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

KQ10 Spraying vs. Wiping of Health Care Workers- Initial Summary

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Nicole Shaver, nicole.shaver@uottawa.ca, Knowledge Synthesis and Application Unit, School of Epidemiology and Public Health, Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada. ORCID 0000-0003-3210-8895

Ba' Pham, ba.pham@theta.utoronto.ca, Li Ka Shing Knowledge Institute, St. Michael's Hospital, Unity Health Toronto, Toronto, Ontario, Canada

Alexandria Bennett, d.bennett@uottawa.ca, Knowledge Synthesis and Application Unit, School of Epidemiology and Public Health, Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada. ORCID 0000-0002-5977-2094

Andrew Beck, andrew.beck@uottawa.ca, Knowledge Synthesis and Application Unit, School of Epidemiology and Public Health, Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada. ORCID 0000-0002-8308-2202

Becky Skidmore, bskidmore@rogers.com, Independent Information Specialist, Ottawa, Ontario, Canada.

Maura R. Grossman, maura.grossman@uwaterloo.ca, University of Waterloo, Waterloo, Ontario, Canada.

Gordon V. Cormack, gvcormac@uwaterloo.ca, University of Waterloo, Waterloo, Ontario, Canada.

Sharmistha Mishra, Sharmistha.Mishra@toronto.ca, Department of Medicine, St. Michael's Hospital, University of Toronto, Toronto, Ontario, Canada;
MAP Centre for Urban Health Solutions, Li Ka Shing Knowledge Institute, Unity Health Toronto, Toronto, Ontario, Canada;
Epidemiology Division and Institute of Health Policy, Management, and Evaluation, Dalla Lana School of Public Health, University of Toronto, Toronto, Ontario, Canada;
Institute of Medical Science, University of Toronto, Toronto, Ontario, Canada. ORCID: 0000-0001-8492-5470

Adrienne Chan, adrienne.chan@sunnybrook.ca, Sunnybrook Health Sciences Centre, Toronto;
Dalla Lana School of Public Health, University of Toronto, Toronto, Ontario, Canada.

Lan Xu, lan.xu@sjtu.edu.cn, School of Medicine, Shanghai Jiao Tong University, China.

David Moher, dmoher@ohri.ca, Knowledge Synthesis and Application Unit, School of Epidemiology and Public Health, Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada.

Melissa Brouwers, Melissa.Brouwers@uottawa.ca, Knowledge Synthesis and Application Unit, School of Epidemiology and Public Health, Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada.

Andrea C. Tricco, Andrea.Tricco@unityhealth.to, Li Ka Shing Knowledge Institute, St. Michael's Hospital, Unity Health Toronto, Toronto, Ontario, Canada;
Epidemiology Division and Institute of Health Policy, Management, and Evaluation, Dalla Lana School of Public Health, University of Toronto, Toronto, Ontario, Canada;
Queen's Collaboration for Health Care Quality Joanna Briggs Institute Centre of Excellence, Queen's University, Kingston, Ontario, Canada.

Julian Little, jlittle@uottawa.ca, Knowledge Synthesis and Application Unit, School of Epidemiology and Public Health, Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada.

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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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Key Question

KQ10: Should health workers to patients with Ebola or Marburg disease be sprayed versus not sprayed during doffing of personal protective equipment (PPE)?

Methods Summary

This is one of a series of rapid reviews answering 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 used 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 were completed independently by two reviewers with any disagreements resolved by consensus, with arbitration by a third reviewer, when needed.

Findings

A total of 164 studies were screened in the CAL tool software and 32 studies were included for full-text screening. A list of excluded studies with reasons for exclusion can be found in Appendix 1 and the eligibility criteria for each question is in Appendix 2.

Two studies were included. One non-randomized parallel group simulation study[1] assessed viral self-contamination after health care workers performed a 16-step Ebola virus PPE doffing protocol. Participants were assigned to extra glove sanitization through spraying of the hands with hypochlorite solution or use of an alcohol-based hand rub (ABHR). The level of surrogate viruses, MS2 and bacteriophage Φ6, on the hands, face or scrubs of health care workers was ascertained following inner glove removal (Table 2). Overall, there was no detectable transfer of enveloped bacteriophage Φ6 for any participants and the certainty of evidence was judged to be very low comparing the effects of hypochlorite spray and ABHR for prevention of Φ6 transfer (Appendix 3). Additionally, there was low certainty of evidence that additional glove sanitization with hypochlorite prevented transfer of MS2 compared to ABHR (Appendix 3).

One retrospective cohort study[2] assessed the level of Ebola virus IgG antibody and prior exposure events among returned responders of the 2014-2016 West African Ebola epidemic. The study collected information on personal protective equipment used, including whether removal of Ebola PPE was performed with or without chlorine spray. Although reported in Table 3, the data is unreliable due to collinearity between use of spray and health care worker role. Almost all participants who reported performing clinical work used spray and almost all participants who did not use spray reported having a role in laboratory work. The difference in the likelihood of exposure between these two occupational groups makes it impossible to analyze the independent effect of spraying the PPE with chlorine. The overall certainty of evidence for the effectiveness of spraying PPE with chlorine prior to PPE removal to mitigate the risk of Ebola virus transmission was judged to be very low (Appendix 4).

Table 1. Characteristics of Included Studies

Citation [Author, Year]	Study Design	Funding Source	Virus Species	Setting	# Total Health Workers	# Health Care Facilities	Description of Health Worker Care/contact with patients	Study Objectives [as reported by study authors]
Casanova, 2016, [1]	Non-randomized simulation study	Non-profit organization (CDC)	Mixture of MS2 (non-enveloped virus surrogate) and Φ6 (enveloped virus surrogate) suspended in phosphate-buffered saline	Patient room in a large tertiary care academic medical center	15 HCWs from an Ebola care team (11 RNs and 4 MDs)[a]	1	Mixture of virus surrogate applied to four PPE sites on HCWs to simulate contamination through droplet exposure during patient care[b]	The goal of this research was to assess viral self-contamination of skin and clothes during a standard EVD PPE doffing protocol performed by trained HCWs using PPE artificially contaminated with 2 surrogate viruses: MS2 (a surrogate for non-enveloped human viruses) and bacteriophage Φ6 (a surrogate for enveloped viruses such as Ebola)
Houlihan, 2017, [2]	Retrospective cohort study	Non-profit organization (Wellcome Trust)	Level of Ebola virus IgG antibody (indicator of previous infection)	West Africa 2014-2016 (94% participants Sierra Leone, 4.5% Liberia, 1.1% Guinea)	268 UK/Irish workers who responded to 2014-2016 West African Ebola epidemic[c]	Not reported	Risk of Ebola virus disease exposure/ transmission ranged from high risk (n=1, 0%) to very low (n=27, 10%) risk	The aim of this project was to assess the prevalence of asymptomatic or pauci-symptomatic infection, and of exposure events, among returned responders to the West African Ebola epidemic 2014–2016

Abbreviations: HCW, health care workers, MD, medical doctor, PPE, personal protective equipment, RN, registered nurse

a. Members of the Ebola team were > 18 years of age and had undergone extensive training in a simulation laboratory in the use of EVD-specific PPE, including donning and doffing.
b. Mixture (25 μL in 5 drops of 5 μL) was applied to 4 sites: (1) the palm of the dominant hand, (2) the shoulder of the gown opposite the dominant hand, (3) the top side of the face shield on the same side as the dominant hand, and (4) the toe of the rubber boot opposite the dominant hand.
c. Roles included clinical (physician/nurse), laboratory, research, as well as management/operations, trainer, epidemiologist, community engagement/tracing, WASH staff, finance, engineer, pharmacist, and social worker/burial team/information technology/journalist/visitor/logistician/nutritionist.

Table 2. Summary of Findings: Transfer of Phi6 or MS2

Study details	***Intervention*** (Spraying with chlorine solution prior to removing PPE)	***Comparator(s)*** (No spraying with chlorine solution prior to removing PPE)	***Outcome in intervention group***	***Outcome in control group***	***Quality Assessment***[a]	***GRADE***	***Notes***
Transfer of Φ6 (n/N, %) to inner gloves, hands, face or scrubs following doffing protocol							
Casanova, 2016, [1]	Doffing protocol with extra glove sanitization with sprayed hypochlorite sanitizer[b]	Doffing protocol with alcohol-based hand rub for extra glove sanitization[c]	0/5, (0%)	0/10, (0%)	Moderate risk of bias	⊕◯◯◯ Very low	Hypochlorite spray or ABHR use for extra hand sanitization was the only alteration between doffing protocols
Transfer of MS2 (n/N, %) to inner gloves following doffing protocol							
Casanova, 2016, [1]	Doffing protocol with extra glove sanitization with sprayed hypochlorite sanitizer[b]	Doffing protocol with alcohol-based hand rub for extra glove sanitization[c]	0/5, (0%)	8/10, (80%)	Moderate risk of bias	⊕◯◯◯ Very low	Hypochlorite spray or ABHR use for extra hand sanitization was the only alteration between doffing protocols
Transfer of MS2 (n/N, %) to hands following doffing protocol							
Casanova, 2016, [1]	Doffing protocol with extra glove sanitization with sprayed	Doffing protocol with alcohol-based hand rub for extra glove sanitization[c]	1/5, (20%)	0/10, (0%)	Moderate risk of bias	⊕◯◯◯ Very low	Hypochlorite spray or ABHR use for extra hand sanitization was

Study details	***Intervention*** (Spraying with chlorine solution prior to removing PPE)	***Comparator(s)*** (No spraying with chlorine solution prior to removing PPE)	***Outcome in intervention group***	***Outcome in control group***	***Quality Assessment***[a]	***GRADE***	***Notes***
	hypochlorite sanitizer[b]						the only alteration between doffing protocols
Transfer of MS2 (n/N, %) to face following doffing protocol							
Casanova, 2016, [1]	Doffing protocol with extra glove sanitization with sprayed hypochlorite sanitizer[b]	Doffing protocol with alcohol-based hand rub for extra glove sanitization[c]	0/5, (0%)	0/10, (0%)	Moderate risk of bias	⊕◯◯◯ Very low	Hypochlorite spray or ABHR use for extra hand sanitization was the only alteration between doffing protocols
Transfer of MS2 (n/N, %) to scrubs following doffing protocol							
Casanova, 2016, [1]	Doffing protocol with extra glove sanitization with sprayed hypochlorite sanitizer[b]	Doffing protocol with alcohol-based hand rub for extra glove sanitization[c]	1/5, (20%)	0/10, (0%)	Moderate risk of bias	⊕◯◯◯ Very low	Hypochlorite spray or ABHR use for extra hand sanitization was the only alteration between doffing protocols

a. Quality assessment of studies was completed using the ROBINS-I tool for non-randomized studies.
b. For each glove sanitizing step in steps 1-12 of the 16-step doffing protocol, liquid hypochlorite (Fuzion Healthcare Disinfectant, Clorox Co., Pleasanton, CA) at a concentration of 1850 ppm was sprayed onto gloves. The final hand hygiene steps (Steps 13 and 16) that called for sanitizing bare hands were performed using ABHR.

c. For each glove sanitizing step in steps 1-12 of the 16-step doffing protocol, 70% ethanol gel was applied to gloves. The final hand hygiene steps (Steps 13 and 16) that called for sanitizing bare hands were performed using ABHR.

Table 3. Summary of Findings: Infection with Ebola virus

Study details	***Intervention*** (Spraying with chlorine solution prior to removing PPE)	***Comparator(s)*** (No spraying with chlorine solution prior to removing PPE)	***Outcome in intervention group***	***Outcome in control group***	***Quality Assessment***[a]	***GRADE***	***Notes***
IgG antibody against Ebola Virus [as an indicator of previous infection]							
Houlihan, 2017, [2]	PPE removal with chlorine spray	PPE removal without chlorine spray	33/132, (25%)	7/98, (7.1%)	High risk of bias (6/9 star rating)	⊕◯◯◯ Very low	Authors did not include PPE removal in their analysis since method of PPE removal was almost collinear with HCW role. Almost all HCWs in clinical roles were sprayed with chlorine and had assistance, and almost all HCWs in laboratory roles were not sprayed and removed PPE without assistance.

a. Quality assessment of studies was completed using the Newcastle Ottawa Scale (NOS) for observational studies. 7-9 stars was judged to be low risk of bias, 4-6 high risk of bias, and 0-3 stars very high risk of bias.

References:

1. Casanova LM, Teal LJ, Sickbert-Bennett EE, et al. Assessment of Self-Contamination During Removal of Personal Protective Equipment for Ebola Patient Care. *Infect Control Hosp Epidemiol.* 2016;37(10):1156-1161. doi:10.1017/ice.2016.169

2. Houlihan CF, McGowan CR, Dicks S, et al. Ebola exposure, illness experience, and Ebola antibody prevalence in international responders to the West African Ebola epidemic 2014–2016: A cross-sectional study. Boyles T, ed. *PLOS Med.* 2017;14(5):e1002300. doi:10.1371/journal.pmed.1002300

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

Does not examine Ebola or Marburg

Martin D, Balermpas P, Gollrad J, et al. RADIANCE – Radiochemotherapy with or without Durvalumab in the treatment of anal squamous cell carcinoma: A randomized multicenter phase II trial. Clinical and Translational Radiation Oncology. 2020;23:43-49. doi:10.1016/j.ctro.2020.04.010

Full-text unavailable

Drew J, Turner J, Cooper D, Zaiser R, Duncan T, Mugele J. Novel use of ultraviolet tracer contagion in multiple-patient simulation and the effect of personal protective equipment on contagion spread: A feasibility study. Academic Emergency Medicine. Published online 2015.

Garibaldi BT, Rainwater-Lovett K, Pilholski T, et al. Transmission of fluorescent aerosolized particles in a clinical biocontainment unit. American Journal of Respiratory and Critical Care Medicine Conference: American Thoracic Society International Conference ATS. Published online 2017.

Somers Y, Verbiest M. Suspecting ebola: When the dress code becomes life saving! Personal protective equipment-a practical demonstration. Anaesthesiology Intensive Therapy. Published online 2014.

Narrative review

Fischer WA, Weber DJ, Wohl DA. Personal Protective Equipment: Protecting Health Care Providers in an Ebola Outbreak. Clinical Therapeutics. 2015;37(11):2402-2410. doi:10.1016/j.clinthera.2015.07.007

Non comparative study

Casanova LM, Erukunuakpor K, Kraft CS, et al. Assessing Viral Transfer During Doffing of Ebola-Level Personal Protective Equipment in a Biocontainment Unit. Clinical Infectious Diseases. 2018;66(6):945-949. doi:10.1093/cid/cix956

Ortega R, Bhadelia N, Obanor O, et al. Putting On and Removing Personal Protective Equipment. N Engl J Med. 2015;372(25):2464-2465. doi:10.1056/NEJMc1504851

Lee M a, Huh K, Jeong J, et al. Adherence to Protocols by Healthcare Workers and Self-Contamination During Doffing of Personal Protective Equipment. American Journal of Infection Control. 2018;46(6):S11. doi:10.1016/j.ajic.2018.04.024

Lim SM, Cha WC, Chae MK, Jo IJ. Contamination during doffing of personal protective equipment by healthcare providers. Clin Exp Emerg Med. 2015;2(3):162-167. doi:10.15441/ceem.15.019

Russo N, Archer M, Kinzie L, Pfeiffer CD. Beyond Ebola: Standardizing the Approach to High Consequence Infection Preparation. American Journal of Infection Control. 2018;46(6):S110-S111. doi:10.1016/j.ajic.2018.04.196

No outcome data

McLaws ML, Chughtai AA, Salmon S, MacIntyre CR. A highly precautionary doffing sequence for health care workers after caring for wet Ebola patients to further reduce occupational acquisition of Ebola. American Journal of Infection Control. 2016;44(7):740-744. doi:10.1016/j.ajic.2015.12.034

Systematic review (references screened)

Verbeek JH, Rajamaki B, Ijaz S, et al. Personal protective equipment for preventing highly infectious diseases due to exposure to contaminated body fluids in healthcare staff. Cochrane Work Group, ed. Cochrane Database of Systematic Reviews. Published online April 15, 2020. doi:10.1002/14651858.CD011621.pub4

Wrong intervention/comparator (Does not compare spraying vs. not spraying for HCWs)

Andonian J, Kazi S, Therkorn J, et al. Effect of an Intervention Package and Teamwork Training to Prevent Healthcare Personnel Self-contamination During Personal Protective Equipment Doffing. Clinical Infectious Diseases. 2019;69(Supplement_3):S248-S255. doi:10.1093/cid/ciz618

Bell T, Smoot J, Patterson J, Smalligan R, Jordan R. Ebola virus disease: The use of fluorescents as markers of contamination for personal protective equipment. IDCases. 2015;2(1):27-30. doi:10.1016/j.idcr.2014.12.003

Berry L, Button T, Fonnie C, King M. How to set up an Ebola isolation unit: Lessons learned from Rokupa. Journal of Clinical Virology. 2015;70:S17. doi:10.1016/j.jcv.2015.07.046

Chughtai AA, Chen X, Macintyre CR. Risk of self-contamination during doffing of personal protective equipment. American Journal of Infection Control. 2018;46(12):1329-1334. doi:10.1016/j.ajic.2018.06.003

Cummings KJ, Choi MJ, Esswein EJ, et al. Addressing Infection Prevention and Control in the First U.S. Community Hospital to Care for Patients With Ebola Virus Disease: Context for National Recommendations and Future Strategies. Ann Intern Med. 2016;165(1):41. doi:10.7326/M15-2944

Drew JL, Turner J, Mugele J, et al. Beating the Spread: Developing a Simulation Analog for Contagious Body Fluids. Simulation in Healthcare: The Journal of the Society for Simulation in Healthcare. 2016;11(2):100-105. doi:10.1097/SIH.0000000000000157

DuBose JR, Matić Z, Sala MFW, et al. Design strategies to improve healthcare worker safety in biocontainment units: learning from ebola preparedness. Infect Control Hosp Epidemiol. 2018;39(8):961-967. doi:10.1017/ice.2018.125

Kwon JH, Burnham CAD, Reske K, et al. Healthcare Worker Self-Contamination During Standard and Ebola Virus Disease Personal Protective Equipment Doffing. Open Forum Infectious Diseases. 2016;3(suppl_1):1387. doi:10.1093/ofid/ofw172.1090

Kwon JH, Burnham CAD, Reske KA, et al. Assessment of Healthcare Worker Protocol Deviations and Self-Contamination During Personal Protective Equipment Donning and Doffing. Infect Control Hosp Epidemiol. 2017;38(9):1077-1083. doi:10.1017/ice.2017.121

Mumma JM, Durso FT, Casanova LM, et al. Common Behaviors and Faults When Doffing Personal Protective Equipment for Patients With Serious Communicable Diseases. Clinical Infectious Diseases. 2019;69(Supplement_3):S214-S220. doi:10.1093/cid/ciz614

Mumma JM, Durso FT, Ferguson AN, et al. Human Factors Risk Analyses of a Doffing Protocol for Ebola-Level Personal Protective Equipment: Mapping Errors to Contamination. Clinical Infectious Diseases. 2018;66(6):950-958. doi:10.1093/cid/cix957

Poller B, Hall S, Bailey C, et al. 'VIOLET': a fluorescence-based simulation exercise for training healthcare workers in the use of personal protective equipment. Journal of Hospital Infection. 2018;99(2):229-235. doi:10.1016/j.jhin.2018.01.021

Poller B, Tunbridge A, Hall S, et al. A unified personal protective equipment ensemble for clinical response to possible high consequence infectious diseases: A consensus document on behalf of the HCID programme. Journal of Infection. 2018;77(6):496-502. doi:10.1016/j.jinf.2018.08.016
Reidy P, Fletcher T, Shieber C, et al. Personal protective equipment solution for UK military medical personnel working in an Ebola virus disease treatment unit in Sierra Leone. Journal of Hospital Infection. 2017;96(1):42-48. doi:10.1016/j.jhin.2017.03.018

Suen LKP, Guo YP, Tong DWK, et al. Self-contamination during doffing of personal protective equipment by healthcare workers to prevent Ebola transmission. Antimicrob Resist Infect Control. 2018;7(1):157. doi:10.1186/s13756-018-0433-y

Tartari E, Parascandalo AF, Borg M. Ensuring healthcare workers' safety in the management of Ebola virus disease: a novel competency assessment checklist for proper PPE use. Antimicrob Resist Infect Control. 2015;4(S1):P6, 2047-2994-4-S1-P6. doi:10.1186/2047-2994-4-S1-P6

Zellmer C, Van Hoof S, Safdar N. Variation in health care worker removal of personal protective equipment. American Journal of Infection Control. 2015;43(7):750-751. doi:10.1016/j.ajic.2015.02.005

Wrong intervention (UV radiation)

Jinadatha C, Simmons S, Dale C, et al. Disinfecting personal protective equipment with pulsed xenon ultraviolet as a risk mitigation strategy for health care workers. American Journal of Infection Control. 2015;43(4):412-414. doi:10.1016/j.ajic.2015.01.013

Appendix 2. Eligibility Criteria

Question (10): Should health workers to patients with Ebola or Marburg disease be sprayed versus not sprayed during doffing of personal protective equipment (PPE)?

Population	Staff in HCF, ETU and community (e.g., burial teams)
Background interventions (Standard of care)	Varies by organization. WHO recommends staff remove PPE in correct order, no spraying
Intervention	Staff spraying with chlorine solution prior to removing PPE
Comparator(s)	No Staff spraying with chlorine solution prior to removing PPE
Outcome	Adverse effects associated with chemical exposure, infection with Ebola virus or Marburg, *health worker confidence*
Potential effect modifiers	Decontamination method and the types of PPE, *Chlorine concentration, chlorine type*
Setting	Health Care Facilities, ETU *Contexts to consider: ETU use vs. healthcare facility; outbreak vs readiness vs. high alert scenario.

Appendix 3. GRADE Assessment: Transfer of Phi6 or MS2

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	chlorine spray of PPE	no chlorine spray of PPE	Relative (95% CI)	Absolute (95% CI)		
Transfer of Phi6 to inner gloves, hands, face or scrubs following doffing protocol												
1	observational studies	not serious[a]	not serious[b]	serious[c]	very serious[d]	none	0/5 (0.0%)	0/10 (0.0%)	not estimable	-	⨁◯◯◯ Very low	
Transfer of MS2 to inner gloves following doffing protocol												
1	observational studies	not serious[a]	not serious[b]	serious[e]	very serious[f]	none	0/5 (0.0%)	8/10 (80.0%)	not estimable	-	⨁◯◯◯ Very low	
Transfer of MS2 to hands following doffing protocol												
1	observational studies	not serious[a]	not serious[b]	serious[e]	very serious[g]	none	1/5 (20.0%)	0/10 (0.0%)	not estimable	-	⨁◯◯◯ Very low	
Transfer of MS2 to face following doffing protocol												
1	observational studies	not serious[a]	not serious[b]	serious[e]	very serious[d]	none	0/5 (0.0%)	0/10 (0.0%)	not estimable	-	⨁◯◯◯ Very low	
Transfer of MS2 to scrubs following doffing protocol												
1	observational studies	not serious[a]	not serious[b]	serious[e]	very serious[g]	none	1/5 (20.0%)	0/10 (0.0%)	not estimable	-	⨁◯◯◯ Very low	

CI: confidence interval

Explanations

a. The overall risk of bias rated to be "moderate" using the ROBINS-I tool for non-randomized studies. The study was judged to be of low risk of bias for all but one domain. One domain was rated at moderate risk of bias due to a lack of blinding of the participants of the intervention and the trained monitor guiding participants through the doffing process.
b. Judged to be not serious as there was only one relevant study for this outcome.
c. Downrated once due to simulation study. Phi6 is a surrogate for enveloped viruses such as Ebola.
d. No events in either group, very small sample size and optimal information size (OIS) not met.
e. Downrated twice due to simulation study and use of MS2 as surrogate agent (non-enveloped virus surrogate).
f. Few events, very small sample size and OIS not met.
g. Only one event, very small samples size and OIS not met.

Appendix 4. GRADE Assessment: Infection with Ebola virus

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	chlorine spray of PPE	no chlorine spray of PPE	Relative (95% CI)	Absolute (95% CI)		
Infection with Ebola Virus												
1	observational studies	serious[a]	not serious[b]	not serious	serious[c]	none	33/132 (25.0%)	7/98 (7.1%)	**RR 3.52** (1.62 to 7.58)	**180 more per 1,000** (from 44 more to 470 more)	⨁◯◯◯ Very low	

CI: confidence interval; **RR:** risk ratio

Explanations

a. Risk of bias was judged to be high using the Newcastle Ottawa Scale. The study was awarded 6/9 stars based on use snowball sampling for a convenience sample, relying on self-reports for ascertainment of exposures and lack of reporting of details on PPE equipment or doffing protocols used between HCW roles.
b. No inconsistency detected as only one study included for this outcome.
c. Optimal information size not met and not a large sample size.