recorded by the CDC [19], there appears to be a declining trend in CFR (Fig. 1). This trend does not, in all likelihood, reflect a decline in *Ebolavirus* virulence with time, but rather improved diagnostics, and better recognition of cases that do not present with a full blown viral hemorrhagic fever syndrome. This conclusion is corroborated by serosurveys in Guinea that suggested that the actual number of infected individuals may have been twice that initially recognized [20].

Compared to the locally reported rate, the CFR among all EVD cases treated outside Africa (which includes two Russian fatalities resulting from laboratory exposure), appears to be much lower (Fig. 2), especially when one considers that most of these cases were infected by the more virulent Zaire *Ebolavirus* strain. If one considers only the 24 cases reported in resource-rich countries during the 2014–2016 West African epidemic [18], the CFR is 21%, approximately half that recorded in Africa. It can only be assumed that

the difference reflects early recognition and the availability of adequate intensive care facilities on the one hand, and late presentation combined with a tragic insufficiency of advanced care on the other hand.

Marburgvirus Case Fatality Rate (CFR): A Comparison of Cases Treated in Resource-Poor and Resource-Rich Countries

Compared with EVD, the total number of MVD outbreaks and cases is small, and there has been no equivalent to the West African EVD epidemic to date. The CDC compilation includes only 15 MVD outbreaks with a total of 474 cases, 85% of which were recorded in two severe African outbreaks [21]. The overall reported mortality was 80%, however so, the difference in CFRs between resource-rich and resource-poor countries is even more striking that in EVD (Fig. 2). In the eponymous event in Marburg, Germany, and Belgrade, Yugoslavia, (Today Serbia), the CFR was 23%. Six of the 31 cases (19%) were secondary and occurred in family caregivers (probably infected by contact with soiled linen) and healthcare personnel, including four cases acquired by contact with contaminated sharps [22]. Another case cluster diagnosed and treated in Johannesburg included one index case who died, and two secondary cases in spouse and healthcare worker infected during resuscitation, both of whom recovered. Since nearly all cases seen in
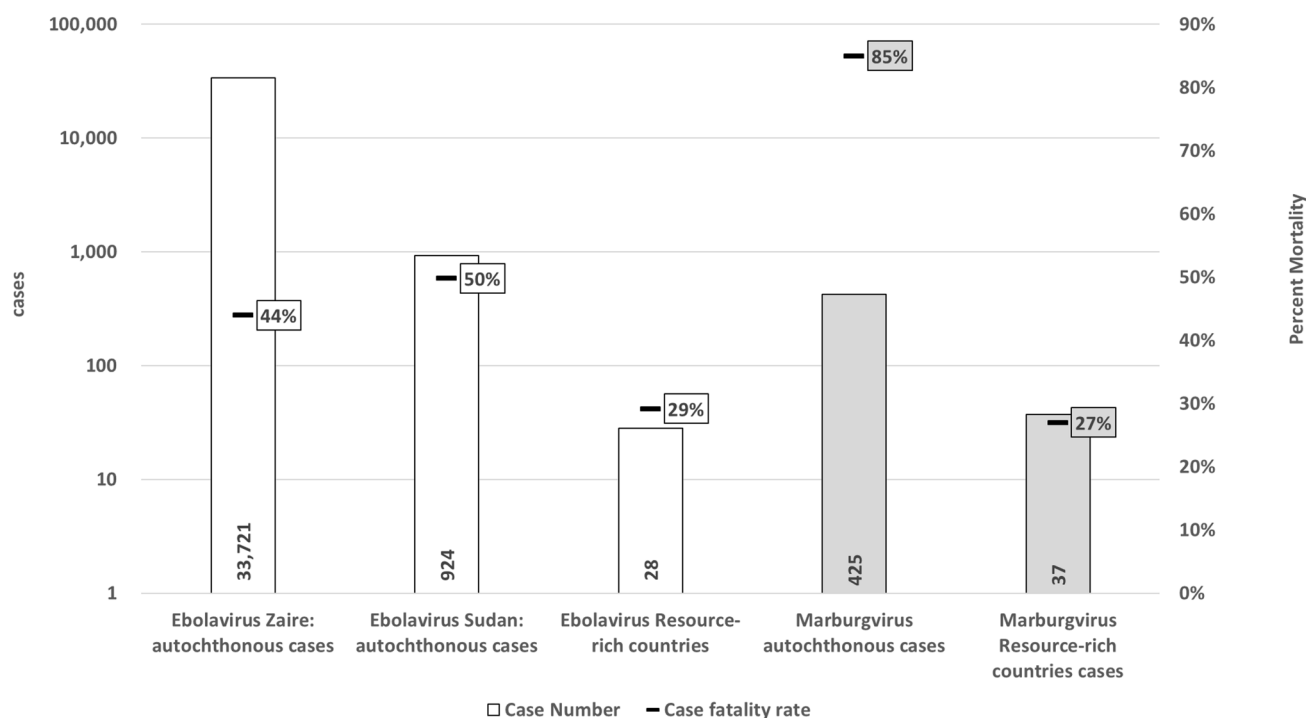
Fig. 2 Ebola/Marburg viral disease outbreaks: case fatality rates recorded in Africa and in resource-rich countries: superscript letter (a): Ebola virus (white bars) and Marburgvirus (gray bars) numbers were compiled from EVD & MVD reports summarized by the CDC [19] and the New York Times Ebola report [18]

resource-rich countries originated from laboratory accidents, early recognition and thorough epidemiological surveillance may cause bias by increased inclusion of milder cases.

Ebolavirus Modes of Transmission and the Risk of Secondary Cases Among Community Contacts in Africa

Ebolavirus is transmitted mostly by contact with infected body fluids. Practically, all body fluids can contain virions including tears, sweat, genital secretions, semen, and breast milk, but with the highest burden in blood and feces. The viral burden changes according to disease severity, with high viremia recorded in critically ill and fatal cases [23]. Viable, infective virus is still present after the patient had died, and one of the important amplifiers of the West African epidemic was the customary preparation of the deceased for burial by multiple family members. In one study, unsafe funerals were associated with a doubling of the secondary case rate [24].

Evidence for the essential role direct contact plays in EVD transmission comes from studies of family caregivers. The secondary attack rate among direct caregivers within households is many times higher than that of household members not involved in direct patient care. For example, in one outbreak, the secondary attack rate among caregivers

was 47%, whereas the rate among non-caregivers was 2.1%. Similarly, a meta-analysis of the secondary attack rates found that the rate among direct caregivers was 17-fold that of household members not directly involved in patient care [25]. The mere fact of being aware of the EVD diagnosis was associated with a significant decrease in the forward transmission rate among family members, presumably through improved vigilance and exposure reduction [24]. In other evidence, the attack rate among children, who are probably less likely to be involved in patient care was much lower than that of adults [25].

The Risk of Secondary Cases Among Community Contacts in Resource-Rich Countries

As was discussed above, close contact with patients, especially with body fluids from severely ill patients, as well as caring for the deceased are strongly associated with EVD transmission in Africa. On the other hand, secondary attack rates are not negligible even for those with minimal contact with EVD cases [26]. However, these data were gathered during outbreak conditions in Africa, where extreme poverty was highly prevalent, with limited access to soap and water, high levels of crowding, etc. [27]. Here again, data on community contacts from resource-rich countries is illuminating. Data from several reports is summarized in Table 2. It shows

an absence of even one secondary case of EVD among more than 600 contacts, which included shared commercial air travel, casual, and household contacts.

Nosocomial EVD Transmission and the Risk of Secondary Cases Among Healthcare Workers

Nosocomial transmission of EVD had been a concern ever since the 1976 outbreaks in both the Democratic Republic of the Congo and Sudan [28, 29]. In both instances, local hospitals became amplifying nodes of EVD, often in association with the use of unsterilized multiple use needles. In Yambuku for example, the administration of anti-malarial injections at the local outpatient clinic resulted in numerous cases including pregnant women. Concomitantly, multiple cases were recorded in hospital staff. Eventually, after the death of eleven nurses (65% of the staff), the Yambuku Mission Hospital shut down. It is sad to note that the closure of the hospital probably contributed to the termination of the outbreak.

In a more recent, well-documented outbreak from the North Kivu region of the Democratic Republic of the Congo, an EVD survivor recrudesced nearly 5 months after recovery. Repeated contacts in several healthcare centers resulted in chains of transmission leading to 91 secondary cases [15••].

Other potential modes of *Ebolavirus* transmission include droplet and airborne infection, but the extent (if at all) of their role in EVD transmission is unclear. To date, although laboratory data suggest that it is possible to mechanically aerosolize *Ebolavirus*, and data in laboratory animals suggest that airborne transmission is possible, no such human data exists [30]. On the other hand, some data suggest that large infective droplets can be created during EVD, which may transmit the infection if they come into contact with mucosal surfaces. This may occur for example during vomiting. A role for droplet inoculation was suggested during the 1995 Kikwit, Democratic Republic of the Congo outbreak:

Table 1 *Ebolavirus* transmission to healthcare workers in cases treated in resource-rich countries

Country	Ref.	Number of healthcare workers followed	Secondary EVD cases N (%)
South Africa	[37]	300	1 (0.3%)
USA: patient 1	[39]	122	2 (1.6%)
USA: patients 2 & 3	[34••]	37	0 (0.0%)
France	[35]	70	0 (0.0%)
Spain: patients 1 & 2	[38]	117	1 (0.8%)
Spain: patients 3	[36]	215	0 (0.0%)
UK	[32]	4	0 (0.0%)
Italy	[33]	16	0 (0.0%)
Total		**881**	**4 (0.45%)**

EVD Ebolavirus disease

Table 2 *Ebolavirus* transmission to community contacts in cases treated in resource-rich countries

Country	Ref.	Number of community contacts followed	Secondary EVD cases N (%)
USA: patient 1	[39]	17	0 (0.0%)
USA: patient 3	[39]	356	0 (0%)
Spain: patients 3	[38]	17	0 (0.0%)
UK	[32]	234	0 (0.0%)
Italy	[33]	3	0 (0.0%)
Total		**627**	**0 (0.0%)**

EVD Ebolavirus disease

here, an outbreak of nosocomial transmission occurred when an undiagnosed EVD patient underwent repeated laparotomy. Fourteen secondary cases including some fatalities were documented in the surgical team. The limited role droplets probably play in EVD transmission is attested by the fact that the implementation of simple barrier precautions in this hospital resulted in the termination of nosocomial transmission [31].

The major role played by direct contact in the transmission of EVD has obvious implications for caregivers. It is safe to conclude that during EVD epidemics, which to date had occurred in some of the world's poorest nations, healthcare workers are faced with a real risk of acquiring EVD, while treating severely ill patients without basic infection control measures. How much of the horrendous toll EVD took among HCW was the result of absent resources? If this is the leading reason, then when such measures are applied, the secondary attack rates among healthcare workers as well as the nosocomial spread of EVD should be greatly reduced.

Here we can also learn from cases treated in resource-rich countries on the actual likelihood of secondary EVD among caregivers. In most cases, the patients were evacuated for treatment outside Africa with an already established diagnosis, and comprehensive infection control measures were in place. However, in a few cases, EVD cases were treated under standard precautions, prior to EVD diagnosis. These reports are summarized in Tables 1 and 2 [32, 33, 34••, 35–39].

One well-researched episode involved a case of EVD treated in Johannesburg, South Africa in 1996. A Gabonese visiting doctor became ill after arrival in the country; he was not diagnosed initially and was treated accordingly under standard precautions. After his recover, the diagnosis of EVD was made in hindsight, after a nurse was diagnosed with, and died from EVD. Investigations revealed that of at least 300 exposed caregivers, this nurse was the only secondary EVD case, which was probably associated with contact with contaminated sharps after assisting in the insertion of a central venous catheter [37].

Another case-cluster was investigated in Atlanta, Georgia, and involved an imported EVD case and subsequent 2 secondary cases [39]. The index case involved a returning traveler from Liberia, who became ill after arrival in the USA, but did not initially disclose his travel itinerary. He was at first treated under standard precautions, with 22 healthcare workers having unprotected high-risk exposure to the patient; later (but prior to diagnosis), he was treated under combined contact and droplet infection control measures due to severe diarrhea. The two secondary cases developed in nurses who cared for the index patient while wearing adequate personal protective equipment. Epidemiological investigation established a total of 149 contacts, of whom 122 were health care workers. No secondary cases were reported among household contacts of all three cases.

A third investigated transmission event involved an evacuated EVD case that was treated in Madrid, Spain. In August 2014, two healthcare workers diagnosed with EVD were repatriated to Spain. A total of 117 personnel were involved in the care of these patients. One nurse assistant developed EVD despite self-reported full adherence to the recommended strict contact and droplet PPE use [36]. A total of 232 contacts at her home and at healthcare facilities including 15 high-risk contacts were followed, but none developed EVD [38].

Potential Implications of Infection Control Measures on the Care of Other "Tropical" Infections

All the above data suggest that in resource-rich countries much of the explosive nature of African EVD outbreaks fails to materialize. It is likely that in affluent countries with universal access to soap and safe running water and totally different mortuary practices, the actual risk of secondary EVD cases even among household contacts (let alone more casual contacts such as during air travel) is much lower. It is also probable that the likelihood of secondary EVD among healthcare workers, even while following standard infection control practices and in the absence of specific "counter-Ebola" measures, is low. The data also suggest that our understanding of EVD epidemiology is not complete, and that some scenarios, such as dying, critically ill EVD patients, or major surgery during critical-illness EVD, may represent "super-spreading" events, where transmission to healthcare workers can occur despite full compliance with infection control measures.

Employing extreme precautions while evaluating "patients under investigation" (PUI's), i.e., when there is only the epidemiological possibility of EVD, can have a downside. When PUIs are shunted to strict isolation, the possibility of other infections may be overlooked. Consider a PUI, a business traveler with fever who returned from Dar-Es-Salaam, Tanzania, some 1400 km from a documented MVD outbreak, and had no contact with sick people. His likelihood of having falciparum malaria,

where timely diagnosis and treatment are essential, is much higher than MVD. Unfortunately, neglecting to consider, and therefore delays in diagnosis and treatment of malaria, has been recorded in the past, both in the local population and in returning travelers. During the West-Africa EVD, excess mortality due to malaria mismanagement was documented in Guinea [40, 41], with similar cases documented among returning travelers as well [42]. Similar unfortunate delays have occurred during the height of the COVID-19 outbreak in 2020 [43]. The need to consider non-Filoviral diseases should be stressed to all teams evaluating PUI's returning from EVD/MVD outbreak destinations.

Conclusions

EVD and MVD outbreaks can develop rapidly into epidemic events of international concern. Such events will continue to occur since the interface of humans and wildlife is increasing. Rapid engagement of the international community is essential to help prevent a severe epidemic such as the West-Africa EVD outbreak.

Data on cases of EVD/MVD cases diagnosed/treated in resource-rich countries suggest that the very high CFR reported from Africa is at least in part a reflection of limited medical infra-structure and delayed care. These data also suggest that in environments where hygiene maintenance is easy, community transmission of EVD/MVD is infrequent, and that even with routine infection control practices, secondary cases among healthcare workers are far less common than was reported during African outbreaks.

Febrile Travelers/passengers who return from a country with a documented outbreak, but with no contact with sick people should always be assessed for treatable causes such as malaria as soon as possible.

Compliance with Ethical Standards

Conflict of Interest The authors declare no competing interests.

References

1. Meltzer E. Arboviruses and viral hemorrhagic fevers (VHF). Infect Dis Clin North Am. 2012;26(2):479–96.

2. WHO. Marburg virus disease - Equatorial Guinea. 2023. Available from: https://www.who.int/emergencies/disease-outbreak-news/item/2023-DON449.

3. Africa CDC. Republic of Tanzania declares Marburg Virus Disease (MVD) Outbreak: African Union. 2023. Available from: https://africacdc.org/news-item/republic-of-tanzania-declares-marburg-virus-disease-mvd-outbreak/.

4. WHO. Ebola, Uganda 2022. 2023. Available from: https://www.who.int/emergencies/situations/ebola-uganda-2022.

5. Feinmann J, The BMJ. Appeal 2022–23: How safe burial helped end the 2022 Ebola epidemic. BMJ. 2023;380:92.

6.• CDC CfDC. The U.S. Response to Ebola Outbreaks in Uganda. 2022. Available from: https://www.cdc.gov/media/releases/2022/s1018-ebola-outbreaks-uganda.html. **A description of the rapid and effective US response to the EVD outbreaks: this prompt and effective response probably assisted Uganda in aborting an extensive outbreak. As such, it stands in contrast to the belated international response to the West African ebola crisis in 2014.**

7. Samarasekera U. Solidarity against Ebola: an update. The Lancet Microbe. 2023;4(3):e139.

8. Simon-Loriere E, Faye O, Faye O, Koivogui L, Magassouba N, Keita S, et al. Distinct lineages of Ebola virus in Guinea during the 2014 West African epidemic. Nature. 2015;524(7563):102–4.

9. WHO. Statement on the 1st meeting of the IHR Emergency Committee on the 2014 Ebola outbreak in West Africa. 2014. Available from: https://www.who.int/news/item/08-08-2014-statement-on-the-1st-meeting-of-the-ihr-emergency-committee-on-the-2014-ebola-outbreak-in-west-africa.

10. Kaner J, Schaack S. Understanding Ebola: the 2014 epidemic. Glob Health. 2016;12(1):53.

11. Bell BP, Damon IK, Jernigan DB, Kenyon TA, Nichol ST, O'Connor JP, et al. Overview, control strategies, and lessons learned in the CDC response to the 2014–2016 Ebola epidemic. MMWR supplements Internet. 2016. 65(3):4–11. Available from: http://europepmc.org/abstract/MED/27389903. https://doi.org/10.15585/mmwr.su6503a2.

12. Ohimain EI, Silas-Olu D. The 2013–2016 Ebola virus disease outbreak in West Africa. Curr Opin Pharmacol. 2021;60:360–5.

13. The PREVAIL III Study Group. A longitudinal study of Ebola sequelae in Liberia. N Engl J Med. 2019;380(10):924–34.

14. Tompkins K, Brown J, Tozay S, Reeves E, Pewu K, Johnson H, et al. The impact of semen testing for Ebola virus RNA on sexual behavior of male Ebola survivors in Liberia. PLoS Negl Trop Dis. 2020;14(9):e0008556.

15.•• Mbala-Kingebeni P, Pratt C, Mutafali-Ruffin M, Pauthner MG, Bile F, Nkuba-Ndaye A, et al. Ebola virus transmission initiated by relapse of systemic Ebola virus disease. N Engl J Med. 2021;384(13):1240–7. **Important study demonstrating the long-term risk of resurgent EVD disease among survivors.**

16. Keita AK, Koundouno FR, Faye M, Düx A, Hinzmann J, Diallo H, et al. Resurgence of Ebola virus in 2021 in Guinea suggests a new paradigm for outbreaks. Nature. 2021;597(7877):539–43.

17.•• Chevalier MS, Chung W, Smith J, Weil LM, Hughes SM, Joyner SN, et al. Ebola virus disease cluster in the United States-Dallas County, Texas, 2014. MMWR Morb Mortal Wkly Rep. 2014;63(46):1087–8. **An epidemiological assessment of exposure to EVD and subsequent outcome among healthcare workers in a resource rich environment.**

18. New York Times. How many Ebola patients have been treated outside of Africa? Available from: https://www.nytimes.com/interactive/2014/07/31/world/africa/ebola-virus-outbreak-qa.html#:~:text=At%20least%2024%20cases%20have,their%20home%20countries%20for%20treatment. New York Times. 2015;2023(12 06 2023).

19. CDC. History of Ebola Disease Outbreaks. 2023. Available from: https://www.cdc.gov/vhf/ebola/history/chronology.html.

20. Timothy JWS, Hall Y, Akoi-Boré J, Diallo B, Tipton TRW, Bower H, et al. Early transmission and case fatality of Ebola virus at the index site of the 2013–16 west African Ebola outbreak: a cross-sectional seroprevalence survey. Lancet Infect Dis. 2019;19(4):429–38.

21. CDC- the Centers for disease Control. Marburg Virus Disease Outbreaks: CDC. Available from: https://www.cdc.gov/vhf/marburg/outbreaks/chronology.html.

22. Slenczka W, Klenk HD. Forty Years of Marburg Virus. J Infect Dis. 2007;196(Supplement_2):S131-S5.

23. Ksiazek TG, Rollin PE, Williams AJ, Bressler DS, Martin ML, Swanepoel R, et al. Clinical virology of Ebola hemorrhagic fever (EHF): virus, virus antigen, and IgG and IgM antibody findings among EHF patients in Kikwit, Democratic Republic of the Congo, 1995. J Infect Dis. 1999;179(Supplement_1):S177-S87.

24. Robert A, Edmunds WJ, Watson CH, Henao-Restrepo AM, Gsell P-S, Williamson E, et al. Determinants of transmission risk during the late stage of the West African Ebola epidemic. Am J Epidemiol. 2019;188(7):1319–27.

25. Dean NE, Halloran ME, Yang Y, Longini IM. Transmissibility and pathogenicity of Ebola virus: a systematic review and meta-analysis of household secondary attack rate and asymptomatic infection. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2016;62(10):1277–86.

26. Bower H, Johnson S, Bangura MS, Kamara AJ, Kamara O, Mansaray SH, et al. Exposure-specific and age-specific attack rates for Ebola virus disease in Ebola-affected households. Sierra Leone Emerging infectious diseases. 2016;22(8):1403–11.

27. Glynn JR, Bower H, Johnson S, Turay C, Sesay D, Mansaray SH, et al. Variability in intrahousehold transmission of Ebola virus, and estimation of the household secondary attack rate. J Infect Dis. 2018;217(2):232–7.

28. Ebola haemorrhagic fever in Zaire, 1976. Bulletin of the World Health Organization. 1978;56(2):271–93.

29. Ebola haemorrhagic fever in Sudan, 1976. Report of a WHO/International Study Team. Bulletin of the World Health Organization. 1978;56(2):247–70.

30. Judson S, Prescott J, Munster V. Understanding Ebola virus transmission. Viruses. 2015;7(2):511–21.

31. Khan AS, Tshioko FK, Heymann DL, Le Guenno B, Nabeth P, Kerstiëns B, et al. The reemergence of Ebola hemorrhagic fever, Democratic Republic of the Congo, 1995. J Infect Dis. 1999;179(Supplement_1):S76-S86.

32. Crook P, Smith-Palmer A, Maguire H, McCarthy N, Kirkbride H, Court B, et al. Lack of secondary transmission of Ebola virus from healthcare worker to 238 contacts, United Kingdom, December 2014. Emerg Infect Dis. 2017;23(12):2081–4.

33. Bertoli G, Mannazzu M, Madeddu G, Are R, Muredda A, Babudieri S, et al. Ebola virus disease: case management in the Institute of Infectious Diseases, University Hospital of Sassari, Sardinia, Italy. J Infect Dev Ctries. 2016;10(5):537–43.

34.•• Regan JJ, Jungerman R, Montiel SH, Newsome K, Objio T, Washburn F, et al. Public health response to commercial airline travel of a person with Ebola virus infection - United States, 2014. MMWR Morb Mortal Wkly Rep. 2015;64(3):63–6. **This unique case shows the crucial role of resource availability in disease transmission on one hand, and also the probable importance of sharps on the other.**

35. RFI RFI. Healthworkers in contact with French Ebola nurse given all-clear press communique. 2014. Available from: https://www.rfi.fr/en/africa/20141028-ebola-end-monitoring-workers-contact-french-nurse.

36. Parra JM, Salmerón OJ, Velasco M. The first case of Ebola virus disease acquired outside Africa. N Engl J Med. 2014;371(25):2439–40.

37. Richards GA, Murphy S, Jobson R, Mer M, Zinman C, Taylor R, et al. Unexpected Ebola virus in a tertiary setting: clinical and epidemiologic aspects. Crit Care Med. 2000;28(1):240–4.

38. Lopaz MA, Amela C, Ordobas M, Dominguez-Berjon MF, Alvarez C, Martinez M, et al. First secondary case of Ebola outside Africa: epidemiological characteristics and contact monitoring, Spain, September to November 2014. Euro surveillance : bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin. 2015;20(1).

39. Chung WM, Smith JC, Weil LM, Hughes SM, Joyner SN, Hall EM, et al. Active tracing and monitoring of contacts associated with the first cluster of Ebola in the United States. Ann Intern Med. 2015;163(3):164–73.

40. Plucinski MM, Guilavogui T, Sidikiba S, Diakité N, Diakité S, Dioubaté M, et al. Effect of the Ebola-virus-disease epidemic on malaria case management in Guinea, 2014: a cross-sectional survey of health facilities. Lancet Infect Dis. 2015;15(9):1017–23.

41. Kolie D, Camara BS, Delamou A, Béavogui AH, Hermans V, Edwards JK, et al. The Ebola-effect in Guinea 2014–15: tangled trends of malaria care in children under-five. PLoS ONE. 2018;13(2):e0192798.

42. Tan KR, Cullen KA, Koumans EH, Arguin PM. Inadequate diagnosis and treatment of malaria among travelers returning from Africa during the Ebola epidemic—United States, 2014–2015. Morb Mortal Wkly Rep. 2016;65(2):27–9.

43. Lev D, Biber A, Lachish T, Leshem E, Schwartz E. Malaria in travellers in the time of corona. Journal of travel medicine. 2020;27(6).