

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

KQ1 Work Exclusion- Initial Summary

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

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Question

Should health workers who have had Ebola Virus Disease (EVD) exposure other than high-risk be excluded versus not excluded from work?

- No studies specifically addressing this question were identified. Therefore, additional searches were completed to address a revised question to provide information on occupational risks of EVD acquisition and transmission that might help in decision-making about work exclusion.
- **Revised PICO Question:**
 - What is the risk of EVD acquisition with different types of occupational exposures?
 - If acquired, what is the risk of transmitting the virus?

Methods Summary

This is one of a series of rapid reviews that will answer 12 key questions related to three themes on infection prevention and control measures for filoviruses: (i) transmission/exposure (n=3 questions), (ii) personal protective equipment (PPE) (n=5), and (iii) decontamination and disinfection (n=4). Data sources include Medline, Embase, bio/medRxiv pre-print servers, Global Medicus Index, Epistemonikos, China National Knowledge Infrastructure (CNKI) and Wangfang database. We will use an automation tool (CAL® tool) for titles/abstracts screening for relevant systematic reviews and primary comparative studies. Full-text screening, data extraction, risk of bias assessment, and GRADE (Grading of Recommendations Assessment, Development and Evaluation) for the certainty of evidence will be completed independently by two reviewers with any disagreements resolved by consensus, with arbitration by a third reviewer, if needed. Results from included studies will be synthesized narratively by theme and key question and pooled via random effects meta-analysis when appropriate.

Initial findings relating to work exclusion

We present study characteristics in Table 1 and a summary of findings in Table 2 and Table 3.

Initially, 203 studies were screened in the CAL tool software and 32 studies were included for full-text screening. Of these 32 studies, none met the eligibility criteria for the primary question (Appendix 2). However, 4 studies were deemed to provide information on occupational risks of EVD acquisition and transmission and were included to address the revised question. To capture additional information related to vaccination status of healthcare workers, an additional 203 studies were reviewed in the CAL tool and 34 of these studies were included. Following full-text screening, an additional 2 studies were deemed relevant. A list of excluded studies with reasons for exclusion can be found in Appendix 1.

Table 1. Characteristics of Included Studies

Citation [Author, Year]	Funding Source	Country	Dates of Outbreak	Study Type	Virus Species	Setting	# Total Health Workers	Study Objectives [as reported by study authors]
Doshi, 2020, [Cross-sectional] ¹	Private research grant	Congo, DR	2014 outbreak	Serologic survey	Ebola	Individuals providing care to local populations in Boende	611	“To conduct a serosurvey in November 2015 among HCWs providing care in Boende to improve our understanding of EBOV transmission dynamics”
Dunn, 2016, [Cross-sectional] ²	Not reported	Sierra Leone	2014 outbreak	Contact-tracing/identifying occupational exposures	Ebola	Health facility	64	“To determine the compliance with personal protective equipment (PPE) usage of HCWs during the follow-up of patients with CCHF; HCWs worked on the wards or handled contaminated materials from these patients in the laboratory”
Gsell, 2017, [Cohort] ³	Private, not-for-profit, research grants	Guinea	2016	Ring Vaccination study (Prospective)	Ebola	Health facility	1510 participants (307 HWs)	“To evaluate the vaccine safety in different populations and examine the transmission dynamics at the level of the rings”
Hoff, 2019, [Cross-sectional] ⁴	Private grant making foundation funding	Congo, DR	2014 outbreak	Seroprevalence survey	Ebola	Health facility	565	“To determine seroprevalence against multiple EBOV antigens among HCWs of Boende Health Zone, Democratic Republic of the Congo, the site of a 2014 EBOV outbreak”

Hoff, 2019, [Cross-sectional] ⁵	Not reported	Congo, DR	Unclear	Serologic survey/Interview	Ebola	Health facility	250	“To conduct a serosurvey among formal and informal HCWs in the Boende health zone in Tshuapa District, DRC”
Samai, 2018, [RCT] ⁶	Not reported	Sierra Leone	2014 outbreak	Randomized, unblinded Phase 2 trial	Ebola	ETU or hospital	8651	“To describe safety results from STRIVE, the largest cohort vaccinated with rVSVΔG-ZEBOV-GP.”

Table 2. Summary of Findings: Exposure to high-risk activity^a vs. no exposure to high-risk activity

<i>Study details</i>	<i>Activity Exposure vs Non-Exposure</i>	<i>Outcome details</i>	<i>Exposed with outcome (n/N, %)</i>	<i>Non-exposed with outcome (n/N, %)</i>	<i>Summary Effect Measure</i>	<i>Quality Assessment^b</i>	<i>GRADE</i>	<i>Notes</i>
Incidence of EVD								
Doshi, 2020, [Cross-sectional] ¹	Washed a cadaver	Seroreactivity (GP > 2.5) to anti-EBOV glycoprotein IgG	NR	NR	1.28 (95% CI 0.13–12.76)	Moderate Risk of Bias	⊕○○○ Very low	None
Dunn, 2016, [Cross-sectional] ²	Performed\assisted in cesarean [No comparator]	PCR-confirmed EVD	0/3	N/A	N/A	Moderate Risk of Bias	⊕○○○ Very low	PPE used: Gown; short gloves (three pairs); mask; goggles; shoe covers
	Placed urinary catheter [No comparator]	PCR-confirmed EVD	0/1	N/A	N/A		⊕○○○ Very low	PPE used: Short gloves; gown
	Placed intravenous line [No comparator]	PCR-confirmed EVD	1/9 (11%)	N/A	N/A		⊕○○○ Very low	PPE used: Short gloves
	Blood draw [No comparator]	PCR-confirmed EVD	0/4	N/A	N/A		⊕○○○ Very low	PPE used: Gown; apron; short gloves (2 pairs); mask
	Discontinued intravenous line [No comparator]	PCR-confirmed EVD	0/1	N/A	N/A		⊕○○○ Very low	PPE used: Short gloves
Gsell, 2017, [Cohort] ³	High-risk contact [No comparator]	Secondary cases of EVD	0/239 ^c	N/A	N/A	Low Risk of Bias	⊕○○○ Very low	All HCWs received the

<i>Study details</i>	<i>Activity Exposure vs Non-Exposure</i>	<i>Outcome details</i>	<i>Exposed with outcome (n/N, %)</i>	<i>Non-exposed with outcome (n/N, %)</i>	<i>Summary Effect Measure</i>	<i>Quality Assessment^b</i>	<i>GRADE</i>	<i>Notes</i>
								rVSV-ZEBOV vaccine. The median delay from confirmation of index case to vaccination of individuals in the ring ranged from 2-10 days over the outbreak.
Samai, 2018, [RCT] ⁶	High perceived risk of Ebola infection [No comparator]	Laboratory-confirmed EVD	0 /2995	N/A	N/A	Moderate Risk of Bias	⊕○○○ Very low	Unvaccinated HWs
	High perceived risk of Ebola infection [No comparator]	Laboratory-confirmed EVD	0/2811	N/A	N/A		⊕○○○ Very low	HWs vaccinated with VSVΔG-ZEBOV-GP
	High perceived risk of Ebola infection [No comparator]	Laboratory-confirmed EVD	0/927	N/A	N/A		⊕○○○ Very low	Crossover vaccinated (deferred)

- a. Activity risk classifications were based on the list provided by the WHO (see Appendix 2).
- b. Quality assessment of studies was completed using the ROBINS-I scale for observational studies. Scores from 7-9 were considered to be high quality (low risk of bias), scores of 4-6 of moderate quality (moderate risk of bias) and scores of 0-3 of low quality (high risk of bias). RCTs were assessed using the Cochrane ROB-2 tool.
- c. Population consisted of 632 vaccinated individuals, 91 of these were frontline workers.

Table 3. Summary of Findings: Exposure to low or medium-risk activity^a vs. no exposure to low or medium-risk activity

<i>Study details</i>	<i>Activity Exposure vs Non-Exposure</i>	<i>Outcome details</i>	<i>Exposed with outcome (n/N)</i>	<i>Non-exposed with outcome (n/N)</i>	<i>Summary Effect Measure</i>	<i>Quality Assessment^b</i>	<i>GRADE</i>	<i>Notes</i>
<i>Incidence of EVD</i>								
Doshi, 2020, [Cross-sectional] ¹	Been in the patient's room vs. Not exposed	Seroreactivity (GP > 2.5) to anti-EBOV glycoprotein IgG	NR	NR	0.79 (95% CI 0.22–2.83)	Moderate Risk of Bias	⊕○○○ Very low	None
	Performed examinations (clinical or laboratory) vs. Not exposed	Seroreactivity (GP > 2.5) to anti-EBOV glycoprotein IgG	NR	NR	0.86 (95% CI 0.17–4.44)		⊕○○○ Very low	
	Given food to a patient vs. Not exposed	Seroreactivity (GP > 2.5) to anti-EBOV glycoprotein IgG	NR	NR	1.13 (95% CI 0.32–3.99)		⊕○○○ Very low	
	Conversed with a patient vs. Not exposed	Seroreactivity (GP > 2.5) to anti-EBOV glycoprotein IgG	NR	NR	3.80 (95% CI 0.73–19.83)		⊕○○○ Very low	
	Washed the patient's clothes vs. Not exposed	Seroreactivity (GP > 2.5) to anti-EBOV glycoprotein IgG	NR	NR	0.99 (95% CI 0.10–10.41)		⊕○○○ Very low	
	Had contact with patient's bodily fluids	Seroreactivity (GP > 2.5) to	NR	NR	2.39 (95% CI 0.79–7.30)		⊕○○○ Very low	

	vs. Not exposed	anti-EBOV glycoprotein IgG						
	Cleaned patient's room vs. Not exposed	Seroreactivity (GP > 2.5) to anti-EBOV glycoprotein IgG	NR	NR	1.40 (95% CI 0.34–5.83)		⊕○○○ Very low	
Dunn, 2016, [Cross-sectional] ²	Shared ward\latrine [No comparator]	PCR-confirmed EVD	3/15 (20%)	N/A	N/A	Moderate Risk of Bias	⊕○○○ Very low	PPE used: None
	Took vital signs [No comparator]	PCR-confirmed EVD	0/16	N/A	N/A		⊕○○○ Very low	PPE used: Short gloves
	Cleaned linens [No comparator]	PCR-confirmed EVD	1/2 (50%)	N/A	N/A		⊕○○○ Very low	PPE used: Short gloves
	Cleaned body fluids [No comparator]	PCR-confirmed EVD	1/4 (25%)	N/A	N/A		⊕○○○ Very low	PPE used: Short gloves
	Cleaned body fluids [No comparator]	PCR-confirmed EVD	1/1 (100%)	N/A	N/A		⊕○○○ Very low	PPE used: None
	Cleaned surfaces: floor, walls, bed [No comparator]	PCR-confirmed EVD	0/3	N/A	N/A		⊕○○○ Very low	PPE used: Gown; apron; short gloves (2 pairs); mask
	Cleaned surgical instruments [No comparator]	PCR-confirmed EVD	0/1	N/A	N/A		⊕○○○ Very low	PPE used: Short gloves

	Moved patient [No comparator]	PCR-confirmed EVD	1/4 (25%)	N/A	N/A			PPE used: Short gloves
	Gave intravenous medications [No comparator]	PCR-confirmed EVD	0/15	N/A	N/A		⊕○○○ Very low	PPE used: Short gloves: gown
	Gave intramuscular medications [No comparator]	PCR-confirmed EVD	0/1	N/A	N/A		⊕○○○ Very low	PPE used: Short gloves
	Changed surgical site dressing [No comparator]	PCR-confirmed EVD	0/3	N/A	N/A		⊕○○○ Very low	PPE used: Short gloves: gown
	General touching patient [No comparator]	PCR-confirmed EVD	0/5	N/A	N/A		⊕○○○ Very low	PPE used: Short gloves
	General touching patient [No comparator]	PCR-confirmed EVD	2/4 (50%)	N/A	N/A		⊕○○○ Very low	PPE used: None
Gsell, 2017, [Cohort] ³	Non-high-risk contact [No comparator]	Secondary cases of EVD	0/237 ^c	N/A	N/A	Low Risk of Bias	⊕○○○ Very low	All HCWs received the rVSV-ZEBOV vaccine. The median delay from confirmation

								of index case to vaccination of individuals in the ring ranged from 2-10 days over the outbreak.
Hoff, 2019, [Cross-sectional] ⁴	Direct contact with patients [No comparator]	Glycoprotein reactivity as >2.5 units/mL	57/279 (20%)	N/A	N/A	Moderate Risk of Bias	⊕○○○ Very low	None
	Indirect contact with patients [No comparator]	Glycoprotein reactivity as >2.5 units/mL	29/177 (16%)	N/A	N/A		⊕○○○ Very low	None
Hoff, 2019, [Cross-sectional] ⁵	Direct contact with patients [No comparator]	Seropositivity to anti-EBOV glycoprotein Ig	38/113 (34%)	N/A	N/A	High Risk of Bias	⊕○○○ Very low	None
	Indirect contact with patients [No comparator]	Seropositivity to anti-EBOV glycoprotein Ig	7/18 (39%)	N/A	N/A		⊕○○○ Very low	None
	Limited contact with patients [No comparator]	Seropositivity to anti-EBOV glycoprotein Ig	3/7 (43%)	N/A	N/A		⊕○○○ Very low	None
Samai, 2018, [RCT] ⁶	Average perceived risk of Ebola infection [No comparator]	Laboratory-confirmed EVD	0/773	N/A	N/A	Moderate Risk of Bias	⊕○○○ Very low	Unvaccinated HWs

	Average perceived risk of Ebola infection [No comparator]	Laboratory-confirmed EVD	0/760	N/A	N/A		⊕○○○ Very low	HWs vaccinated with VSVΔG-ZEBOV-GP
	Average perceived risk of Ebola infection [No comparator]	Laboratory-confirmed EVD	0/724	N/A	N/A		⊕○○○ Very low	Crossover vaccinated (deferred)
	Low perceived risk of Ebola infection [No comparator]	Laboratory-confirmed EVD	0/705	N/A	N/A		⊕○○○ Very low	Unvaccinated HWs
	Low perceived risk of Ebola infection [No comparator]	Laboratory-confirmed EVD	0/606	N/A	N/A		⊕○○○ Very low	HWs vaccinated with VSVΔG-ZEBOV-GP
	Low perceived risk of Ebola infection [No comparator]	Laboratory-confirmed EVD	0/2170	N/A	N/A		⊕○○○ Very low	Crossover vaccinated (deferred)

- a. Activity risk classifications were based on the list provided by the WHO (see Appendix 2).
- b. Quality assessment of studies was completed using the ROBINS-I scale for observational studies. Scores from 7-9 were considered to be high quality (low risk of bias), scores of 4-6 of moderate quality (moderate risk of bias) and scores of 0-3 of low quality (high risk of bias). RCTs were assessed using the Cochrane ROB-2 tool.
- c. Population consisted of 632 vaccinated individuals, 91 of these were frontline workers.

Citations:

1. Doshi RH, Hoff NA, Bratcher A, et al. Risk Factors for Ebola Exposure in Health Care Workers in Boende, Tshuapa Province, Democratic Republic of the Congo. *J Infect Dis.* Published online 2020;jiaa747. doi:10.1093/infdis/jiaa747
2. Dunn AC, Walker TA, Redd J, et al. Nosocomial transmission of Ebola virus disease on pediatric and maternity wards: Bombali and Tonkolili, Sierra Leone, 2014. *Am J Infect Control.* 2016;44(3):269-272. doi:10.1016/j.ajic.2015.09.016
3. Gsell PS, Camacho A, Kucharski AJ, et al. Ring vaccination with rVSV-ZEBOV under expanded access in response to an outbreak of Ebola virus disease in Guinea, 2016: an operational and vaccine safety report. *Lancet Infect Dis.* 2017;17(12):1276-1284. doi:10.1016/S1473-3099(17)30541-8
4. Hoff NA, Mukadi P, Doshi RH, et al. Serologic Markers for Ebolavirus Among Healthcare Workers in the Democratic Republic of the Congo. *J Infect Dis.* 2019;219(4):517-525. doi:10.1093/infdis/jiy499
5. Hoff NA, Mukadi P, Mukadi D, et al. Seroprevalence of ebola virus among health care workers in yambuku health zone Democratic Republic of Congo. *Am J Trop Med Hyg.* Published online 2019.
6. Samai M, Seward JF, Goldstein ST, et al. The Sierra Leone Trial to Introduce a Vaccine Against Ebola: An Evaluation of rVSVΔG-ZEBOV-GP Vaccine Tolerability and Safety During the West Africa Ebola Outbreak. *J Infect Dis.* 2018;217(suppl_1):S6-S15. doi:10.1093/infdis/jiy020

Appendix 1. Excluded Studies List – By Reason for Exclusion:

Does not provide risk of infection for HCWs for activities of interest (see Appendix 2)

Borchert M, Mulangu S, Lefèvre P, et al. Use of Protective Gear and the Occurrence of Occupational Marburg Hemorrhagic Fever in Health Workers from Watsa Health Zone, Democratic Republic of the Congo. *J Infect Dis.* 2007;196(s2):S168-S175. doi:10.1086/520540

Carnino L, Vetter P, Peyraud N, et al. Feasibility and safety of rVSV-ZEBOV vaccination of humanitarian health workers against Ebola virus disease: an observational study. *Journal of Travel Medicine.* 2021;28(8):taab086. doi:10.1093/jtm/taab086

Gozel MG, Dokmetas I, Oztop AY, Engin A, Elaldi N, Bakir M. Recommended precaution procedures protect healthcare workers from Crimean-Congo hemorrhagic fever virus. *Int J Infect Dis.* 2013;17(11):e1046-e1050. doi:10.1016/j.ijid.2013.05.005

Grinnell M, Dixon MG, Patton M, et al. Ebola Virus Disease in Health Care Workers — Guinea, 2014. *MMWR Morb Mortal Wkly Rep.* 2015;64(38):1083-1087. doi:10.15585/mmwr.mm6438a1

Hoff NA, Mwanza A, Doshi RH, et al. Possible high exposure to ebola among non-formal health care providers in a previous outbreak site boende democratic republic of congo. *J Infect Dis.* 2016;219:517-525.

Juan-Giner A, Tchaton M, Jemmy JP, et al. Safety of the rVSV ZEBOV vaccine against Ebola Zaire among frontline workers in Guinea. *Vaccine.* 2019;37(48):7171-7177. doi:10.1016/j.vaccine.2018.09.009

López MA, Amela C, Ordobas M, et al. First secondary case of Ebola outside Africa: epidemiological characteristics and contact monitoring, Spain, September to November 2014. *Eurosurveillance.* 2015;20(1). doi:10.2807/1560-7917.ES2015.20.1.21003

Matanock A, Arwady MA, Ayscue P, et al. Ebola Virus Disease Cases Among Health Care Workers Not Working in Ebola Treatment Units — Liberia, June–August, 2014. *2014;63(46):5.*

Tomori O, Bertolli J, Rollin PE, et al. Serologic Survey among Hospital and Health Center Workers during the Ebola Hemorrhagic Fever Outbreak in Kikwit, Democratic Republic of the Congo, 1995. *J Infect Dis.* 1999;179(s1):S98-S101. doi:10.1086/514307

Case Report

Günther S, Feldmann H, Geisbert TW, et al. Management of Accidental Exposure to Ebola Virus in the Biosafety Level 4 Laboratory, Hamburg, Germany. *The Journal of Infectious Diseases.* 2011;204(suppl_3):S785-S790. doi:10.1093/infdis/jir298

Jacobs M, Aarons E, Bhagani S, et al. Post-exposure prophylaxis against Ebola virus disease with experimental antiviral agents: a case-series of health-care workers. *The Lancet Infectious Diseases.* 2015;15(11):1300-1304. doi:10.1016/S1473-3099(15)00228-5

Lai L, Davey R, Beck A, et al. Emergency Postexposure Vaccination With Vesicular Stomatitis Virus–Vectored Ebola Vaccine After Needlestick. *JAMA*. 2015;313(12):1249. doi:10.1001/jama.2015.1995

Wong KK, Davey RT, Hewlett AL, et al. Use of Postexposure Prophylaxis After Occupational Exposure to Zaire ebolavirus. *Clin Infect Dis*. 2016;63(3):376-379. doi:10.1093/cid/ciw256

Not about EVD or Marburg

Ergönül Ö, Keske Ş, Çeldir MG, et al. Systematic Review and Meta-analysis of Postexposure Prophylaxis for Crimean-Congo Hemorrhagic Fever Virus among Healthcare Workers. *Emerg Infect Dis*. 2018;24(9):1642-1648. doi:10.3201/eid2409.171709

Ergonul O, Zeller H, Celikbas A, Dokuzoguz B. The lack of Crimean-Congo hemorrhagic fever virus antibodies in healthcare workers in an endemic region. *International Journal of Infectious Diseases*. 2007;11(1):48-51. doi:10.1016/j.ijid.2005.10.009

Güven G, Talan L, Altıntaş ND, Memikoglu KO, Yoruk F, Azap A. An Unexpected Fatal CCHF Case and Management of Exposed Health Care Workers. *International Journal of Infectious Diseases*. 2017;55:118-121. doi:10.1016/j.ijid.2016.12.026

Maltezou HC, Maltezos E, Papa A. Contact tracing and serosurvey among healthcare workers exposed to Crimean-Congo haemorrhagic fever in Greece. *Scandinavian Journal of Infectious Diseases*. 2009;41(11-12):877-880. doi:10.3109/00365540903173619

Pshenichnaya NY, Nenadskaya SA. Probable Crimean-Congo hemorrhagic fever virus transmission occurred after aerosol-generating medical procedures in Russia: nosocomial cluster. *International Journal of Infectious Diseases*. 2015;33:120-122. doi:10.1016/j.ijid.2014.12.047

Study does not provide details on the exposure

Adedire EB, Fatiregun A, Olayinka A, Sabitu K, Nguku P. Descriptive epidemiology of the EBOLA virus disease outbreak in Nigeria July to September 2014. 2015; *Am J Trop Med Hygiene*.

Bausch DG. The Year That Ebola Virus Took Over West Africa: Missed Opportunities for Prevention. *The American Journal of Tropical Medicine and Hygiene*. 2015;92(2):229-232. doi:10.4269/ajtmh.14-0818

Doshi RH, Hoff NA, Mukadi P, et al. Seroprevalence of ebola virus among health care workers in the Tshuapa district democratic republic of congo. *Am J Tropic Med Hygiene*. Published online 2016.

Mba S, Ukponu W, Saleh M, et al. Lassa fever infection among health care workers in Nigeria, 2019. *International Journal of Infectious Diseases*. 2020;101:279. doi:10.1016/j.ijid.2020.09.731

Study does not provide risk of infection by exposure

Calkin S. British ebola nurse's African colleague dies of the virus. *Nursing Times*. 2014;110(38).

Chevalier MS, Chung W, Smith J, et al. Ebola Virus Disease Cluster in the United States — Dallas County, Texas, 2014. :2.

Chung WM, Smith JC, Weil LM, 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):164-173. doi:10.7326/M15-0968

Clausen, L, Bothwell TH, Isaacson M, et al. Isolation and Handling of Patients with Dangerous Infectious Disease. *S Afr med J*. 1978;53(238):5.

Gear JSS, Cassel GA, Gear AJ, et al. Outbreak of Marburg virus disease in Johannesburg. *BRITISH MEDICAL JOURNAL*. Published online 1975:5.

Grinnell M, Dixon MG, Patton M, et al. Ebola Virus Disease in Health Care Workers — Guinea, 2014. *MMWR Morb Mortal Wkly Rep*. 2015;64(38):1083-1087. doi:10.15585/mmwr.mm6438a1

Kilmarx PH, Clarke KR, Dietz PM, et al. Ebola Virus Disease in Health Care Workers — Sierra Leone, 2014. 2014;63(49):4.

Musene KK, Hoff NA, Spencer D, et al. Occupational exposure of health care workers in Kinshasa Democratic Republic of the Congo. *Am J Trop Med Hygiene*. Published online 2018.

Nyenswah T, Fallah M, Sieh S, et al. Controlling the last known cluster of Ebola virus disease - Liberia, January-February 2015. *MMWR Morb Mortal Wkly Rep*. 2015;64(18):500-504.

Olu O, Kargbo B, Kamara S, et al. Epidemiology of Ebola virus disease transmission among health care workers in Sierra Leone, May to December 2014: a retrospective descriptive study. *BMC Infect Dis*. 2015;15(1):416. doi:10.1186/s12879-015-1166-7

Report of a WHO/International Study Team. Ebola haemorrhagic fever in Sudan, 1976. Report of a WHO/International Study Team. *Bull World Health Organ*. 1978;56(2):247-270.

Report of an International Commission. Ebola haemorrhagic fever in Zaire, 1976. *Bull World Health Organ*. 1978;56(2):271-293.

Senga M, Pringle K, Brett-Major D, et al. Largest documented cluster of ebola virus disease among health workers. Published online 2015.

Senga M, Pringle K, Ramsay A, et al. Factors Underlying Ebola Virus Infection Among Health Workers, Kenema, Sierra Leone, 2014–2015. *Clin Infect Dis*. 2016;63(4):454-459. doi:10.1093/cid/ciw327

No data from health workers

Bolay FK, Grandits G, Lane HC, et al. PREVAIL I Cluster Vaccination Study With rVSVΔG-ZEBOV-GP as Part of a Public Health Response in Liberia. *The Journal of Infectious Diseases*. 2019;219(10):1634-1641. doi:10.1093/infdis/jiy698

Davis C, Tipton T, Sabir S, et al. Postexposure Prophylaxis With rVSV-ZEBOV Following Exposure to a Patient With Ebola Virus Disease Relapse in the United Kingdom: An Operational, Safety, and Immunogenicity Report. *Clinical Infectious Diseases*. 2020;71(11):2872-2879. doi:10.1093/cid/ciz1165

Henao-Restrepo AM, Camacho A, Longini IM, et al. Efficacy and effectiveness of an rVSV-vectored vaccine in preventing Ebola virus disease: final results from the Guinea ring vaccination, open-label, cluster-randomised trial (Ebola Ça Suffit!). *The Lancet*. 2017;389(10068):505-518. doi:10.1016/S0140-6736(16)32621-6

Henao-Restrepo AM, Longini IM, Egger M, et al. Efficacy and effectiveness of an rVSV-vectored vaccine expressing Ebola surface glycoprotein: interim results from the Guinea ring vaccination cluster-randomised trial. *The Lancet*. 2015;386(9996):857-866. doi:10.1016/S0140-6736(15)61117-5

Hoff NA, Bratcher A, Kelly JD, et al. Immunogenicity of rVSVΔG-ZEBOV-GP Ebola vaccination in exposed and potentially exposed persons in the Democratic Republic of the Congo. *Proc Natl Acad Sci USA*. 2022;119(6):e2118895119. doi:10.1073/pnas.2118895119

Kennedy SB, Bolay F, Kieh M, et al. Phase 2 Placebo-Controlled Trial of Two Vaccines to Prevent Ebola in Liberia. *N Engl J Med*. 2017;377(15):1438-1447. doi:10.1056/NEJMoa1614067

Olugbade OT, Israel O, Fadahunsi R, Ogunniyi A, Oladimeji A, Olayinka A. Outbreak of lassa fever in a healthcare setting : Epidemiologic surveillance and risk stratification for contact persons-Saki Oyo State Nigeria 2014. *Antimicrob Resist Infect Contr*. Published online 2017.

Xie Z. Data Fitting and Scenario Analysis of Vaccination in the 2014 Ebola Outbreak in Liberia. *Osong Public Health and Research Perspectives*. 2019;10(3):187–201.

Duplicate reference, included

Borchert M, Mulangu S, Lefèvre P, et al. Use of Protective Gear and the Occurrence of Occupational Marburg Hemorrhagic Fever in Health Workers from Watsa Health Zone, Democratic Republic of the Congo. *J INFECT DIS*. 2007;196(s2):S168-S175. doi:10.1086/520540

Modelling Data Only

Ajelli M, Merler S, Fumanelli L, et al. Spatiotemporal dynamics of the Ebola epidemic in Guinea and implications for vaccination and disease elimination: a computational modeling analysis. *BMC Med*. 2016;14(1):130. doi:10.1186/s12916-016-0678-3

Bodine EN, Cook C, Shorten M. The potential impact of a prophylactic vaccine for Ebola in Sierra Leone. *MBE*. 2017;15(2):337-359. doi:10.3934/mbe.2018015

Chen P, Fan W, Guo X. A hybrid simulation model to study the impact of combined interventions on Ebola epidemic. Siettos C, ed. PLoS ONE. 2021;16(7):e0254044. doi:10.1371/journal.pone.0254044

Coltart CEM, Johnson AM, Whitty CJM. Role of healthcare workers in early epidemic spread of Ebola: policy implications of prophylactic compared to reactive vaccination policy in outbreak prevention and control. BMC Med. 2015;13(1):271. doi:10.1186/s12916-015-0477-2

Jones-Konneh TEC, Suda T, Sasaki H, Egawa S. Agent-Based Modeling and Simulation of Nosocomial Infection among Healthcare Workers during Ebola Virus Disease Outbreak in Sierra Leone. Tohoku J Exp Med. 2018;245(4):231-238. doi:10.1620/tjem.245.231

Merler S, Ajelli M, Fumanelli L, et al. Containing Ebola at the Source with Ring Vaccination. Bottomley C, ed. PLoS Negl Trop Dis. 2016;10(11):e0005093. doi:10.1371/journal.pntd.0005093
Potluri R, Kumar A, Maheshwari V, et al. Impact of prophylactic vaccination strategies on Ebola virus transmission: A modeling analysis. Sahoo MK, ed. PLoS ONE. 2020;15(4):e0230406. doi:10.1371/journal.pone.0230406

Robert A, Camacho A, Edmunds WJ, et al. Control of Ebola virus disease outbreaks: Comparison of health care worker-targeted and community vaccination strategies. Epidemics. 2019;27:106-114. doi:10.1016/j.epidem.2019.03.001

Wells CR, Pandey A, Ndeffo Mbah ML, et al. The exacerbation of Ebola outbreaks by conflict in the Democratic Republic of the Congo. Proc Natl Acad Sci USA. 2019;116(48):24366-24372. doi:10.1073/pnas.1913980116

Wells CR, Pandey A, Parpia AS, et al. Ebola vaccination in the Democratic Republic of the Congo. Proc Natl Acad Sci USA. 2019;116(20):10178-10183. doi:10.1073/pnas.1817329116

Wells C, Yamin D, Ndeffo-Mbah ML, et al. Harnessing Case Isolation and Ring Vaccination to Control Ebola. Bausch DG, ed. PLoS Negl Trop Dis. 2015;9(5):e0003794. doi:10.1371/journal.pntd.0003794

Unavailable Full-text

Massy N, Boulay C, Andriamanantena D, Ficko C, Chartier C. One-year cumulative safety review of adverse effects reported after vaccination with Ervebo (rVSV-ZEBOV) in French volunteer professionals leaving for Ebola virus disease (EVD) epidemic areas in Democratic Republic of Congo (DRC).

Mukadi PK, Hoff NA, Mukadi D, et al. Serologic profiling of the humoral immune response to ebola virus minimally or asymptotically infected subjects.

Non-English

Adachi T, Komiya N, Kato Y. Ebola Virus Disease Outbreak Response in West Africa.
Kansenshogaku Zasshi. 2015;89(2):223-229. doi:doi: 10.11150/kansenshogakuzasshi.89.223.

Appendix 2. Eligibility Criteria

Question (1): Should health workers who have had EVD or Marburg exposure other than high-risk be excluded versus not excluded from work?

Background: 1) What is the risk of EVD acquisition with different types of occupational exposures?

2) If acquired, what is the risk of transmitting the virus?

Setting	Health care facilities, ETU, <i>community</i>
Population	<p>Staff working in health care facilities, ETU</p> <p>Sub-groups:</p> <p>High risk patient care activity Broken skin or mucous membrane contact with a patient with Ebola virus disease (alive or deceased) or their bodily fluids:</p> <ul style="list-style-type: none"> • Bodily fluid in direct contact with mucous membrane (e.g. eyes, nose or mouth) • Penetrating sharps injury from used device or through contaminate • Performed finger prick • Put in IV • Delivered babies • Performed invasive procedure • Performed major surgery • Performed autopsy • Drew blood • Cleaned blood spill • Controlled bleeding • Performed minor surgery • Moved dead bodies • Cleaned or disinfected latrines <p>Intermediate risk patient care activities (intact-skin-only contact with a patient with Ebola virus disease or their body fluids):d</p> <ul style="list-style-type: none"> • Clinical assessment of an individual with suspected Ebola virus disease before diagnosis without appropriate personal protective equipment (PPE)Close contact with a patient, body or body fluid, linen or clothes of an infected patient/person • Bathes or cleaned patients • Gave injection • Handled urinary catheter • Contact with contaminated surfaces • Recapped needle

	<ul style="list-style-type: none"> • Handled IV line (e.g., gave IV medications) • Handled waste • Handled linen or clothes or mattresses <p>Low risk patient care activities (No direct contact with a patient with Ebola virus disease or their body fluids):</p> <ul style="list-style-type: none"> • Living in the same house as a patient with Ebola virus disease but no direct contact with their bodily fluids) • Breach of personal protective equipment (PPE) without risk of contamination • Provided general patient care (took vital signs, examined patients, moved patients) • Fed patients or administered oral medications • Discarded sharps (appropriately) • Cleaned patient room or ward Living in same house as a patient with EVD but no direct contact with their body fluids • Moved/ transported patients
Background interventions (Standard of care)	Continue with normal duties (no work exclusion)
Intervention	Continue with normal duties (no work exclusion)
Comparator(s)	Exclude from work for 21 days
Outcome	<p>Infection with Ebola or Marburg virus, <i>health-care associated transmission of Ebola</i></p> <p>Indirect evidence: Lassa fever</p>
Potential effect modifiers	<p>Impact of vaccination status on post exposure actions <i>Community exposures during exclusion period, type of exposure, vaccination</i></p>

Appendix 3. GRADE Assessment (High Risk Exposures)

<i>Number of studies</i>	<i>Study Design</i>	<i>Risk of Bias^a</i>	<i>Inconsistency</i>	<i>Indirectness</i>	<i>Imprecision</i>	<i>Other Considerations</i>	<i>Quality</i>
Incidence of EVD							
Washed a cadaver [No comparator]							
1 ¹	[Cross-sectional]	Serious ^b	No serious ^c	Serious ^d	Serious ^e	None	⊕○○○ Very low
Performed\assisted in cesarean [No comparator]							
1 ²	[Cross-sectional]	Serious ^f	No serious ^c	Serious ^d	Very Serious ^g	None	⊕○○○ Very low
Placed urinary catheter [No comparator]							
1 ²	[Cross-sectional]	Serious ^f	No serious ^c	Serious ^d	Very Serious ^g	None	⊕○○○ Very low
Placed intravenous line [No comparator]							
1 ²	[Cross-sectional]	Serious ^f	No serious ^c	Serious ^d	Very Serious ^g	None	⊕○○○ Very low
Blood draw [No comparator]							
1 ²	[Cross-sectional]	Serious ^f	No serious ^c	Serious ^d	Very Serious ^g	None	⊕○○○ Very low
Discontinued intravenous line [No comparator]							
1 ²	[Cross-sectional]	Serious ^f	No serious ^c	Serious ^d	Very Serious ^g	None	⊕○○○ Very low
High-risk contact [No comparator]							
1 ³	[Cohort]	Not Serious ^h	No serious ^c	Serious ^d	Very Serious ^g	None	⊕○○○ Very low
High perceived risk of Ebola infection [No comparator]							
1 ⁶	[RCT]	Serious ⁱ	No serious ^c	Serious ^d	Very Serious ^g	None	⊕○○○ Very low

- d. Individual quality assessment of studies was completed using the ROBINS-I scale for observational studies. Scores from 7-9 were considered to be high quality (low risk of bias), scores of 4-6 of moderate quality (moderate risk of bias) and scores of 0-3 of low quality (high risk of bias).
- e. 5/9 on NOS; downrated for lack of controls, no reporting on non-response rate.
- f. No inconsistency as only one study evaluated.

- g. Downrated by 1 for failure to provide information on PICO intervention of work exclusion for 21 days.
- h. Downrated by 1 as CI crosses null + appreciable benefit or harm.
- i. 6/9 on NOS; downrated for lack of non-exposed cohort, failure to adjust for key confounders.
- j. Downrated by 2 as very few or no events, and no relative effects reported.
- k. 7/9 on NOS; downrated for failure to adjust for confounders.
- l. Some concerns of risk of bias assessed using Cochrane ROB-2.

Appendix 4. GRADE Assessment (Low or Medium Risk Exposures)

<i>Number of studies</i>	<i>Study Design</i>	<i>Risk of Bias^a</i>	<i>Inconsistency</i>	<i>Indirectness</i>	<i>Imprecision</i>	<i>Other Considerations</i>	<i>Quality</i>
Incidence of EVD							
Been in the patient's room [No comparator]							
1 ¹	[Cross-sectional]	Serious ^b	No serious ^c	Serious ^d	Serious ^e	None	⊕○○○ Very low
Performed examinations (clinical or laboratory) [No comparator]							
1 ¹	[Cross-sectional]	Serious ^b	No serious ^c	Serious ^d	Serious ^e	None	⊕○○○ Very low
Given food to a patient [No comparator]							
1 ¹	[Cross-sectional]	Serious ^b	No serious ^c	Serious ^d	Serious ^e	None	⊕○○○ Very low
Conversed with a patient [No comparator]							
1 ¹	[Cross-sectional]	Serious ^b	No serious ^c	Serious ^d	Serious ^e	None	⊕○○○ Very low
Washed the patient's clothes [No comparator]							
1 ¹	[Cross-sectional]	Serious ^b	No serious ^c	Serious ^d	Serious ^e	None	⊕○○○ Very low
Had contact with patient's bodily fluids [No comparator]							
1 ¹	[Cross-sectional]	Serious ^b	No serious ^c	Serious ^d	Serious ^e	None	⊕○○○ Very low
Shared ward/latrine [No comparator]							
1 ²	[Cross-sectional]	Serious ^f	No serious ^c	Serious ^d	Very Serious ^g	None	⊕○○○ Very low
Took vital signs [No comparator]							
1 ²	[Cross-sectional]	Serious ^f	No serious ^c	Serious ^d	Very Serious ^g	None	⊕○○○ Very low
Cleaned linens [No comparator]							
1 ²	[Cross-sectional]	Serious ^f	No serious ^c	Serious ^d	Very Serious ^g	None	⊕○○○ Very low
Cleaned body fluids [No comparator]							

<i>Number of studies</i>	<i>Study Design</i>	<i>Risk of Bias^a</i>	<i>Inconsistency</i>	<i>Indirectness</i>	<i>Imprecision</i>	<i>Other Considerations</i>	<i>Quality</i>
1 ²	[Cross-sectional]	Serious ^f	No serious ^c	Serious ^d	Very Serious ^g	None	⊕○○○ Very low
Cleaned body fluids [No comparator]							
1 ²	[Cross-sectional]	Serious ^f	No serious ^c	Serious ^d	Very Serious ^g	None	⊕○○○ Very low
Cleaned surfaces: floor, walls, bed [No comparator]							
1 ²	[Cross-sectional]	Serious ^f	No serious ^c	Serious ^d	Very Serious ^g	None	⊕○○○ Very low
Cleaned surgical instruments [No comparator]							
1 ²	[Cross-sectional]	Serious ^f	No serious ^c	Serious ^d	Very Serious ^g	None	⊕○○○ Very low
Moved patient [No comparator]							
1 ²	[Cross-sectional]	Serious ^f	No serious ^c	Serious ^d	Very Serious ^g	None	⊕○○○ Very low
Gave intravenous medications [No comparator]							
1 ²	[Cross-sectional]	Serious ^f	No serious ^c	Serious ^d	Very Serious ^g	None	⊕○○○ Very low
Gave intramuscular medications [No comparator]							
1 ²	[Cross-sectional]	Serious ^f	No serious ^c	Serious ^d	Very Serious ^g	None	⊕○○○ Very low
Changed surgical site dressing [No comparator]							
1 ²	[Cross-sectional]	Serious ^f	No serious ^c	Serious ^d	Very Serious ^g	None	⊕○○○ Very low
General touching patient [No comparator]							
1 ²	[Cross-sectional]	Serious ^f	No serious ^c	Serious ^d	Very Serious ^g	None	⊕○○○ Very low
Non-high-risk contact [No comparator]							
1 ³	[Cohort]	Not Serious ^h	No serious ^c	Serious ^d	Very Serious ^g	None	⊕○○○ Very low
Direct contact with patients [No comparator]							

<i>Number of studies</i>	<i>Study Design</i>	<i>Risk of Bias^a</i>	<i>Inconsistency</i>	<i>Indirectness</i>	<i>Imprecision</i>	<i>Other Considerations</i>	<i>Quality</i>
2 ⁴⁵	[Cross-sectional]	Serious ⁱ	No serious ^j	Serious ^d	Serious ^k	None	⊕○○○ Very low
Indirect contact with patients [No comparator]							
2 ⁴⁵	[Cross-sectional]	Serious ⁱ	No serious ^j	Serious ^d	Serious ^k	None	⊕○○○ Very low
Limited contact with patients [No comparator]							
1 ⁵	[Cross-sectional]	Very Serious ^l	No serious ^c	Serious ^d	Serious ^k	None	⊕○○○ Very low
Average perceived risk of Ebola infection [No comparator]							
1 ⁶	[RCT]	Serious ^m	No serious ^c	Serious ^d	Very Serious ^g	None	⊕○○○ Very low
Low perceived risk of Ebola infection [No comparator]							
1 ⁶	[RCT]	Serious ^m	No serious ^c	Serious ^d	Very Serious ^g	None	⊕○○○ Very low

- a. Individual quality assessment of studies was completed using the ROBINS-I scale for observational studies. Scores from 7-9 were considered to be high quality (low risk of bias), scores of 4-6 of moderate quality (moderate risk of bias) and scores of 0-3 of low quality (high risk of bias).
- b. 5/9 on NOS; downrated for lack of controls, no reporting on non-response rate.
- c. No inconsistency as only one study evaluated.
- d. Downrated by 1 for failure to provide information on PICO intervention of work exclusion for 21 days.
- e. Downrated by 1 as CI crosses null + appreciable benefit or harm.
- f. 6/9 on NOS; downrated for lack of non-exposed cohort, failure to adjust for key confounders.
- g. Downrated by 2 as very few or no events and no relative effects reported.
- h. 7/9 on NOS; downrated for failure to adjust for confounders.
- i. Both studies rated “serious” to “very serious” risk of bias on NOS.
- j. No inconsistency; rates are similar across both studies.
- k. Downrated by 1 due to small sample size; unable to evaluate relative effects.
- l. 3/9 on NOS; Downrated for lack of controls, failure to adjust for confounders and no reporting on non-response rate.
- m. Some concerns of risk of bias assessed using Cochrane ROB-2.