Infection prevention and control measures for Ebola and Marburg Virus disease: A series of rapid reviews

Modes of Transmission of Ebola and Marburg Virus – A Rapid Scoping Review

(Version 2, 19 October 2022)

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Funding: Funding for this protocol and the subsequent reviews was provided by the World Health Organization (Funding # 202818287). The working group (WG) from the WHO/HQ Country Readiness Strengthening Health Care Readiness Unit was consulted to develop and refine the scope, and review and approve the protocol. The WG was not be involved in the conduct of the review including selection of studies and data analysis but advised as needed on priority population(s), interventions, and outcomes in an iterative process during the review process based on the available evidence. The WG will also comment on the draft report and provide input on interpretations of findings. AT is funded by a Tier 2 Canada Research Chair in Knowledge Synthesis. SM is funded by a Tier 2 Canada Research Chair in Mathematical Modeling and Program Science.

Competing interests: DM was involved in the 2015 rapid review by Hersi et al. [1] There are no other competing interests to acknowledge.

Acknowledgements: We thank Kaitryn Campbell, MLIS, MSc (St. Joseph's Healthcare Hamilton/McMaster University) for peer review of the Embase search strategy.

Key Question

What is currently understood about the modes of transmission of Ebola and Marburg diseases from individuals infected with EVD/Marburg virus?

Methods Summary

We conducted a rapid scoping review to synthesize evidence on the contribution of different modes of transmission (direct or indirect) of Ebola or Marburg virus to overall Ebola or Marburg transmission. Data sources include Medline, Embase, bio/medRxiv pre-print servers, Global Medicus Index, and Epistemonikos. We used an automation tool (CAL® tool) for titles/abstracts screening for relevant systematic reviews and primary studies. Full-text screening and data extraction were completed independently by two reviewers with any disagreements resolved by consensus, with arbitration by a third reviewer, when needed. As the review was scoping in nature, we did not perform quality assessments of included studies or assess the overall certainty of evidence through GRADE ratings. Data was charted against the known modes of direct or indirect transmission (see Appendix 1.) and narratively synthesized by mode of transmission.

Findings

Search Results Summary

We screened 680 studies at the title/abstract stage and 188 studies at the full-text review stage. In total, 47 articles were included. We included seven evidence syntheses that address the primary direct/indirect modes of human-to-human transmission. Three systematic reviews assessed for risk factors and transmissibility of the Ebola virus in the general population[1,2] and in health care workers.[3] Four evidence syntheses addressed viral persistence, sexual transmission and vertical transmission.[4–7]

We supplemented the included systematic reviews with 30 primary studies that we captured in our searches that were not already included in the systematic reviews. Thirteen of these studies addressed zoonotic transmission for Ebola or Marburg viruses.

No systematic reviews or primary studies in humans were found that directly captured data on aerosol transmission (either droplet or airborne). To fill in these evidence gaps, we expanded our inclusion criteria to review all study designs that addressed aerosol transmission. We deemed that 10 of these studies provided relevant data, seven of which were narrative reviews and three experimental studies on animals or on particle dynamics.

Direct Physical Contact and Fomite Transmission

A 2016 systematic review by Brainard et al. evaluated the risk factors for Ebola or Marburg virus disease transmission.[1] The review highlighted three groups of behaviours primarily associated with the infection risk within the community. First, close contact with individuals in the later stages of Ebola or Marburg disease, when bodily fluids which contain high viral loads are more likely to be shed, and even non-intimate contact (e.g., conversation, prevalence rate ratio (PRR)= 3.9, 95% CI (1.2-12.2)) poses some infection risk even after adjustment for direct contact. Other activities like sharing a meal, a bed or sleeping mat, and touching and contact with body fluids show a high risk of disease transmission, suggesting probable fomite transmission. Second, caring for, or visiting, a sick person during EBOV or MARV illness. Visiting or caring for actively ill filovirus cases in hospitals or at home raised transmission risks across most outbreaks. Caring for Ebola or Marburg patients at home until death raised the disease transmission risk (OR = 13.33; 95% CI; 3.2 - 55.6). Third,

preparing a recently deceased body for burial. Those engaged in behaviours such as washing, dressing, and preparing a body for a funeral are at high risk; however, the evidence is inconsistent (range from unadjusted OR 1.07, 95% CI 0.63–1.82, to matched OR 13.1, 95% CI 1.4–631). Moreover, not all included studies found an association between attending funerals and disease risk. The review authors concluded that although certain behaviours suggest an increased risk of Ebola or Marburg virus transmission, limited pooled estimates restrict them from specifying the degree of certainty across evidence sources. Additional sources of uncertainty included the potential introduction of bias due to the use of anecdotal data in primary study reports and a lack of precision in estimates.

Dean et al., 2016, summarized the transmissibility and pathogenicity of the Ebola virus among household contacts.[2] The overall estimated household secondary attack rate (SAR) based on the nine studies was 12.5% (95% CI: 8.6%-16.3%). The risk was highest for those exposed to infectious body fluids while providing nursing care (SAR = 48% (95% CI: 25.5% - 70.9%). Additionally, the members of the immediate family members were found to be at a greater risk. The nine studies had limited data with variable quality, leading to uncertainty in the evidence for household spread of EVD.[2]

A 2018 review identified five most frequently cited categories of risk situation or factors contributing to exposure to, or infection with Ebola or Marburg virus among health care workers (HCWs).[3] First, insufficient/incorrect PPE use was the most frequently cited exposure risk. Also, deficiencies in PPE and lack of training in PPE use during patient care, transport or cleaning contributed to the exposure risk. Second, exposure at the point of care, particularly to patients with unrecognized Ebola or Marburg virus disease and cadavers during unsafe burial practices. Third, inappropriate risk assessment, including a lack of identification of potential EVD in corpses. Fourth, lack of environmental and engineering controls, including delays in laboratory EVD/MVD diagnosis. Fifth, lack of healthcare staff, no standard IPC protocols at the hospital, and IPC breaches during patient care contribute to risk exposure. The authors concluded that the high rates of HCWs infection highlight an urgent need to strengthen IPC measures.

We included 30 primary studies not captured by the included evidence syntheses. Most recent studies highlighted the same risk factors described in the Brainard review. High-risk exposures for transmission included having direct contact with another confirmed or probably EVD or Marburg case[8–15], exposure to body fluids[14–18], participation in a funeral[8–10,19–22], touching bodies of a deceased patient infected with EBOV or MARV [11,12,17,18,20,22], and care provision.[13,17,19–22] Studies reported higher transmission rates when exposure was direct rather than indirect and when primary contacts had wet rather than dry symptoms.[17,23] Of note, studies highlighted contact with a case's clothing or bed linens,[13,14] sleeping in the same room/spending time in the same physical space with the case,[13,14] touching the clothes or eating utensils of the case as sources of EVD transmission.[14] Two included studies examined the risk of fomite transmission by assessing the presence of EBOV RNA in the vicinity of EVD patients.[24,25] Palich and colleagues found evidence of persistence of EBOV RNA in the environment of Ebola patients, with a higher level of positivity in the vicinity of patients with a very high plasma viral load. Of swabs collected from fomites following contact with infected patients (e.g., mattress, clothes, blanket, bucket for digestive losses), 41.2% were positive.[25] In two Ebola treatment centers in Sierra Leone during the 2014–2016 West African Ebola outbreak, Poliquin and colleagues found that general areas, were negative for EBOV RNA, but higher levels of EBOV RNA were observed in the immediate vicinity of patients.[24] Personal protective equipment showed positivity for EBOV RNA, but chlorine solution washes were shown to render samples

negative for infectious material. EBOV RNA was commonly detected from material in direct contact with the patients, with less contamination in the immediate patient environment. Medical supplies and disposal containers showed positivity for EBOV RNA, whereas the pit latrine floor and shower floors did not.

Viral Presence/Persistence

A 2016 rapid review by Brainard and colleagues examined evidence of the presence/persistence of Ebola or Marburg viruses in body fluids from infected and convalescent individuals.[7] The authors found that blood from actively infected patients was likely to be positive for the virus, but seldom later than 16 days after illness onset. Blood appeared to be the most infectious body fluid due to high viral loads during illness. Ebola and Marburg were reported in most body fluids, including breastmilk, saliva, semen, sputum, stools, sweat, tears, urine or vomit. However, most non-blood or semen samples from patients were negative in patients or survivors, suggesting that these other fluids may be of low infectious risk. The authors could not draw any definite conclusions about relative infectivity due to inconsistent testing techniques and a lack of data on viral loads throughout patient illness and recovery.

Sexual transmission

A 2018 review examined eight Ebola flare-up events after the peak of the 2014-2016 Ebola epidemic in West Africa.[5] Reviewers defined Ebola flare-ups as new cases or clusters of cases occurring since January 2015 - i.e., when the number of EVD cases started to decline - with no epidemiological link with the ongoing chain of transmission. Results from the three affected countries (Guinea, Liberia, and Sierra Leone) showed that in half of those events sexual intercourse was the most likely transmission route from male survivors confirmed or suspected to be persistently infected. Case reports from two flare-up events also suggested that infectious semen may have infected humans (without sexual contact), e.g., through small lesions. In addition, results from the other two flare-up events suggested an underestimation of survivors with persisting EBOV in semen and other body fluids. The authors recommended continuing biological monitoring of survivors' body fluids (i.e., semen, breast milk, aqueous humour) for at least 18 months after their release from the ETU or until their body fluids tested negative at least twice. The study called for additional research on EBOV persistence and estimating EBOV transmission risk isolated from different body fluids.

A 2015 systematic review by Thorson et al. presented evidence of EBOV persistence in body fluids and sexual transmission from recovered Ebola survivors.[4] Evidence showed that viable EBOV persists in semen for at least 82 days and up to 284 days post-symptom onset. They reported no viable EBOV was isolated from the vaginal secretions; however, the detection of EBOV RNA on day 33 in the vaginal secretions of one of six women tested in the Kikwit (DRC) epidemic warrants additional research. Additionally, there was evidence of persisting Ebola virus in feces, saliva, sweat and urine. The authors concluded that there was a risk of sexual transmission of Ebola from convalescent patients, but that in-depth investigations
of putative sexual transmission with RT-PCR analyses, virus isolation and genetic sequencing was needed to confirm this.

In addition, we identified and included one primary cohort study that analyzed EBOV RNA persistence rates in semen over time in 220 male survivors from Sierra Leone.[26] The median duration was 204 days, and longer virus persistence was significantly associated with severe acute EVD and older age. The study authors noted that there remains a need for additional research to confirm the impact of viral RNA in semen on the transmission of Ebola virus.

Vertical transmission (Parent-to-Offspring)

Filovirus infection poses a substantial risk to susceptible populations like pregnant women and young children. EBOV infection during pregnancy is associated with fatal obstetrical and neonatal complications, like bleeding, miscarriage, stillbirth, and preterm delivery; however, evidence of mother-to-child EBOV transmission is limited.[6] Evidence confirms the presence of EBOV in maternal fluids, such as blood, vagina secretions, placenta, breast milk, urine, saliva, and sweat, acquired during maternal acute and convalescent states of EBOV disease. A recent 2021 evidence synthesis by Medina-Rivera et al. assessed EBOV transmission through breast milk and the outcomes of the infants who ingested EBOV laboratory-confirmed breast milk.[6] It was found that EBOV RNA shedding through breast milk may increase the risk of mother-to-child EBOV transmission; however, the limited number of reports and low certainty of evidence did not allow the reviewers to draw any definitive conclusions. The authors recommend additional research that simultaneously evaluates other potential modes of transmission and in-depth characterization of maternal body fluids.

Aerosol Transmission (Airborne or Droplet)

To discuss aerosol transmission, we refer to the modes of transmission as defined by the CDC[27]:

- Droplet transmission is a form of direct contact transmission in which droplets carrying infectious pathogens transmit infection when they travel directly from the respiratory tract of the infectious individual to susceptible mucosal surfaces of the recipient. This generally occurs over short distances and droplets have been traditionally defined as being >5 micrometers in size.
- Airborne transmission is a form of transmission resulting from the inhalation of small infectious particles or droplet nuclei (<= 5 micrometres) that can remain infectious over time and distance and be dispersed over long distances by air currents.

Droplet and airborne transmission can both fit under the broader category of aerosol transmission. Aerosols are typically defined as particles less than 50 micrometres in size.

Epidemiological Data

Epidemiological evidence of aerosol transmission is limited, partially due to the nature of outbreak investigations and the opportunity for recall bias when characterizing exposures. However, some studies of prior outbreaks have pointed to alternative routes of transmission beyond direct physical contact with infected patients or fluids. For example, 6.6% of the 274 cases in the 1976 SUDV EVD outbreak in Nzara (Sudan)and 17.4% of the 316 cases during the 1995 EBOV EVD outbreak in Kikwit (DRC) had no direct physical contact with a known source of infection or body fluid.[28–30] One case report on two American nurses who acquired EVD while caring for a patient in Dallas (Texas, USA) postulated that aerosol-generating procedures may have contributed to the transmission of the virus, as the nurses did not report direct contact with the infected patient.[30] While aerosol transmission may have occurred, it is impossible to rule out other modes of transmission from these reports (e.g., fomite transmission). Another study examining the risk of illness among household contacts found no evidence of Ebola virus transmission in any 23 familial contacts who had been in the same room as the primary case but had no direct contact with them. The authors concluded that the risk of aerosol transmission for Ebola virus was likely low.[30] Vetter and colleagues concluded that the risk of airborne transmission is also likely low, as the use of surgical masks that prevent contamination of the oral mucosa, but not airborne transmission, have

been sufficient to prevent nosocomial transmission in prior outbreaks.[31] The lack of evidence of aerosol transmission supports that aerosol transmission is not the most likely route of person-to-person transmission for Ebola or Marburg viruses.[32] However, this does not mean that aerosol transmission is impossible. One review noted that it may have been difficult to detect the contribution of coughing and aerosol transmission due to the high ambient temperature in African villages.[29] Aerosol transmission may occur in conditions of lower temperature and humidity not seen in prior Ebola virus or Marburg virus outbreaks.[29] Additional research is needed to confirm how the environmental conditions may have affected aerosol transmission during these outbreaks.

Other Evidence

Despite the lack of epidemiological evidence supporting aerosol transmission, we found several studies and reviews discussing the possibility of airborne or droplet transmission of filoviruses. Jones et al. discussed three conditions for the biological plausibility of aerosol transmission: (1) aerosols containing the pathogen are generated by or from an infectious person, (2) the pathogen remains viable in the environment for some period of time, and (3) the target tissues in which the pathogen initiates infection are accessible to the aerosol.[32] The additional information we found supporting the possibility of aerosol transmission will be organized according to these principles.

1. Aerosols containing the pathogen are generated by or from an infectious person

Autopsies performed on a small sample of EVD victims during the 1976 SUDV and 1995 EBOV EVD outbreaks revealed congestion, focal intra-alveolar edema, diffuse alveolar damage, and hemorrhage in the lungs, suggesting a potential pathogenic role of the virus in the respiratory system.[28,29] EBOV inclusions within alveolar macrophages and free viral particles within alveolar spaces in the lungs have also suggested that infectious aerosols could potentially be emitted from the respiratory tract.[29,31]

Aerosol generation is also possible in filovirus patients. Ebola and Marburg viruses are present in several bodily fluids in infected individuals, including saliva, stool, feces, and blood.[4,7] It is possible that these fluids may become aerosolized through symptoms or routine health care procedures. Droplets of various sizes may be emitted by coughing, talking, sneezing or vomiting, as well as aerosol-generating medical procedures.[29,33]

However, studies have noted that the risk of droplet transmission to nearby workers appears to be limited to within 3 feet (<1 metre) of an infectious patient.[29] The time, duration, and amount of virus shed from infected EVD or Marburg virus disease patients remains uncertain, as does how these factors may contribute to aerosol and droplet transmission at various stages of illness.[29]

2. The pathogen remains viable in the environment for some period of time

For Ebola virus or Marburg virus to be transmitted through aerosols, viral particles would need to be able to survive in the air and remain infectious until inhalation.[29] Piercy and colleagues calculated the theoretical survival of filoviruses in an aerosol over time based on their observed decay rates. They found that MARV, EBOV and RESTV can survive in aerosols for approximately 90 min, 100 min, 160 min, respectively (at 50% to 55% relative humidity and 22°C).[34] This showed that Ebola and Marburg viruses could remain in the air for 60–90 min within small droplets in African climatological conditions. The authors also noted that if filoviruses were aerosolized during laboratory or clinical practices (either by accident or deliberately), they may pose a significant threat to humans due to their significant length of infectivity. Another laboratory investigation of filovirus

particle dynamics showed that Ebola virus (Mayinga 1976 and EBOV Makona 2014 strains) could survive for 3 hours as an aerosol at 22°C and 80% relative humidity.[35]

3. The target tissues in which the pathogen initiates infection are accessible to the aerosol
Several sources discussed the possibility that Ebola and Marburg may be able to cause respiratory infections through aerosol inhalation. As noted above, Ebola viruses have been shown to initiate infection in diverse target tissues, including respiratory tract cells. Beyond pathophysiological evidence, animal studies have shown evidence of filovirus infection after artificial virus inoculation by aerosol challenge to mucus membranes. Experimental studies on guinea pigs and non-human primates (NHPs) found that transmission of the Marburg virus (Popp strain) through aerosol exposure is possible.[36] Infection of NHPs after aerosol exposure to EBOV has also been reported, with both low and high inhaled doses resulting in fatal EVD.[28–30,36] However, a recent 2022 study of EBOV transmissibility reported that aerosol EBOV-Makona-exposed NHPs did not succumb to infection or demonstrate any observable signs of disease.[37] Nevertheless, the animals did exhibit seropositivity to EBOV.

Some experimental studies have also reported on natural animal-to-animal aerosol transmission. In one study, piglets were infected with EBOV and then housed with macaques, separated by a 20 cm wire barrier to block direct contact. All NHPs subsequently developed an infection and respiratory lesions, further supporting respiratory involvement.[28–30] Similarly, other experimental studies on NHPs have reported primate-to-primate transmission of Ebola virus.[30,36] One study of EBOV-inoculated rhesus monkeys reported that control monkeys housed in the same room but 3 metres from the inoculated monkeys developed EVD.[30] The control monkeys were postulated to have been infected from aerosol, oral, or conjunctival exposure to virus-laden droplets. While the pattern of pulmonary antigen staining on pathology specimens suggested aerosol infection, transmission from other behaviours of NHPs, such as spitting or throwing feces, or other potential sources of cross-contamination, cannot be ruled out.

Overall, based on the principles outlined by Jones et al., there is evidence that aerosol transmission for Ebola and Marburg viruses is biologically plausible. The majority of reviews argued that droplet transmission may be more likely than true airborne transmission, but there was no strong epidemiological evidence supporting a high-risk from either mode of transmission.

Zoonotic Transmission

Marburg
Bausch and colleagues investigated chains of transmission from the outbreak of Marburg hemorrhagic fever in the DRC in 1998-2000.[38] A seasonal transmission pattern was observed over the two years, showing multiple, short, independent chains of human-to-human transmission. The pattern consisted of a seasonal upsurge in cases, primarily among miners, followed by the spread to close contacts or nosocomial infection. Of 154 cases, 52% were in young male miners, and only 27% of these cases reported direct contact with other affected cases. 67% of cases who were not miners did report direct contact with infected cases. A subsequent phylogenetic analysis of bat specimens captured from the mine associated with this outbreak found that isolated bat gene fragments corresponded to virus sequences previously isolated from humans during the epidemic.[39]

A retrospective 2020 study reported that Ugandan gold miners who work in bat-inhabited caves had a 5.4 times risk of being seropositive for filoviruses compared to the unexposed group in central Uganda (RR= 5.4, 95% CI 1.5–19.7).[12] Another epidemiological investigation of the Marburg outbreak in Kween District (Uganda) in 2017 concluded that rock salt mining in a bat cave led to a spill-over of the virus into the human population.[11] Similarly, a 2007 outbreak of Marburg hemorrhagic fever was detected among 4 Ugandan gold miners and was reported to likely have been due to exposure to bat secretions from Egyptian fruit bats (*Rousettus aegyptiacus*).[40]
The *Rousettus aegyptiacus* species of bat was also found to have virus-specific RNA and IgG antibody in 2007 in Gabon, suggesting that it may be a natural reservoir for these viruses.[41] Following virus isolation and phylogenetic sequencing, a recent study of bats in Sierra Leone showed active infection in 2.5% of *Rousettus aegyptiacus* bats with a Marburg strain similar to the Angola strain.[42] Towner and colleagues estimated that approximately 5% of *Rousettus aegyptiacus* bats were infected in Kitaka Cave (Uganda).[43] A similar analysis of bat liver/spleen tissues from bats in Python Cave (Uganda) found that 2.5% of 1,622 captured bats were actively infected with Marburg virus and the strains were genetically similar to those from infected tourists who had been exposed to bats in the cave.[44] Additionally, the authors reported pulses of virus infection in older juvenile bats, possibly explaining prior spillover events where there were seasonal periods of increased risk of human infection.

Ebola
During EVD outbreaks, the typical pattern of transmission is a single primary introduction of infection into humans, followed by human-to-human transmission.[45] This was thought to be the case in the 2017 EBOV outbreak in the DRC.[46] The epidemiological investigation concluded that the index case was infected from zoonotic transmission through close contact with bush meat (butchering wild boar, contact with a non-human primate). However, the presence of EBOV could not be confirmed with viral samples from the animals.

Bratcher 2021 reported that zoonotic exposures were associated with EBOV GP seroreactivity in the absence of diagnosed EVD. Significant associations were reported between seroreactivity to Ebola virus and having contact with bats, rodents, and eating non-human primate meat.[47] An earlier seroprevalence study of risk factors in the pygmy population of the Watsa region, found no association between exposure to risk factors (contacts with rats, bats, monkeys, or entry into caves) and seropositivity for IgG antibody against EBOV.[48] However, the study authors noted that their study may have failed to detect differences by not accounting for the level of exposure between participants.[48] Another 2018 seropositivity study in southwest Uganda found that touching duikers was the most significant risk factor associated with EBOV seropositivity, while hunting primates and touching and eating cane rats were significant risk factors for SUDV seropositivity.[49]

Table 1. Characteristics of Included Evidence Syntheses

Citation [Author, Year of Publication]	Study Design	Funding Source	Virus Species	Mode of Transmission	# Studies included in review	Study Objectives [as reported by study authors]
Brainard 2016[1]	Systematic review and Meta-analysis	National Institute for Health Research Health Protection Research Unit in Emergency Preparedness and Response in partnership with Public Health England	Ebola/ Marburg	Direct physical /Fomite	31	"In this systematic review we searched for all published evidence which identified and/or quantified the risk factors for community acquisition of filovirus infection"
Brainard 2016 [2][7]	Rapid Systematic Review	National Institute for Health Research Health Protection Research Unit in Emergency Preparedness and Response in partnership with Public Health England	Ebola/ Marburg	Viral Persistence	33	"We report a rapid systematic review of published evidence on the presence of filoviruses in body fluids of infected people and survivors."
Dean 2016[2]	Systematic review and Meta-analysis	National Institutes of Health	Ebola	Direct physical /Fomite	9	"We performed a meta-analysis of Ebola household secondary attack rate (SAR), disaggregating by type of exposure (direct contact, no direct contact, nursing care, direct contact but no nursing care)."
Medina-Rivera 2021[6]	Systematic review and meta-analysis	Division of Nutritional Sciences, Cornell University, Ithaca, New York, and the World Health Organization, Geneva, Switzerland	Ebola	Vertical transmission	8	"To determine whether EBOV can be transmitted through breast milk and to describe the outcomes of the infants who ingested EBOV laboratory-confirmed breast milk"
Selvaraj 2018[3]	Systematic review	World Health Organization	Ebola/ Marburg	Direct physical /Fomite	69	"We conducted a systematic review to investigate infection and mortality rates and common exposure risks in HWs in EVD and MVD outbreaks."
Subissi 2018[5]	Review	Not reported	Ebola	Sexual transmission	8 Flare-up events	"To review the knowledge on the Ebola flare-ups that occurred after the peak of the 2014–2016 Ebola epidemic in West Africa"
Thorson 2015[4]	Systematic review	None	Ebola	Sexual transmission	13	"To present a comprehensive, systematic review on evidence of sexual transmission from Ebola survivors and persistence of Ebola virus in body fluids of relevance to sexual transmission, and

						additionally to review condom effectiveness against sexual transmission of Ebola"

Table 2. Characteristics of Included Primary Studies

Citation [Author, Year of Publication]	Study Design	Funding Source	Virus Species	Primary Mode of Transmission Reported	Outbreak Setting	# Total Participants	Study Objectives [as reported by study authors]
Adjemian 2011[40]	Contact tracing/ surveillance	Viral Special Pathogens Branch, Division of High-Consequence Pathogens and Pathology, National Center for Emerging and Zoonotic Infectious Diseases, CDC	Marburg	Zoonotic	Uganda 2007	4 cases	"Marburg hemorrhagic fever was detected among 4 miners in Ibanda District, Uganda, from June through September, 2007. Infection was likely acquired through exposure to bats or bat secretions in a mine in Kamwenge District, Uganda, and possibly human-to-human transmission between some patients. We describe the epidemiologic investigation and the health education response."
Amman 2012[44]	Immunohistochemical analyses	Department of Health and Human Services	Marburg	Zoonotic	N/A	N/A	"In the present study, we report a multi-year investigation of natural Marburg virus circulation among *R. aegyptiacus* in southwest Uganda, with emphasis on bats inhabiting Python Cave"
Amman 2020[42]	Phylogenetic analyses	Government of Sierra Leone, United States Agency for International Development (USAID) Emerging Pandemic Threats PREDICT project, CDC and Prevention's Division of High Consequence Pathogens and Pathology and the Viral Special Pathogens Branch	Marburg	Zoonotic	Sierra Leone	N/A	"Here, collaborative studies by the Centers for Disease Control and Prevention, Njala University, University of California, Davis USAID-PREDICT, and the University of Makeni identify MARV circulating in ERBs in Sierra Leone. PCR, antibody and virus isolation data from 1755 bats of 42 species shows active MARV infection in approximately 2.5% of ERBs"

Barry 2018[8]	Contact tracing/ surveillance	None	Ebola (Zaire)	Direct physical/fomite	DRC 2018	50 cases	"On May 8, 2018, the Government of the Democratic Republic of the Congo reported an outbreak of Ebola virus disease in Équateur Province in the northwest of the country. […] We provide early epidemiological information arising from the ongoing investigation of this outbreak"
Bausch 2003[38]	Contact tracing/ surveillance	Office of Foreign Disaster Assistance of the U.S. Agency for International Development and the Department of Communicable Disease Surveillance and Response, WHO	Marburg	Zoonotic	DRC 1998	912 participants	"We conducted two antibody surveys to assess risk factors for Marburg hemorrhagic fever in an area of confirmed Marburg virus transmission in the Democratic Republic of the Congo"
Bower 2016[17]	Contact tracing	Save the Children internal funds and the Wellcome Trust's Enhancing Research Activity in Epidemic Situations program	Ebola (Unclear strain)	Direct physical/fomite	Sierra Leone 2014–2015	937 participants	"Using histories of household members of Ebola virus disease (EVD) survivors in Sierra Leone, we calculated risk of EVD by age and exposure level, adjusting for confounding and clustering, and estimated relative risks"
Bratcher 2021[47]	Cross-sectional serosurvey	Bill & Melinda Gates Foundation, The Faucett Catalyst Fund, the Shaffer Family Foundation, and the US Food and Drug Administration	Ebola (Zaire)	Zoonotic	DRC 2015 - 2017	1366	"This study aims to identify risk factors associated with detectable antibody levels in the absence of an EVD diagnosis."
Cleaton 2016[19]	Cross-sectional	Division of International Epidemiology and Population Studies, the Fogarty International Center, US National Institutes of Health, Office of Pandemics and Emerging Threats at the US Department of Health and Human Services, National Science Foundation, Research and Policy for Infectious Disease Dynamics Program of the US Department of Homeland Security, Lundbeck Foundation, Denmark.	Ebola (Unclear strain)	Direct Physical	Guinea, Sierra Leone, and Liberia 2014-2015	286 cases	"Here, we validate the systematic collection of Internet news reports to characterize epidemiological patterns of Ebola virus disease (EVD) infections during the West African 2014–2015 outbreak"

Curran 2016[20]	Contact tracing/ surveillance	Not reported	Ebola (Unclear strain)	Direct physical/f omite	Sierra Leone 2014	281 cases	"The Sierra Leone Ministry of Health and Sanitation and CDC conducted a retrospective analysis of laboratory-con- firmed Ebola cases in Moyamba during July 11–October 31, to investigate the increase in cases in September 2014, determine the source and risk factors, and recommend prevention and control measures."
Diallo 2019[16]	Cross-sectional observational study	Funding Institut National de la Santé et de la Recherche Médicale, Reacting, the French Ebola Task Force, Institut de Recherche pour le Développement, and Montpellier University Of Excellence-University of Montpellier.	Ebola (Unclear strain)	Direct physical/f omite	Guinea 2016-2017	1390 participants	"This study aimed to identify risk factors for seropositivity and to estimate the prevalence of Ebola virus infection in unvaccinated contact persons."
Glynn 2018[23]	Cross-sectional	Save the Children internal funds and the Wellcome Trust's Enhancing Research Activity in Epidemic Situations program	Ebola (Unclear strain)	Direct physical/f omite	Sierra Leone 2015	109 primary cases, 317 subsequent	"From detailed exposure histories, intrahousehold transmission chains were created for 94 households of Ebola survivors in Sierra Leone"
Knust 2015[9]	Cross-sectional serosurvey	CDC, the Uganda Ministry of Health, Médecins sans Frontières, WHO	Ebola (Unclear strain)	Direct physical/f omite	Uganda 2012	26 cases	"In this article, we describe findings of the outbreak investigation and diagnostic testing and review the clinical symptoms of cases"
Miglietta 2019[10]	Retrospective surveillance data analysis	None	Marburg	Direct physical/f omite	Sierra Leone 2014-2015	454 cases	"We analysed the VHF database of Tonkolili district to describe the epidemiology of the EVD outbreak during July 2014–June 2015"
Mulangu 2016[48]	Cross-sectional serosurvey	'Fonds voor Wetenschappelijk Onderzoek—Vlaanderen' Antwerp; the Framework Agreement between the Belgian Directorate for Development Co-operation and the Institute of Tropical Medicine, Antwerp and the Wellcome Trust Grant to the	Ebola (Unclear strain)	Zoonotic	N/A	300 participants	"We studied the pygmy population of Watsa region to determine seroprevalence to EBOV infection and possible risks factors"

		Southern African Centre for Infectious Diseases and Surveillance					
Nsio 2019[46]	Phylogenetic analyses	DRC Ministry of Health; the Global Outbreak Alert and Response Network, World Health Organization; and Médecins sans Fontières	Ebola (Zaire)	Zoonotic	DRC 2017	8 cases	"In this article, we report the clinical and epidemiological information related to the 2017 EBOV outbreak in the DRC, as well as the characterization of the causative agent, a novel Ebolavirus variant from the Zaire ebolavirus species"
Nyakarahuka 2020[12]	Cross-sectional serosurvey	UgandaVirus Research Institute and CDC	Ebola (Zaire)	Direct physical/Zoonotic	N/A	724 participants	"We investigated the seroprevalence and risk factors for Marburg virus and ebolaviruses in gold mining communities around Kitaka gold mine in Western Uganda and compared them to non-mining communities in Central Uganda"
Nyakarahuka 2019[11]	Outbreak investigation (epidemiological and laboratory analyses)	CDC, Ministry of Health of Uganda and WHO	Marburg, Sudan	Direct physical/Zoonotic	Uganda 2017	70	"In October 2017, a blood sample from a resident of Kween District, Eastern Uganda, tested positive for Marburg virus. Within 24 hour of confirmation, a rapid outbreak response was initiated. Here, we present results of epidemiological and laboratory investigations."
Palich 2017[25]	Cross-sectional	None	Marburg	Fomite	Guinea 2015	N/A	"Our study aims todetect Ebola virus (EBOV) RNA within the high- and low-risk areas ofan Ebola treatment unit (ETU) located ininland Guinea during the 2014–2015 West African Ebola epidemics"
Poliquin 2016[24]	Cross-sectional	Public Health Agency of Canada	Ebola (Zaire)	Fomite	Sierra Leone 2015	N/A	"This study conducted environmental surveillance in 2 ETCs in Freetown, Sierra Leone, during the 2014–2016 West African Ebola outbreak"
Reichler 2018[13]	Contact tracing/surveillance (prospective)	Centers for Disease Control and Prevention and by the CDC Foundation.	Ebola (Unclear strain)	Fomite	Sierra Leone 2015	150 cases and 838 contacts	"From this prospective investigation of households with a first case of EVD in Freetown, Sierra Leone, we present the rates and risk factors associated with transmission to household contacts"

Senga 2017[18]	Retrospective surveillance data analysis	None	Ebola (Unclear strain)	Direct physical/fomite	Sierra Leone 2014	261 cases	"We performed a retrospective data analysis of 261 probable and confirmed EVD cases in the national EVD database and 2525 contacts in the Contact Line Lists in Kenema district, Sierra Leone between 27 April and 4 September 2014 to assess the performance of contact tracing during the initial stage of the outbreak"
Skrip 2017[14]	Contact tracing/surveillance	NIH and MIDAS	Ebola (Unclear strain)	Direct physical/fomite	Liberia 2014	4373	"To investigate potential differences in the risk of transmission and susceptibility to disease, we analysed contact-tracing data collected in Montserrado County, Liberia, during the 2013 – 2016 Ebola outbreak in West Africa"
Smiley Evans 2018[49]	Cross-sectional	William J. Fulbright Foundation, the US Agency for International Development Emerging Pandemic Threats PREDICT project and the Intramural Research Program of the National Institute of Allergy and Infectious Diseases, National Institutes of Health	Ebola (Unclear strain)	Zoonotic	Uganda 2013	331	"In this study, we investigated potential exposures to filoviruses among acutely febrile patients from the Bakiga and Batwa tribes in southwestern Uganda, and identified possible risk factors for filovirus seropositive status using detailed livelihood and behavior surveys"
Stehling-Ariza 2016[21]	Contact tracing/ surveillance	None	Ebola and Marburg	Direct physical	Sierra Leone 2014-2015	50 cases	"We conducted a field investigation to determine the likely sources of Ebola infection for the index case and other cases in the village, and potential opportunities for prevention of future Ebola infections"
Swanepoel 2007[39]	Ecological investigations	Department of Communicable Disease Surveillance and Response, WHO	Ebola (Zaire)	Zoonotic	DRC 1999	N/A	"To determine reservoir hosts for Marburg virus (MARV), we examined the fauna of a mine in northeastern Democratic Republic of the Congo"
Swanson 2018[15]	Retrospective descriptive	U.S. Agency for International Development Office of Foreign Disaster Assistance	Marburg	Direct physical/fomite	Liberia, 2014–2015	25,651 contacts; 2,465 index cases	"We performed a retrospective descriptive analysis of data collection forms for contact tracing conducted in six counties during June 2014–July 2015"

Thorson 2007	Prospective cohort	Paul Allen family foundation, WHO Ebola Response Program, the Paul G.Allen Family Foundation, the UNDP, UNFPA UNICEF–WHO–WorldBank Special Program ofResearch, Developmentand Research Training inHuman Reproduction(HRP), CDC, Chinese CDC, Sierra Leone Ministry of Health and Sanitation and the Ministry of Defence, and theJoint United Nations Program on HIV/AIDS in support of the Sierra Leone Ebola Virus Persistence Study	Ebola (Zaire)	Direct physical (Sexual Transmission)	Sierra Leone 2015-2017	220	"This cohort study aimed to analyze population estimates of EBOV RNA persistence rates in semen over time, and associated risk factors in a population of survivors from Sierra Leone"
Tiffany 2017[22]	Contact tracing/ surveillance	International Federation of the Red Cross and Red Crescent Societies	Ebola (Unclear strain)	Direct physical/fomite	Sierra Leone, Liberia and Guinea 2015	310	"Using data collected during epidemiological investigations, we estimate the number of secondary cases that were potentially averted by safe burials, and describe risk factors for EVD transmission during funerals and burial rituals (unsafe burials)."
Towner 2007[41]	Phylogenetic analysis	CDC, CIRMF, Government of Gabon, Total-Fina-Elf Gabon, and the Ministere de la Coope □ ration Francaise, Fonds de Solidarite □ Prioritaire grant	Marburg	Zoonotic	Gabon [no outbreak]	N/A	"Here, we report the discovery of Marburg virus in a common species of fruit bat (Rousettusaegyptiacus) in Gabon as shown by finding virus-specific RNA and IgG antibody in individual bats"
Towner 2009[43]	Ecological investigations	CDC, Battelle National Biodefense Insitute, Frederick	Ebola (Unclear strain)	Zoonotic	Uganda 2007-2008	N/A	"In July 2007, a small outbreak of MHF occurred in workers mining lead and gold in Kitaka Cave near Ibanda village in western Uganda. Large numbers of R. aegyptiacus and insectivorous Hipposideros species bats were present in this mine. Ecological investigations were conducted in August 2007 and May 2008, and the findings are presented here"

Table 3. Characteristics of Included Aerosol Studies

Citation [Author, Year of Publication]	Study Design	Funding Source	Virus Species	Study Objectives [as reported by study authors]
De la Vega 2022[37]	Experimental animal study	Canadian Institutes of Health Research	Ebola (EBOV)	"We sought to characterize the impact by route of infection, viremia, and viral shedding through various mucosae, with regards to intraspecies transmission of Ebola virus in a nonhuman primate model"
Fischer 2016[35]	Experimental study	Intramural Research Program of the National Institute of Allergy and Infectious Diseases, National Institutes of Health	Ebola (EBOV Mayinga 1976 and EBOV Makona 2014)	"This study investigates the viability of 2 Zaire ebolavirus strains within aerosols at 22°C and 80% relative humidity over time"
Jones 2015[32]	Literature review	None	Infectious aerosols, including Ebola virus	"The concept of aerosol transmission is developed to resolve limitations in conventional definitions of airborne and droplet transmission"
Lalle 2019[28]	Literature review	Italian Ministry of Health; the European and Developing Countries Clinical Trials Partnership (EDCTP2); PANDORA-ID-NET project	Ebola (EBOV, SUDV, RESTV)	"This review highlights the pulmonary involvement in EVD, with a special focus on the new data emerging from the 2013–2016 Ebola outbreak"
Leffel 2004[36]	Perspective/Literature Review	US Army Medical Research Material Command Research Plan	Marburg/Ebola viruses	"Building on published results from aerosol studies, as well as a review of the history, epidemiology, and disease course of naturally occurring outbreaks, we offer an aerobiologist's perspective on the threat posed by aerosolized filoviruses."
Mekibib 2016[29]	Literature review	Fund for Scientific Research Flanders (FWO) and the Agency for Innovation by Science and Technology (IWT)	Ebola (EBOV, SUDV, RESTV, MARV	"This review deals with the controversial issue of aerosol transmission of filoviruses"
Osterholm 2015[30]	Literature review	Center for Infectious Disease Research and Policy (CIDRAP)	Ebola (EBOV, SUDV, RESTV)	"In this review, we address what we know and what we do not know about Ebola virus transmission. We also hypothesize that Ebola viruses have the potential to be respiratory pathogens with primary respiratory spread"

Passi 2015[33]	Literature review	Not reported	Ebola (EBOV, SUDV, RESTV)	"Idea behind this article is to briefly review the history and present recent updates on Ebola virus, its pathogenesis and possible hopes for treatment"
Piercy 2010[34]	Experimental study	Not reported	Ebola (EBOV, MARV, RESTV)	"Filoviruses were tested for their ability to survive in different liquids and on different solid substrates at different temperatures. The decay rates of filoviruses in a dynamic aerosol were also determined."
Vetter 2016[31]	Literature review	Geneva University Hospitals, the Swiss Agency for Development and Cooperation, and the Tulane University	Ebola	"We performed an extensive PubMed literature review encompassing the period from discovery of Ebola virus, in 1976, until 1 June 2016 to evaluate the evidence on modes of Ebola virus shedding and transmission"

Table 4. Summary of Findings by Mode of Transmission

Mode of Transmission	***Virus Species***	***Results***	***Conclusions***

Aerosol	Ebola	• Prior outbreaks have reported EVD cases with no direct physical contact with infected patients or their body fluids (6.6% and 17.4% of cases respectively in the 1976 SUDV EVD outbreak and the 1995 EBOV EVD[28–30]; case report of two nurses in Dallas Texas[30]
		  ○ Unclear if these cases were due to aerosol transmission or other modes (e.g., fomite transmission).
		• One study examining risk of illness among household contacts, found no evidence of Ebola virus transmission in any of 23 familial contacts who had been in the same room as the primary case[30]
		  ○ Authors concluded that the risk of aerosol transmission for Ebola virus was likely low
		• Use of surgical masks that prevent contamination of the oral mucosa, but not airborne transmission, have been sufficient to prevent nosocomial transmission in prior outbreaks[31]
		• One review noted that it may have been difficult to see the contribution of coughing and aerosol transmission due to the hostile ambient temperature in African villages[29]
			• Limited epidemiological data supports aerosol transmission (either droplet or airborne)
			• Aerosol transmission did not appear to be the primary source of transmission during prior EVD outbreaks
			• Some studies have concluded that the risk of aerosol transmission (and particularly airborne transmission) is low
			• More research is needed to assess how environmental conditions affected aerosol

Mode of Transmission	***Virus Species***	***Results***	***Conclusions***
			transmission during prior outbreaks
Aerosol	Ebola/Marburg	Evidence that aerosols containing Ebola or Marburg viruses could generated by or from an infectious person: • Autopsies studies have suggested from 1976 SUDV and 1995 EBOV EVD outbreaks suggested a potential pathogenic role of the virus in the respiratory system[28,29] • EBOV inclusions within alveolar macrophages and free viral particles within alveolar spaces in the lungs have also suggested that infectious aerosols could potentially be emitted from the respiratory tract[29,31] • Ebola and Marburg viruses are present in several bodily fluids in infected individuals, including saliva, stool, feces, and blood[7,31] and may become aerosolized through symptoms or routine health care procedures • Risk of droplet transmission to nearby workers appears to be limited to within 3 feet of an infectious patient[29] • The time, duration, and amount of virus that is shed from infected EVD or Marburg virus disease patients remains uncertain, as does how these factors may contribute to aerosol and droplet transmission at various stages of illness[29] Evidence that the filoviruses could remain viable in the environment for some period of time: • MARV, EBOV and RESTV can survive in aerosols for approximately 90 min, 100 min, 160 min, respectively (at 50% to 55% relative humidity and 22°C)[34] • Ebola virus (Mayinga 1976 and EBOV Makona 2014 strains) can survive for 3 hours as an aerosol at 22°C and 80% relative humidity[35]	• Based on the principles outlined by Jones et al., there is evidence that aerosol transmission for Ebola and Marburg viruses is biologically plausible

Mode of Transmission	***Virus Species***	***Results***	***Conclusions***
		Evidence that Ebola and Marburg may be able to cause respiratory infections through aerosol inhalation: • Animal studies of guinea pigs and NHPs have shown evidence of Marburg and Ebola virus infection with respiratory involvement after artificial virus inoculation by aerosol challenge to mucus membranes[28–30,36] • Experimental studies have also reported on natural animal-to-animal aerosol transmission of EBOV[28–30,36] ○ Pulmonary samples suggested respiratory involvement suggesting aerosol infection, but other modes of transmission cannot be ruled out (e.g., direct contact with body fluids, fomites)	

Direct contact/Fomite	Ebola/Marburg	• A 2016 systematic review evaluated the risk factors for Ebola or Marburg virus disease transmission[1] highlighted three groups of behaviours primarily associated with the infection risk within the community[1]
		  1) Close contact with individuals in the later stages of Ebola or Marburg disease due to the presence of high viral loads in bodily fluids. Other activities like sharing a meal, a bed or sleeping mat, and touching and contact with body fluids show high risk of disease transmission, suggesting probable fomite transmission.
		  2) Caring for a sick person during EBOV or MARV illness
		  3) Preparing the recently deceased body for burial.
		  ○ Not all included studies found an association between attending funerals and disease risk. However, those engaged in certain behaviours (e.g., washing, dressing, and preparing for a funeral) are at increased risk, although the evidence is inconsistent
		• Dean et al., 2016, summarized the transmissibility and pathogenicity of Ebola virus among household contacts[2] and found that risk was highest for those exposed to infectious body fluids while providing nursing care (SAR = 48% (95% CI: 25.5% - 70.9%)
			• Behaviours that involve direct physical contact with an EVD/Marburg patient, including contact with body fluids from infected patients, patient care or touching deceased bodies consistently pose the highest risk of EVD/MARV transmission.
			• The certainty of evidence is lowered by a limited ability to pool estimates likely introduction of bias due to use of anecdotal data in primary study reports and a lack of precision in estimates
			• A lack of properly implemented IPC measures, including PPE,

Mode of Transmission	*Virus Species*	*Results*	*Conclusions*
		• A 2018 review identified Ebola or Marburg virus infection risk factors among HWs and categorized the five significant categories contributing to the infection risk:[3] 1. Insufficient/incorrect PPE, including deficiencies in PPE and lack of training in PPE use during patient care, transport or cleaning contributed to the exposure risk 2. Exposure at the point of care, particularly to patients with unrecognized Ebola or Marburg virus disease and cadavers during unsafe burial practices 3. Inappropriate risk assessment, including a lack of identifying potential EVD in corpses 4. Lack of environmental and engineering controls, including delays in laboratory EVD/MVD diagnosis 5. Lack of healthcare staff, no standard IPC protocols in place at the hospital, and IPC breaches during patient care contribute to risk exposure. • Recent studies highlighted the same risk factors as previously described in the Brainard review, including having direct contact with another confirmed or probably EVD or Marburg case[8–15], exposure to body fluids[14–18], participation in a funeral[8–10,19–22], touching bodies of a deceased patient infected with EBOV or MARV [11,12,17,18,20,22], and care provision.[13,17,19–22] • Studies reported higher rates of transmission when exposure was direct than indirect, and when primary contacts had wet rather than dry symptoms.[17,23] • Studies highlighted contact with a case's clothing or bed linens,[13,14] sleeping in the same room/spending time in the same physical space with the case,[13,14] touching the clothes or eating utensils of the case as sources of EVD transmission.[14]	inappropriate risk assessment, lack of environmental/engineering controls, play a large role in the risk of infection for HCWs • Limited epidemiological evidence confirms fomite transmission, but studies have shown the presence of EBOV RNA in the vicinity of EVD patients

Mode of Transmission	***Virus Species***	***Results***	***Conclusions***

		• Two included studies examined the risk of fomite transmission by assessing the presence of EBOV RNA in the vicinity of EVD patients.[24,25]
		  ○ Palich and colleagues found evidence of persistence of EBOV RNA in the environment of Ebola patients, with a higher level positivity in the vicinity of patients with a very high plasma viral load. Of swabs collected from fomites following contact with infected patients (e.g., mattress, clothes, blanket, bucket for digestive losses), 41.2% were positive.[25]
		  ○ Poliquin and colleagues found that general areas in two Ebola treatment centers in Sierra Leone during the 2014–2016 West African Ebola outbreak, were negative for EBOV RNA, with higher levels of EBOV RNA observed in the immediate vicinity of patients.[24] Personal protective equipment showed positivity for EBOV RNA, but chlorine solution washes were show to render samples negative for infectious material. EBOV RNA was commonly detected from material in direct contact with the patients, with less contamination in the immediate patient environment. Medical supplies and disposal containers showed positivity for EBOV RNA, whereas the pit latrine floor and shower floors did not.	

Direct contact (sexual transmission)	Ebola Virus	• A 2018 review examined eight Ebola flare-up events after the peak of the 2014-2016 Ebola epidemic in West Africa[5] ○ Sexual intercourse was the most likely transmission route from the persistently infected male survivors (confirmed or suspected) in half of flare-up events • A 2015 systematic review by Thorson et al. presented evidence of EBOV persistence in body fluids and sexual transmission from recovered Ebola survivors[4]	• Viral persistence has been recorded in human semen • Authors recommended continuing biological monitoring of survivors' body fluids (i.e., semen, breast milk, aqueous humour) for at least 18 months after their release

Mode of Transmission	***Virus Species***	***Results***	***Conclusions***
		○ Evidence showed that viable EBOV persisted in semen from a range of 82 days up to 284 days post-symptom onset ○ No viable EBOV was isolated from the vaginal secretions • A primary cohort study that analyzed EBOV RNA persistence rates in semen over time in 220 male survivors from Sierra Leone found a median persistence duration (50% of men with clear semen samples of EBOV RNA) of 204 days[26]	from the ETU or until their body fluids tested negative at least twice • Additional research is required on EBOV persistence and estimating EBOV transmission risk isolated from different body fluids
Direct contact (vertical transmission)	Ebola	• EBOV infection during pregnancy is associated with fatal obstetrical and neonatal complications, like bleeding, miscarriage, stillbirth, and preterm delivery[6] • EBOV has been shown to be present in maternal fluids, such as blood, vagina secretions, placenta, breast milk, urine, saliva, and sweat, including in convalescent EVD patients[6] • A systematic review found that EBOV RNA shedding through breast milk may increase the risk of mother-to-child EBOV transmission; however, the limited number of reports and low certainty of evidence did not allow the reviewers to draw any definitive conclusions[6] • Additional research that simultaneously evaluates other potential modes of transmission and in-depth maternal body fluids characterization is required[6]	• Evidence of mother-to-child EBOV transmission is limited • EBOV infection during pregnancy has been associated with adverse pregnancy and neonatal complications
Zoonotic Transmission	Ebola (EBOV/SUDV)	• An investigation of the 2017 EBOV outbreak in the Democratic Republic of Congo concluded that the index case was infected from zoonotic transmission through close contact with bush meat (butchering wild boar, contact with a nonhuman primate)[46] • Zoonotic exposures were associated with EBOV GP seroreactivity in the absence of diagnosed EVD. Significant associations were	• During EVD outbreaks, the typical pattern of transmission is a single primary introduction of infection into humans, followed by human-to-human transmission

Mode of Transmission	***Virus Species***	***Results***	***Conclusions***
		reported between seroreactivity to Ebola virus include having contact with bats, rodents, and eating non-human primate meat[47] • An earlier seroprevalence study of risk factors in the pygmy population of the Watsa region, found no association between exposure to risk factors (contacts with rats, bats, monkeys, or entry into caves) and seropositivity for IgG antibody against EBOV[48] • A 2018 seropositivity study in southwest Uganda, found that touching duikers was the most significant risk factor associated with EBOV seropositivity, while hunting primates and touching and/or eating cane rats were significant risk factors for SUDV seropositivity[49]	• Seropositivity to EBOV/SUDV has been associated with zoonotic exposures, although the species associated with highest risk of seroreactivity varied between studies and Ebola virus species
Zoonotic transmission	Marburg	• A seasonal pattern of transmission was observed over outbreak of Marburg hemorrhagic fever in the Democratic Republic of the Congo 1998-2000[38] o The pattern consisted of a seasonal upsurge in cases was primarily among miners, followed by spread to close contacts or nosocomial infection o A phylogenetic analysis of bat specimens captured from the mine associated with the DRC 1998-2000 outbreak found that isolated bat gene fragments corresponded to virus sequences previously isolated from humans during the epidemic[39] • An epidemiological investigation of the Marburg outbreak in Kween District, Uganda, in 2017 concluded that rock salt mining in a bat cave led to a spill-over of the virus into the human population.[11] • A 2007 outbreak of Marburg hemorrhagic fever was detected among 4 Ugandan gold miners was reported to likely have been due to exposure to bat secretions from Egyptian fruit bats (Rousettus aegyptiacus)[40] • A retrospective 2020 study found that Ugandan gold miners who work in bat inhabited caves had a 5.4 times the risk of being	• Marburg transmission patterns show seasonal surges with multiple, short, independent chains of human-to-human transmission • Reported pulses of virus infection in older juvenile bats may explain the seasonal pulses of increased risk of human infection • Several outbreaks were reportedly initiated by zoonotic transmission of MARV between bat species (particularly Egyptian fruit bats, *Rousettus aegyptiacus*) and miners • Phylogenetic analyses of bat specimens showed the same

Mode of Transmission	*Virus Species*	*Results*	*Conclusions*
		seropositive for filoviruses compared to the unexposed group in central Uganda[12] • A phylogenetic study estimated that approximately 5% of Egyptian fruit bats (Rousettus aegyptiacus) were infected in Kitaka Cave, Uganda[43] • Another phylogenetic study found that 2.5% of 1,622 captured bats were actively infected with Marburg virus and the strains were genetically similar to those from infected tourists who had been exposed to bats in a nearby cave in Uganda.[44] Additionally, pulses of virus infection in older juvenile bats, possibly explaining prior spillover events were there were seasonal periods of increased risk of human infection.	or similar strains of MARV were present as those isolated from human Marburg patients

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Appendix 2. Eligibility Criteria

Criterion	Inclusion	Exclusion
Population	Patients, health care workers/staff, burial teams, community members	

Concept	• Transmission of Ebola virus or Marburg virus (stratify by virus), including IPC measures to mitigate virus transmission
	• Direct Transmission
	  ○ Person-to-person contact
	  ○ Droplet spread
	• Indirect Transmission
	  ○ Aerosol transmission
	  ○ Vehicles [food/water, biologic products (e.g., blood), and fomites (e.g., linens, surfaces, surgical scalpels)
	  ○ Vector-borne transmission, zoonotic transmission
		• Transmission of other types of haemorrhagic fever viruses (e.g., Lassa fever)
		• Simulation studies using surrogate outcomes (e.g., fluorescent contamination) or viruses (e.g., Phi6, MS2)
		• Modelling studies

Context	Health care facilities, ETU, community No country-based restrictions, but will note the setting context (e.g., geography, country income level, areas with sub-optimal IPC measures)	
Other	None	