HHS Public Access

Author manuscript

BMJ Public Health. Author manuscript; available in PMC 2024 July 16.

Published in final edited form as:

BMJ Public Health. 2024 ; 2(1): . doi:10.1136/bmjph-2023-000556.

Infection prevention and control studies for care of patients with suspected or confirmed filovirus disease in healthcare settings, with focus on Ebola and Marburg: an integrative review

Raphael G Frankfurter[1], **Victoria Willet**[2], **Eugene T Richardson**[3,4], **George W Rutherford**[5], **April Baller**[2], **J Daniel Kelly**[1,5,6,7]

[1]University of California San Francisco School of Medicine, San Francisco, California, USA

[2]WHO Health Emergencies (WHE) Programme, Geneva, Switzerland

[3]Department of Global Health and Social Medicine, Harvard Medical School, Boston, Massachusetts, USA

[4]Department of Medicine, Brigham and Women's Hospital, Boston, Massachusetts, USA

[5]Department of Epidemiology and Biostatistics, University of California San Francisco, San Francisco, California, USA

[6]Department of Medicine, University of California San Francisco, San Francisco, California, USA

[7]Francis I. Proctor Foundation, San Francisco, CA, USA

Abstract

Objective—To review evidence pertaining to methods for preventing healthcare-associated filovirus infections (including the survivability of filoviruses in clinical environments and the chlorine concentration required for effective disinfection), and to assess protocols for determining the risk of health worker (HW) exposures to filoviruses.

Design—Integrative review.

Correspondence to Dr J Daniel Kelly; dan.kelly@ucsf.edu.

Contributors VW and AB proposed the review, and RF and JDK offered refinements to the scope of the review. RF and JDK designed the systematic search strategy, search strings, data extraction tools and conducted the preliminary analysis. VW, AB, GR and ETR provided supervision and edits on search strategy, data extraction tools and analysis. RGF and JDK drafted initial paper and VW, AP, GR and ETR revised and contributed to the paper. JDK is the overall content guarantor.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sources—PubMed, Embase, Google Scholar, internet-based sources of international health organisations (eg, WHO, CDC), references of the included literature and grey literature.

Study selection—Laboratory science, clinical research and real-world observational studies identified through comprehensive search strings that pertained to Ebola disease and Marburg disease and the three research objectives.

Methods—Using the framework of population, intervention or exposure, outcomes, study types and report characteristics, reviewers extracted data and critically appraised the evidence using predefined data extraction forms and summary tables. The extraction forms, summary tables and critical appraisals varied based on the included literature; we used both the QUIPS Risk-of-Bias tool when possible and an internally developed instrument to systematically extract and review the evidence from observational and experimental studies. Evidence was then synthesised and summarised to create summary recommendations.

Results—Thirty-six studies (including duplicates across research questions) were included in our reviews. All studies that related to the review questions were either (1) descriptive, real-world studies (ie, environmental audits of various surfaces in operational Ebola Treatment Units) or (2) controlled, laboratory studies (ie, experimental studies on the survivability of ebolaviruses in controlled conditions), presenting a range of concerns pertaining to bias and external validity. Our reviews of viral survivability evidence revealed significant disconnections between laboratory-based and real-world findings. However, there is greater viral persistence in liquid than dried body fluids, with the possible exception of blood, and ebolaviruses can survive for significant periods of time in dried substrate. Evidence suggests that 0.5% hypochlorite solution should be used for disinfection activity. Spills should be cleaned with covering and soaking for 15 min. Existing literature suggests that within a well-resourced clinical environment with trained, foreign HWs and established protocols, transmission of ebolaviruses as an occupational risk is a rare event. Despite the high rates of HW infections within public African healthcare settings, no evidence with low risk of bias exists to assess the risk of various occupational exposures given that all high-quality studies were conducted on foreign Ebola clinicians who had low overall rates of infection. This review underscores the critical need for better-quality evidence to inform best practices to ensure HW safety during filovirus disease epidemics.

INTRODUCTION

Filovirus disease (FVD) epidemics present a variety of challenges pertaining to health worker (HW) safety and exposure mitigation. The causative agents of these outbreaks —most notably, ebolaviruses—are known to be highly infectious and lead to clinical diseases with high mortality rates, even in the context of supportive care[1] and monoclonal antibody therapies,[2] though there is evidence that effective intensive care unit-level care can significantly improve outcomes.[3] Given that patients suffering from FVDs often produce copious amounts of infectious body fluids at the height of their illness each day, infection prevention and control (IPC) measures are important to adhere to while often being challenging to implement.[4] Compounding this, most haemorrhagic filoviruses are endemic to extremely impoverished regions of the world—particularly Western and Central Africa —and outbreaks emerge in the context of systemically underdeveloped public healthcare systems where frontline HWs often do not have the materials to protect themselves.[5 6]

Health facilities have amplified viral transmission due to the absence of routine personal protective equipment (PPE) and safety protocols.[7 8]

Novel Ebola disease (EBOD) vaccines offer promising approaches for epidemic control, while, at the same time, recent advances in antiviral and monoclonal antibody therapies open up the possibility for effective HW postexposure prophylaxis regimens.[9 10] However, there are not standardised, evidence-based criteria for how to stratify the risk of various forms of occupational exposure, which types of occupational exposures warrant postexposure prophylaxis, nor how these postexposure prophylaxis regimens might be tailored to individuals who have received pre-exposure vaccination. Given the high mortality rates and relative rarity and fast pace of filovirus outbreaks, exposure risk studies have been limited.[11 12 13] As a result, epidemic response institutions and organisations have developed their own protocols for HW safety and risk exposure assessment given the state of scientific knowledge about the infectiousness, transmission dynamics and survivability of filoviruses.

Due to these issues, guidelines issued by international agencies and non-governmental organizations (NGOs) for HW protection are often inconsistent and not always evidence-based. In 2022, the World Health Organization (WHO) established a guideline development group (GDG) to re-evaluate the current IPC recommendations and protocols for HW safety in hopes of disseminating best and evidence-based practices and aligning institutional protocols (the prior guidelines for PPE use were published in 2016[14] and for general interim IPC guidance were published in 2014[15]). In response to a series of priority questions identified by the WHO GDG members, we conducted a review of the literature to provide evidence to support development of key recommendations. As an integrative review, we sought to critically appraise and synthesise findings systematically from multiple types of literature to generate frameworks and summary recommendations (thus our review would not be a purely ‘scoping’ review).[16] Given that this integrative review had no statistical analyses, it fell under the category of ‘Literature reviews that use a systematic search’, which precludes registration in the PROSPERO database.[17]

Our integrative review addresses three priority questions. First, we sought to review the existing literature on established systems used by active epidemic response organisations to classify the level of risk of exposure of an HW to ebolaviruses and Marburg virus (MARV). (Throughout, we use the new WHO filovirus disease classification system, which stipulates that EBOD reference clinical syndromes caused by any of the ebolaviruses, MARD a clinical syndrome caused by marburgvirus infection, EVD a clinical syndrome caused by the *Zaire ebolavirus*, EBOV as the *Zaire ebolavirus,* and MARV as the *Marburg marburgvirus.)*[18] Our reviews focused on the evidence surrounding particular risk-assessment algorithms that can be implemented within high-risk settings rather than particular pathways for Ebola transmission, as the modes of Ebola and Marburg transmission have been well-defined.[19 20] Then, as a secondary aim, we reviewed literature on two more fundamental questions with relevance for HW safety protocols: What is the survivability of ebolaviruses and MARV in the environment (eg, water, septic systems, dirt) and on surfaces? And what is the chlorine concentration and contact time required to disinfect materials or surfaces contaminated with ebolaviruses and MARV, respectively? These latter two more laboratory science questions have also been explored as part of a series of recent systematic

reviews on viral survivability and disinfection practices,[21 22] however, in our review, we sought to address particular gaps in the evidence-base that can readily inform HW protection protocols during (specifically) FVD outbreaks. Together, our reviews on both the basic science and implementation of HW safety in filovirus epidemics can be used to formulate questions for further study and inform the ongoing revision and study of IPC guidelines.

METHODS

We devised a systematic search strategy for each question. To create eligible criteria, we used the framework of population, intervention or exposure, outcomes, study types and report characteristics. To assess the eligible literature, we created comprehensive search strings with terms that included combinations of Medical Subject Headings (MeSH) and text words for Ebola disease (EBOD) and Marburg disease (MARD) (see online supplemental materials). This search strategy was applied against the following information sources to identify and screen for the eligible literature: PubMed, Embase, Google Scholar, internet-based sources of international health organisations (eg, WHO, CDC), references of the included literature and grey literature. Other systematic reviews were not included in our review. The flow from articles identified and screened to articles included is described in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) diagrams.

Two reviewers (RGF, JDK) extracted data and critically appraised the evidence using predefined data extraction forms and summary tables (see online supplemental materials), and in turn verified each other's work. The extraction forms and summary tables for questions 1–3 varied based on the included literature and are also included in online supplemental materials, as are the PICO frameworks for each question and a complete list of studies included in our review for each question. No grey literature manuscripts ended up meeting inclusion criteria and being included in our review. Notably, all studies included in the review that related to the background questions were either (1) descriptive, real-world studies (ie, environmental audits of various surfaces in operational Ebola Treatment Units (ETUs)) or (2) controlled, laboratory studies (ie, experimental studies on the survivability of ebolaviruses in controlled conditions). Since there are no validated risk-of-bias assessment tools for descriptive or controlled, experimental studies, our approach drew both on the QUIPS Risk-of-Bias tool when possible[23] (online supplemental table 1) and an instrument we developed to systematically extract and review the evidence from observational and experimental studies. Thus, while we were not able to consistently perform bias assessments due to the nature of the study designs, we recognise that experimental laboratory studies and descriptive studies are inherently biased by a high likelihood of selection and measurement biases, as well as other issues.

RESULTS

Existing systems to classify level of risk exposure of an HW to filoviruses

The search returned 410 unique results which were screened to assess if they met inclusion or exclusion criteria. Of these screened records, 36 full-text articles were assessed for eligibility, and 6 studies were included in these results. A flow diagram describing the process can be found in figure 1 and the screening eligibility in figure 2. In this search,

we found two types of research studies: high-quality studies of international HWs and one low-quality study of local HWs. Box 1 describes the key findings of this review.

The 2013–2016 Ebola epidemic in West Africa appears to be the first EBOD outbreak during which researchers attempted to develop risk assessment algorithms specifically for HWs involved in the response. These algorithms were largely adapted from existing occupational health literature. The need for risk assessment algorithms emerged from the availability of potential EBOD therapeutics for postexposure prophylaxis, as well as the need to identify the types of exposure that should warrant rapid evacuation to well-equipped intensive care centres. (Of note: it is no coincidence that this effort to define exposure algorithms overlapped with a major influx of European and American HWs to affected regions of West Africa; local HWs who worked on the frontlines in this and other filovirus epidemics often bore the risk of exposure without assurance of evacuation to higher levels of care.)[8]

In a study by Jacobs and colleagues,[9] an initial risk assessment algorithm was proposed based on interviews from eight HWs who were potentially exposed to EBOV. This risk assessment algorithm was further developed and modified in a study by Houlihan and colleagues and used to assess risk among 268 HWs who travelled to West Africa in response to the Ebola epidemic.[24] Key additions to the algorithm this latter study included the addition of PPE and breeches. Both studies were conducted in the UK and considered HWs who responded to the outbreak in Sierra Leone. At the same time, however, a prospective study of French military providers in Guinea sought to classify exposures and present a parallel risk assessment algorithm.[25] Key additions from this study were consideration of HWs' indirect contact with infectious individuals by more than 1 m, and cumulative incidents and exposures to ebolavirus, particularly during the removal of PPE.

All of these studies advanced algorithms for use within ETUs that attempt to stratify risk based off of particular breaches, exposures and pathways. However, none of these studies actually identified any infections by using these risk algorithms, thus rendering the risk assessment algorithms not evidenced-based. Together, these studies suggest that HW infection rates are exceedingly low in the settings in which these algorithms were implemented; with the relatively small cohorts of responding HWs there is no existing, high-quality evidence to link HW infection to particular types of exposure.

In contrast to these research studies, there have been a series of case reports among international laboratory scientists and high-profile media reports of international HWs who have been exposed and subsequently infected with ebolaviruses (with variable clinical outcomes).[26–28] These reports are low quality given the risk of bias and represent a very weak evidence base; however, given that HWs *have* been infected via occupational exposure, the available risk algorithms should be further evaluated with cohorts that include HWs who *do* develop EBOD from occupational exposure.

In contrast to what is suggested by the literature available from international HWs and the relative paucity of HW infections in this population, a considerable number of local healthcare providers from West Africa *were* infected with the disease and thus beckon

further consideration of the highest profile risks. A retrospective descriptive study based in Sierra Leone by Olu *et al* attempted to associate mode and type of exposures with healthcare provider infections.[29] This study is difficult to interpret because of the widespread possibility that national HWs acquired EVD from community sources (ie, through contact within their homes or families) among this study population. This study thus has a high risk of bias and represents weak evidence for consideration in the current development of a risk assessment algorithm. However, this study points to the critical need to pursue high-quality research among national healthcare providers that focus on isolated health facility-based events without potential community-based exposures in future outbreaks, and that the overall risk of HW infections across healthcare settings and with varying resources and safety protocols in place remains unclear. It also reaffirms the fact that local HWs often operate on the front lines of FVD outbreaks at great peril given inadequate supplies and that the safety of future HWs in countries impacted by FVD epidemics depends on further exploration of occupational hazards.[30] Of note, a review of FVD risk factors and HW infection rates by Selvaraj and colleagues likewise found widely variable rates of HW infections depending on context, and affirmed that over multiple outbreaks inadequate PPE supplies were commonly linked to national HW infections.[8] This lends credence to the idea that while there is a critical need for evidence based guidelines to assess occupational exposure risk, many HW infections in frontline clinics may simply be caused by scarce supplies of basic PPE.

SURVIVABILITY OF EBOLAVIRUSES AND MARV IN THE ENVIRONMENT (EG, WATER, SEPTIC SYSTEMS, DIRT) AND ON SURFACES

The second search focused on the survivability of ebolaviruses and MARV and returned 142 unique results, which were screened to assess if they met inclusion or exclusion criteria. Of these screened records, 81 full-text articles were assessed for eligibility, and 20 studies were included in these results. A flow diagram describing the process can be found in figure 3 and the screening eligibility in figure 4. See box 2 for key findings.

Evidence pertaining to the survivability of ebolaviruses and MARV on various relevant surfaces derives from two sources: experimental studies that have assessed the survivability of the viruses in a variety of controlled conditions, and real-world environmental audits in which various surfaces in actively used ETUs were swabbed and then assessed for the presence of viral RNA.

There are fewer studies pertaining to the survivability of MARV than that of ebolaviruses. However, Piercy and colleagues showed that these filoviruses have similar decay rates on both liquid and dried substrates at 4°C.[31] While there is limited data in more real-world conditions of MARV, this study suggests that the general principles pertaining to the survivability of ebolaviruses from other investigations can likely be applied to MARV as well.

Schuit and colleagues found that when multiple strains of ebolaviruses were spiked onto three different dried human body fluid matrices and then inoculated on a variety of clinically relevant non-porous test surfaces in multiple temperatures and humidity levels, the decay rates of ebolaviruses were dependent on the fluid matrix (eg, vomitus, faeces, blood) and the environment (eg, temperature, humidity), not the surface itself.[32] Cook and colleagues found

that ebolaviruses on porous surfaces, such as a cotton gown, survives for much less time than on nonporous clinical surfaces.[33] Sagripanti and colleagues also found a decay rate of nearly 6 days for ebolaviruses inoculated on a non-porous surfaces in darkness.[34]

The Schuit study further showed that ebolaviruses did not survive for significant time periods in dried, simulated vomitus or faeces, but did survive for up to 240 hours in dried blood[32]; multiple other studies also found that ebolaviruses or surrogate viruses may survive within blood and plasma samples for several days or more.[35 36 37 38] One concerning finding from the Schuit study is that ebolaviruses persisted longest in dried blood at higher relative humidity, (conditions most similar to real-world, African ETU settings). Fischer and colleagues revealed similar findings pertaining to surfaces, but showed that ebolaviruses maintained an even longer duration of viability in liquid blood than in dried blood.[39]

Wastewater has been another fluid matrix under consideration in terms of ebolavirus survivability.[40] Bibby and colleagues showed that ebolaviruses may survive in wastewater for up to 8 days; however, the viral titre rapidly declined (approximately 99%) within the first day of the experiment, suggesting diminished risk of transmission via wastewater after 1 day of contamination.[41] Cook and colleagues used viral decay rates to calculate an estimated upper range of survivability. These investigators found that on stainless steel in an organic soil load, in a low-humidity, 22°C setting, ebolaviruses may survive for up to 365 hours.[33]

These findings about the long survivability of filoviruses on relevant fluids and surfaces are, however, belied by real-world descriptive studies. Six such real-world studies report the results of environmental audits, during which high-risk and low-risk surfaces from in-use ETUs were (often unsystematically) swabbed and tested for the presence of viral RNA and, in some cases, live viral particles. Of note: these studies were all carried out in relatively well-resourced clinical contexts that may not resemble the national clinics and hospitals in which FVD epidemics are first managed. In Youkee *et al* (Sierra Leone),[42] Bausch *et al* (Uganda),[43] Poliquin *et al* (Sierra Leone),[44] Puro *et al* (Italy),[45] Palich *et al* (Guinea)[46] and Wu *et al* (Sierra Leone),[47] *ebolaviruses were only recovered in areas in the immediate vicinity to patients or on visibly soiled surfaces*. While Youkee and colleagues suggested that some viral RNA may have been displaced in the process of cleaning (as, for instance, a patients' bedframe was only found to harbour viral RNA *after* a routine cleaning, not before), these studies suggest that while ebolaviruses may survive for an extended period on surfaces (as also evidenced by the experimental studies), current disinfection procedures as used in a variety of well-resourced contexts are generally effective.

All these studies are descriptive and thus may be affected by a high likelihood of selection/measurement bias and other issues. The findings from the experimental studies included are subject to the limitations of the assays and the controlled conditions in which they were carried out. The fact that there are such discrepancies in the implications of the findings from the experimental studies (which suggest potentially weeks-long survivability of ebolaviruses) versus the real-world studies (which suggest that disinfection protocols are effective and ebolaviruses is unlikely to be found outside of direct patient care areas) suggest an urgent need for further high-quality research. More environmental audits that

systematically test for viable viral particles on ETU surfaces would be helpful to elucidate the survivability of these viruses in real-world settings.

CHLORINE CONCENTRATION AND CONTACT TIME REQUIRED TO DISINFECT MATERIALS OR SURFACES SOILED WITH BOLAVIRUSES AND MARV

The third search focused on the concentration and contact time of chlorine as an environmental disinfectant and returned 36 unique results which were screened to assess if they met inclusion or exclusion criteria. Of these screened records, 26 full-text articles were assessed for eligibility, and 10 studies were included in these results. A flow diagram describing the process can be found in figure 5 and the screening eligibility in figure 6. See box 3 for key findings.

There are at least three different institutional protocols (MSF, WHO and CDC) pertaining to chlorine disinfection recommendations for Ebola response efforts,[48] none of which are evidence based. All these protocols, however, call for 0.5% chlorine to be used as the primary surface cleaning solution in ETUs.

In our review of the literature, we again found a range of experimental studies which are subject to the same limitations as stated above: low external validity, limitations with the assays used and more. Cook and colleagues found that solutions of sodium hypochlorite (NaOCl) greater than or equal to 0.5% chlorine inactivated all strains of ebolaviruses in organic soil load after 5 min of contact.[33] Weaker concentrations (for instance 0.05% and 0.1%) were not able to fully inactivate ebolaviruses. Gallandat and colleagues corroborated this finding about the effectiveness of 0.5% chlorine with a viral surrogate inoculated in an organic soil load. They also found that covering spills with a cloth soaked in 0.5% chlorine and leaving it for 15 min was an effective method of disinfection, while avoiding the risk of splash from spraying.[48] Smither and colleagues found that a 0.75% NaOCl exposure for 10 min led to no recoverable ebolavirus on all surface types tested, however this investigation did not assess the effectiveness of 0.5% chlorine.[49]

In another study by Smither and colleagues, neither 0.5% nor 1% hypochlorite was able to completely reduce ebolavirus viability when the virus was inoculated on surfaces in dried blood.[50] More research is needed on whether higher concentrations of chlorine—or chlorine applied during the cover-and-wipe method of disinfection—are effective at disinfecting ebolaviruses in dried blood.

Finally, Cook and colleagues found that high amounts of viral RNA could be recovered in the absence of infectious virus after chlorine disinfection, suggesting that PCR alone likely overestimates the survivability (and thus ineffectiveness) of a disinfection method.[33]

In the context of the real-world studies reviewed for question 2 (above) that have shown low risk of recoverable infectious virus after routine disinfection protocols, and given the several studies that have corroborated the efficacy of 0.5% chlorine, these studies offer ample evidence for 0.5% chlorine being an effective disinfectant for surfaces, with the caveat that the issue of viral persistence in dried blood needs further investigation.

DISCUSSION

In this review, we have surveyed the existing literature on FVD HW exposure risk algorithms, and the survivability and effective disinfection of filoviruses in healthcare settings. Throughout, we found inconsistencies between experimental and real-world findings, but the lack of systematic, high-quality research has likely contributed to conservative IPC practices and other implications for both EBOD and MARD care.

Broadly, the existing literature suggests that within a well-resourced ETU environment with trained HWs, the transmission of ebolaviruses from occupational risks is a rare event (although exposures that result in asymptomatic infection are overlooked).[51 52] Systematic studies that include a larger number of these internationally staffed ETUs would increase the probability of capturing infected HWs who were evacuated to home countries and add power to descriptive and analytical estimates. Given that most transmission of ebolaviruses has been occurring within local HW populations, high-quality studies may be able to identify HWs with isolated occupational exposures and decrease potential biases. We wish to emphasise that these conclusions pertain to the delivery of care within designated treatment units *during* known FVD epidemics, when paradigms of FVD HW protection have been enacted; ‘mistakes’ in FVD identification, diagnosis and HW protection protocols—not to mention scarcities in crucial PPE resources—have historically been drivers of FVD emergence and transmission in both African and, in the case of the small 2014 outbreak in Dallas county, the USA as well.[53 54] Of course, in real-world settings, as HWs must meet the demands of routine care delivery even as ebolaviruses and MARV may be circulating in communities, this distinction is less clear-cut; there is a crucial need for more research to guide the protocols that should be enacted within non-ETU hospitals and clinics in FVD-endemic or high-risk areas, both during and in-between FVD outbreaks. There is also a need for more data on the rates of particular procedural failures and their contribution to disease transmission during care within ETUs and general health facilities.

The studies that have assessed HW exposure algorithms are potentially subject to a range of biases and methodological limitations, including: (1) the lack of a control group (ie, no study randomised ETUs to use vs not use aspects of risk algorithms or algorithms in their entirety); (2) low overall numbers of ebolavirus infections which limit the power of these studies to evaluate algorithms; and (3) publication biases: given that Ebola care is often delivered by humanitarian organisations and public clinical facilities, there may have been other ETUs or response organisations who have used algorithms included in these studies but did not report findings. It is unclear how this lack of publication may have influenced our findings.

Pertaining to viral survivability, we found a significant disconnection between laboratory-based and real-world findings. Still, general principles hold: there is greater viral persistence in liquid than dried body fluids, though ebolaviruses can survive for significant periods of time in dried substrates, particularly dried blood. There is a need for concerted effort to coordinate further environmental contamination studies to learn more about real-world survivability of infectious virus using culture in BSL-4 facilities.

Finally, evidence suggests that 0.5% hypochlorite solution should be used for disinfection activity. Spills should be cleaned with covering and soaking for 15 min. There is a need for further evaluation of decontamination techniques in real-world settings (ie, surfaces for which sustained contact with chlorine is not easy to maintain) and regarding the disinfection of dried spills.

These findings on viral survivability and disinfection practices were also possibly subject to biases including (1) the lack of external validity from laboratory-based experiments to real-world settings; (2) the lack of validated instruments to evaluate risk of biases in such experimental, laboratory studies; and (3) publication bias: given the biosecurity threat of viral haemorrhagic fevers, there are likely other experiments on viral survivability that have been conducted but which are not published due to government restrictions. Finally, in all three of our reviews, our search terms were carefully selected by the study team, but it is possible that we have missed related studies that could contribute to the evidence base presented here.

There continue to be grave disparities in HW FVD infection and mortality rates across contexts, with large numbers of HWs contracting these diseases in under-resourced settings, and very low infection rates and deaths occurring among ‘expatriate’ HWs.[55] These disparities evince the fact that FVD epidemics should be studied as historically-situated phenomena, shaped by legacies of colonialism and ongoing systems of structural violence.[56] As a more proximal intervention to address these disparities, research protocols on HW safety during FVD epidemics could be developed in pre-outbreak periods, so that when the next filovirus outbreak occurs, high-quality research studies can be rapidly enacted and higher-quality evidence produced to inform HW safety protocols. This review underscores the need for ongoing efforts to protect frontline workers from filoviruses with know-how, supplies and other components of comprehensive health systems during future outbreaks.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

We thank other team members involved in the integrative review and appraisal of evidence, including Elie Akl and Miranda Deeves.

Funding

This article was supported by the NIH National Institute of Allergy and Infectious Diseases grants K08-AI139361 (ETR) and K23-AI146268 (JDK) and the National Institute of General Medical Sciences T32GM007618 (RF).

Data availability statement

Data sharing not applicable as no datasets generated and/or analysed for this study.

REFERENCES

1. Lamontagne F, Clément C, Kojan R, et al. The evolution of supportive care for ebola virus disease. The Lancet 2019;393:620–1.

2. Mulangu S, Dodd LE, Davey RT Jr, et al. A randomized, controlled trial of ebola virus disease therapeutics. N Engl J Med 2019;381:2293–303. [PubMed: 31774950]
3. Richardson ET, Fallah MP. The genesis of the ebola virus outbreak in West Africa. Lancet Infect Dis 2019;19:348–9. [PubMed: 30799253]
4. Feldmann H, Sprecher A, Geisbert TW. Ebola. N Engl J Med 2020;382:1832–42. [PubMed: 32441897]
5. Frankfurter R, Kardas-Nelson M, Benton A, et al. Indirect rule redux: the political economy of diamond mining and its relation to the ebola outbreak in Kono district, Sierra Leone. Rev Afr Polit Econ 2019;45:522–40. [PubMed: 31772418]
6. Richardson ET. Epidemic illusions: on the coloniality of global public health. 1st edn. Cambridge, Massachusetts: The MIT Press, 2020.
7. World Health Organization. Health worker ebola infections in guinea, Liberia and Sierra Leone: a preliminary report 21 may 2015. 2015. Available: https://apps.who.int/iris/handle/10665/171823 [Accessed 12 May 2023].
8. Selvaraj SA, Lee KE, Harrell M, et al. Infection rates and risk factors for infection among health workers during Ebola and Marburg virus outbreaks: A systematic review. J Infect Dis 2018;218(suppl_5):S679–89. [PubMed: 30202878]
9. 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. Lancet Infect Dis 2015;15:1300–4. [PubMed: 26321189]
10. Wong KK, Davey RT, Hewlett AL, et al. Use of postexposure prophylaxis after occupational exposure to Zaire ebolavirus. Clin Infect Dis 2016;63:376–9. [PubMed: 27118786]
11. Petti S, Protano C, Messano GA, et al. Ebola virus infection among western healthcare workers unable to recall the transmission route. Biomed Res Int 2016;2016:8054709. [PubMed: 28018915]
12. Kelly JD, Frankfurter RG, Tavs JM, et al. Association of lower exposure risk with paucisymptomatic/asymptomatic infection, less severe disease, and unrecognized Ebola virus disease: a seroepidemiological study. Open Forum Infect Dis 2022;9:ofac052. [PubMed: 35265726]
13. Gayedyu-Dennis D, Fallah MP, Drew C, et al. Identifying paucisymptomatic or asymptomatic and unrecognized ebola virus disease among close contacts based on exposure risk assessments and screening algorithms. J Infect Dis 2023;227:878–87. [PubMed: 36047331]
14. World Health Organization. Personal protective equipment for use in a Filovirus disease outbreak: rapid advice guideline. 2016. Available: https://apps.who.int/iris/handle/10665/251426 [Accessed 18 May 2023].
15. World Health Organization. Interim infection prevention and control guidance for care of patients with suspected or confirmed filovirus haemorrhagic fever in health-care settings, with focus on ebola. 2014.
16. Toronto CE, Remington R, eds. A Step-by-Step Guide to Conducting an Integrative Review. Springer International Publishing, 2020. Available: 10.1007/978-3-030-37504-1
17. Inclusion Criteria. International prospective register of systematic reviews. n.d. Available: https://www.crd.york.ac.uk/prospero/#aboutregpage
18. Kuhn JH, Adachi T, Adhikari NKJ, et al. New Filovirus disease classification and nomenclature. Nature Reviews Microbiology 2019;17:261–3.
19. Vetter P, Fischer WA II, Schibler M, et al. Ebola virus shedding and transmission: review of current evidence. J Infect Dis 2016;214(suppl 3):S177–84. [PubMed: 27443613]
20. Brainard J, Hooper L, Pond K, et al. Risk factors for transmission of ebola or marburg virus disease: a systematic review and meta-analysis. Int J Epidemiol 2016;45:102–16. [PubMed: 26589246]
21. Gallandat K, Kolus RC, Julian TR, et al. A systematic review of chlorine-based surface disinfection efficacy to inform recommendations for low-resource outbreak settings. Am J Infect Control 2021;49:90–103. [PubMed: 32442652]
22. Silverman AI, Boehm AB. Systematic review and meta-analysis of the persistence of enveloped viruses in environmental waters and wastewater in the absence of Disinfectants. Environ Sci Technol 2021;55:14480–93. [PubMed: 34665598]

23. Hayden JA, van der Windt DA, Cartwright JL, et al. Assessing bias in studies of prognostic factors. Ann Intern Med 2013;158:280–6. [PubMed: 23420236]
24. 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. PLoS Med 2017;14:e1002300. [PubMed: 28510604]
25. Savini H, Janvier F, Karkowski L, et al. Occupational exposures to ebola virus in ebola treatment center, Conakry, guinea. Emerg Infect Dis 2017;23:1380–3. [PubMed: 28726614]
26. Fernandez M 2nd Ebola case in U.S. Stokes fears of health care workers [N. Y. Times]. 2014. Available: https://www.nytimes.com/2014/10/13/us/texas-health-worker-tests-positive-for-ebola.html [Accessed 8 May 2023].
27. Goodnough A, Trenchard T. Doctor being treated for Ebola in Omaha dies [N. Y. Times]. 2014. Available: https://www.nytimes.com/2014/11/18/us/martin-salia-omaha-ebola-dead.html
28. Fink S U.S. clinician with Ebola under care in Maryland [N. Y. Times]. 2015. Available: https://www.nytimes.com/2015/03/14/world/africa/us-clinician-with-ebola-under-care-in-maryland.html [Accessed 8 May 2023].
29. 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;15:416. [PubMed: 26464285]
30. Borchert M, Mulangu S, Lefevre 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 Suppl 2:S168–75. [PubMed: 17940946]
31. Piercy TJ, Smither SJ, Steward JA, et al. The survival of Filoviruses in liquids, on solid substrates and in a dynamic aerosol. J Appl Microbiol 2010;109:1531–9. [PubMed: 20553340]
32. Schuit M, Miller DM, Reddick-Elick MS, et al. Differences in the comparative stability of ebola virus Makona-C05 and Yambuku-Mayinga in blood. PLOS ONE 2016;11:e0148476. [PubMed: 26849135]
33. Cook BWM, Cutts TA, Nikiforuk AM, et al. Evaluating environmental persistence and disinfection of the ebola virus Makona variant. Viruses 2015;7:1975–86. [PubMed: 25875372]
34. Sagripanti J-L, Rom AM, Holland LE. Persistence in darkness of virulent alphaviruses, ebola virus, and lassa virus deposited on solid surfaces. Arch Virol 2010;155:2035–9. [PubMed: 20842393]
35. Palyi B, Magyar N, Henczko J, et al. Determining the effect of different environmental conditions on ebola virus viability in clinically relevant specimens. Emerg Microbes Infect 2018;7:52. [PubMed: 29593278]
36. Westhoff Smith D, Hill-Batorski L, N'jai A, et al. Ebola virus stability under hospital and environmental conditions. J Infect Dis 2016;214(suppl 3):S142–4. [PubMed: 27279525]
37. Wood JP, Richter W, Sunderman M, et al. Evaluating the environmental persistence and inactivation of Ms2 Bacteriophage and the presumed ebola virus Surrogate Phi6 using low concentration hydrogen peroxide vapor. Environ Sci Technol 2020;54:3581–90. [PubMed: 32073830]
38. Prescott J, Bushmaker T, Fischer R, et al. Postmortem stability of ebola virus. Emerg Infect Dis 2015;21:856–9. [PubMed: 25897646]
39. Fischer R, Judson S, Miazgowicz K, et al. Ebola virus stability on surfaces and in fluids in simulated outbreak environments. Emerg Infect Dis 2015;21:1243–6. [PubMed: 26079114]
40. Wolfe MK, Gallandat K, Daniels K, et al. Handwashing and ebola virus disease outbreaks: a randomized comparison of soap, hand Sanitizer, and 0.05% chlorine solutions on the inactivation and removal of model organisms Phi6 and E. coli from hands and persistence in rinse water. PLoS One 2017;12:e0172734. [PubMed: 28231311]
41. Bibby K, Fischer RJ, Casson LW, et al. Disinfection of ebola virus in sterilized municipal wastewater. PLoS Negl Trop Dis 2017;11:e0005299. [PubMed: 28146555]
42. Youkee D, Brown CS, Lilburn P, et al. Assessment of environmental contamination and environmental decontamination practices within an ebola holding unit, Freetown, Sierra Leone. PLoS One 2015;10:e0145167. [PubMed: 26692018]
43. Bausch DG, Towner JS, Dowell SF, et al. Assessment of the risk of ebola virus transmission from bodily fluids and fomites. J Infect Dis 2007;196 Suppl 2:S142–7. [PubMed: 17940942]

44. Poliquin PG, Vogt F, Kasztura M, et al. Environmental contamination and persistence of ebola virus RNA in an ebola treatment center. J Infect Dis 2016;214(suppl 3):S145–52. [PubMed: 27365495]
45. Puro V, Fusco FM, Petrecchia A, et al. Sampling surfaces for ebola virus persistence after cleaning procedures in high-level isolation settings: the experience with 2 patients at the Lazzaro Spallanzani National Institute for infectious diseases. Infect Control Hosp Epidemiol 2016;37:723–5. [PubMed: 27198605]
46. Palich R, Irenge LM, Barte de Sainte Fare E, et al. Ebola virus RNA detection on fomites in close proximity to confirmed ebola patients. PLoS ONE 2015;12:e0177350.
47. Wu X, Wang H, Yang Y, et al. Investigation for ebola virus environmental contamination in an ebola virus disease convalescent ward. J Hosp Infect 2015;91:185–6. [PubMed: 26304624]
48. Gallandat K, Wolfe MK, Lantagne D. Surface cleaning and disinfection: efficacy assessment of four chlorine types using escherichia coli and the ebola surrogate Phi6. Environ Sci Technol 2017;51:4624–31. [PubMed: 28294602]
49. Smither S, Phelps A, Eastaugh L, et al. Effectiveness of four disinfectants against ebola virus on different materials. Viruses 2016;8:185. [PubMed: 27399759]
50. Smither SJ, Eastaugh L, Filone CM, et al. Two-center evaluation of disinfectant efficacy against ebola virus in clinical and laboratory matrices. Emerg Infect Dis 2018;24:135–9. [PubMed: 29261093]
51. Richardson ET, Kelly JD, Barrie MB, et al. Minimally symptomatic infection in an ebola 'hotspot': a cross-sectional Serosurvey. PLoS Negl Trop Dis 2016;10:e0005087. [PubMed: 27846221]
52. Kelly JD, Barrie MB, Mesman AW, et al. Anatomy of a hotspot: chain and seroepidemiology of ebola virus transmission, Sukudu, Sierra Leone, 2015–16. J Infect Dis 2018;217:1214–21. [PubMed: 29325149]
53. Chevalier MS, Chung W, Smith J, et al. Ebola virus disease cluster in the United States--Dallas County. MMWR Morb Mortal Wkly Rep 2014;63:1087–8. [PubMed: 25412069]
54. Stephens PR, Sundaram M, Ferreira S, et al. Drivers of African Filovirus (Ebola and Marburg) outbreaks. Vector Borne Zoonotic Dis 2022;22:478–90. [PubMed: 36084314]
55. Farmer P Fevers, feuds, and diamonds: ebola and the ravages of history. New York: Farrar, Straus and Giroux, 2020.
56. Cook BWM, Cutts TA, Nikiforuk AM, et al. The disinfection characteristics of ebola virus outbreak variants. Sci Rep 2016;6:38293. [PubMed: 27910909]

Box 1

Key findings

- There are multiple avenues to develop algorithms to classify level of HW exposure risk.[9 24 25]
- Multiple studies of exposed HWs from Global North countries did not show PCR or antibody evidence of infection with ebolaviruses.[9 24 25]
- Studies of local HWs are difficult to interpret because of community-based exposures without stratifying based on isolated exposure events.[29]

HW, health worker.

Box 2

Key findings

- Ebolaviruses and Marburg virus have similar survivability, and non-pourous surfaces have similar survivability times for ebolaviruses.[31 32]
- Ebolaviruses maintain viability for longer in liquid rather than dried substrates, with the possible exception of blood.[32 39]
- In real-world ETU environmental audit studies, ebolavirus RNA has only been found on visibly soiled surfaces and in immediate vicinity of patients.[42–47]

ETU, Ebola treatment unit.

Box 3

Key findings

- 0.5% hypochlorite solution is effective for surface disinfection activity, though may not be completely effective at disinfecting dried blood.[33 48 50 56]
- On non-porous, contaminated surfaces without visible spills, 10 min of contact time is consistently effective.[33 48 49]
- For visible spills, covering and pouring for 15 min is the most conservative recommendation.[48]

WHAT IS ALREADY KNOWN ON THIS TOPIC

- The strong evidence base related to filovirus disease transmission modes has led to the development of health worker (HW) infection prevention protocols (both disinfection and occupational risk assessments) within designated treatment units, but evaluations of algorithms and disinfection practices within these protocols are relatively few and have generated a weak evidence base.

WHAT THIS STUDY ADDS

- Basic science (laboratory) evidence on safe disinfection protocols is reviewed and specific practices using hypochlorite solution are proposed. Gaps in evidence surrounding algorithms for HW risk assessment are reviewed.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

- Our results and proposed evidence-based protocols contribute to efforts to standardise practices within filovirus treatment units and can be implemented by outbreak response programs.

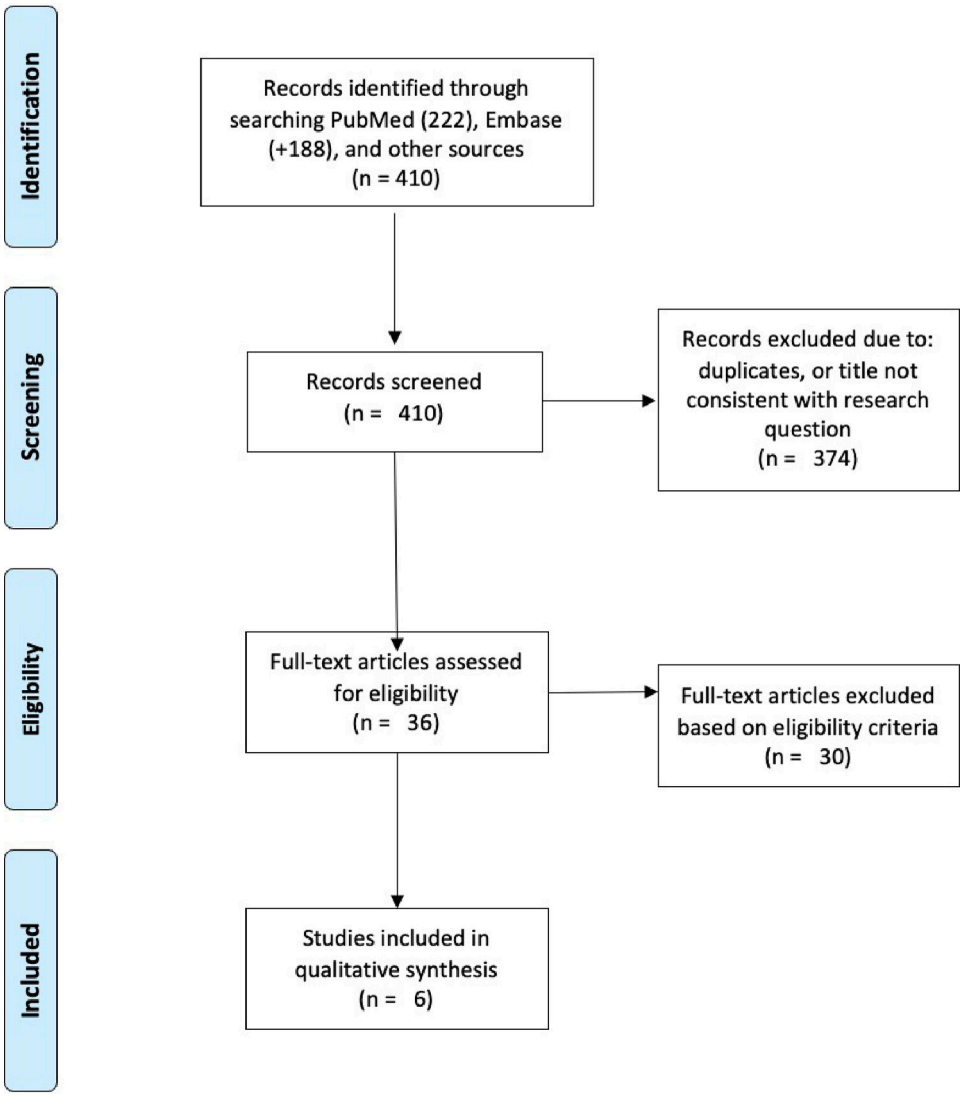

Figure 1.
Question 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses diagram.

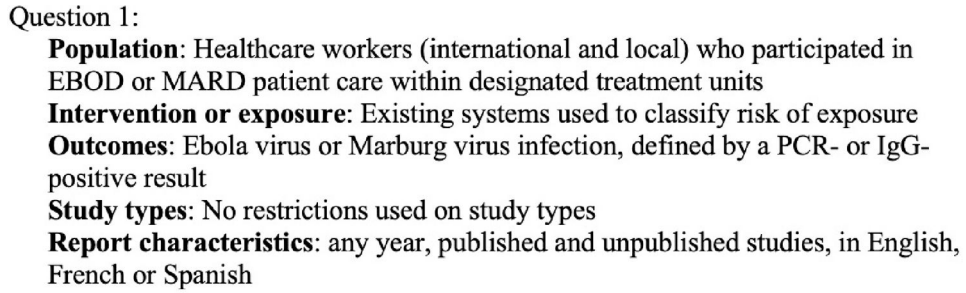

Figure 2.

Question 1 inclusion criteria. EBOD, Ebola disease; MARD, Marburg virus disease

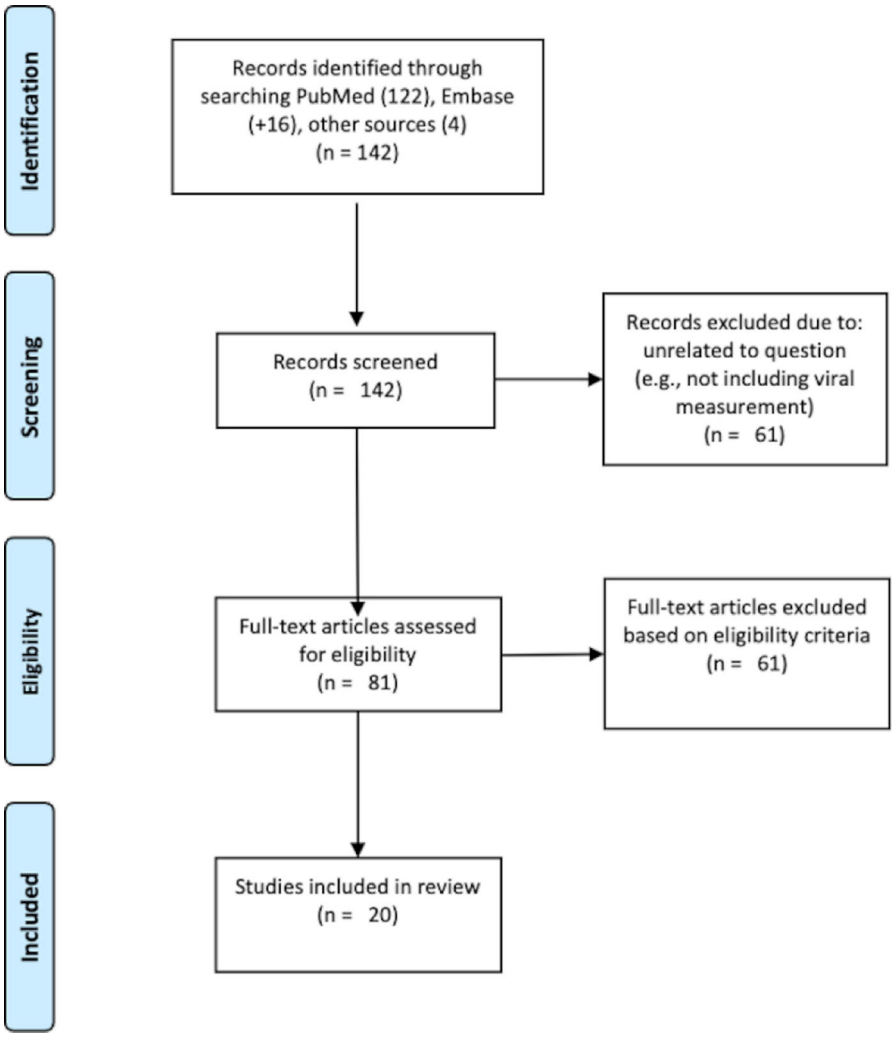

Figure 3.
Question 2 Preferred Reporting Items for Systematic Reviews and Meta-Analyses diagram.

Question 2:

Pathogen of interest: Ebola, Marburg or Surrogate
Intervention: Inoculation on surfaces and measurement of viability
Outcome: Survival time of virus or surrogate
Study Type: No restriction placed on study type, however only studies providing a quantitative outcome for viral survivability included. Studies that included a measurement of survivability as a control (i.e. when evaluating disinfectants) were included
Report characteristics: any year, published and unpublished studies, in English, French or Spanish

Figure 4.
Question 2 inclusion criteria.

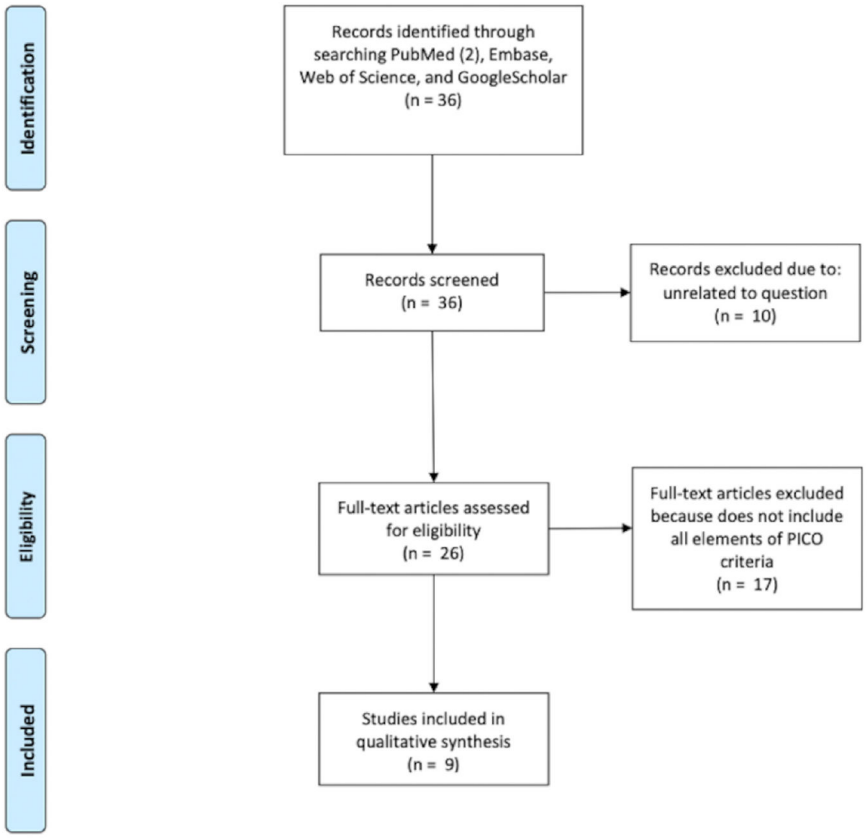

Figure 5.
Question 3 Preferred Reporting Items for Systematic Reviews and Meta-Analyses diagram.

Question 3:

Pathogen: Ebola virus, Marburg virus or Surrogate
Intervention: Exposure to chlorine
Outcome: Disinfection efficacy, defined as proportion of pathogens or pathogen surrogates that are inactivated by disinfection
Study Type: No restriction was placed on study type, however only studies providing a quantitative outcome for disinfection efficacy were included
Report characteristics: Any year, published and unpublished studies

Figure 6.
Question 3 inclusion criteria.