Ebola and Marburg disease outbreaks

Infection prevention and control research priorities in health care settings

World Health Organization

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Contents

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Overall coordination, writing and design of the document

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Abbreviations

EBOD	Ebola disease
EBOV	Ebola virus
GDG	Guideline Development Group
GIPCN	Global Infection Prevention and Control Network
IPC	Infection prevention and control
LMIC	Low- and middle-income country
MARD	Marburg disease
MARV	Marburg virus
PHE	Public health emergencies
PPE	Personal protective equipment
WHO	World Health Organization

Executive summary

Ebola virus (EBOV) and Marburg virus (MARV) are associated with severe, potentially fatal, systemic diseases. During the development of *the Infection Prevention and Control Guideline for Ebola Disease and Marburg Disease*, the Guideline Development Group (GDG) identified multiple research gaps in key areas and practices that lacked strong evidence to help in the formulation of recommendations. Because of the lack of strong evidence, there exists an array of research questions related to infection prevention and control (IPC) in the context of Ebola Disease (EBOD) and Marburg Disease (MARD). Identifying those that are priorities would help policy-makers target efforts and funding to support the most relevant studies. The objective of this research prioritization exercise was to identify the short- to medium-term (over the next two years) priority research questions for IPC in health care settings based on the gaps identified during the EBOD/MARD IPC guideline development process.

For this exercise, a modified Delphi Technique was carried out in three steps; 41 participants were invited. Participants were asked to complete the spreadsheet using a five-point Likert-type scale, from 1 (lowest priority) to 5 (highest priority), according to six pre-established criteria. The sum of each research question's total score and individual criteria score was calculated. The percentile distribution of the sum of the scores was used to stratify the scores based on pre-determined cut-offs. A total of 18 out of 41 (43.9%) participants completed the second round. Nine of the 36 (above percentile 75) research questions were ranked as higher priority, 18 (between percentile 25 and 75) were ranked as intermediate priority and the remaining nine (below percentile 25) were ranked as lower priority.

The results of this exercise demonstrate participants' concerns about the uncertainty of the evidence base supporting protection recommendations for health and care workers as well as supporting personal protective equipment (PPE) use in EBOD/MARD outbreaks. Additionally, higher priority was given to research questions focusing on the evidence related to the impact of different IPC training programme methods (virtual, face-to-face, practical sessions) in the containment of EBOD/MARD outbreaks.

1. Background

EBOV and MARV (*1, 2*) are associated with severe, potentially fatal, systemic diseases *(3, 4*). These pathogens have caused multiple outbreaks, with implications for transmission within health care settings among staff and patients, as well transmission back to communities, in particular related to EBOV (*5, 6*).

During the development of the *Infection Prevention and Control Guideline for Ebola Disease and Marburg Disease*, the GDG identified multiple research gaps in key areas and practices that lacked strong evidence to help in the formulation of recommendations. The GDG noted that, if more robust and direct evidence had been available, "conditional" recommendations could potentially have become "strong" recommendations. This would have resulted in clearer guidance for Member States, their frontline health and care workers and policy-makers.

Because of the lack of strong evidence, there exists an array of research questions related to IPC in the context of EBOD and MARD. Identifying those that are priorities would help policy-makers target efforts and funding to support the most relevant studies. Hence, this research prioritization exercise was initiated to guide researchers, funders, publishers and other key stakeholders involved in the production and dissemination of scientific evidence related to IPC measures during EBOD/MARD outbreaks.

2. Objective

The objective of this research prioritization exercise was to identify the short- to medium-term (over the next two years) priority research questions for IPC in health care settings based on the gaps identified during the EBOD/MARD IPC guideline development process.

3. Methods

Design
For this research-prioritization exercise, a modified Delphi Technique (*7*) was used. In this report, the steps of this exercise and the results are summarized.

Participants
Currently, there is no standard for the number of participants needed to reach consensus by using Delphi methods (*7*). The selection of experts largely depends on the subject that is being explored (*8*). For this exercise, in both the first and second rounds, 41 participants were invited; including:

- Members of IPC Public Health Emergencies (PHE) Working Group within the Global Infection Prevention and Control Network (GIPCN) (for more information on the Public Health Emergencies Working Group within the Global Infection Prevention and Control Network (GIPCN), refer to https://www.who.int/groups/global-infection-prevention-and-control-network);
- Members of the GDG who had expressed interest in participating in this exercise (for more information on the Infection Prevention and Control Ebola Virus Disease Guideline Development Group, refer to https://www.who.int/groups/guideline-development-group-for-infection-prevention-and-control-ebola-virus-disease).

Data collection and prioritization criteria
This prioritization exercise was carried out in three steps:

I. An inception meeting attended by the potential participants in the prioritization exercise;
II. A first round, which sought to establish the list of potential research questions to be prioritized;
III. A second round, which aimed to define a score of priority for each research question.

In the inception meeting, the objectives and methods were presented to the participants. The group discussed the initial list of potential research questions composed during the previous GDG discussions.

In the first round, participants were asked to complete a survey to review the 45 research questions previously collected and organized into 11 categories (Table 1). For each research question, the participants answered the following question: *Should this question be included in the list of research questions to be prioritized?* The options for answers were *yes*, *no* and *yes, with modifications*. Whenever modifications were suggested, the participants could describe the proposed modifications. "Q" and a sequential number (e.g. Q01, Q02, etc.) identified questions without any priority meaning a priori.

After completing the first step, all invited participants received a summary report of the first round, which did not include individual opinions. For the second round, the participants received an Excel® spreadsheet containing 36 research questions resulting from the first round. Participants were asked to complete the spreadsheet using a five-point Likert-type scale, from 1 (lowest priority) to 5 (highest priority), according to six pre-established criteria:

- Criterion 1 (C1): Likelihood of improving IPC practices and reducing EBOD/MARD transmission;
- Criterion 2 (C2): Implementation feasibility for low- and middle-income countries (LMICs);
- Criterion 3 (C3): Access considerations (whether the research solution matches the needs of impoverished population and whether they will be able to afford it and readily implement it);
- Criterion 4 (C4): The potential cost-effectiveness of the intervention to prevent EBOD/MARD transmission;
- Criterion 5 (C5): Ability to strengthen local research capacities;
- Criterion 6 (C6): Ability to reduce the environmental impact of IPC practices.

The criteria were adapted from the WHO, 2020 (*6*) and agreed to by participants during the inception meeting (1 December 2022) and by the potential participants in the prioritization exercise.

Table 1. Number of identified research questions on Ebola Disease/Marburg Disease Infection Prevention and Control for health care facilities according to their categories. January—March 2023.

Category of research question	Number of questions	%
Disinfection – gloves	7	15.6
Disinfection – gloves	7	15.6
Environment – linen	6	13.3
PPE – types and standards	6	13.3
Environment – linen	6	13.3
PPE – types and standards	6	13.3
Methodological issues**	5	11.1
Disinfection – environment	4	8.9
Health and care workers' occupational risk*	4	8.9
Health care-associated infection	4	8.9
Dead body management	3	6.7
PPE – putting on and taking off	3	6.7
PPE – indication	2	4.4
PPE – reuse	1	2.2
Total	45	100

PPE: personal protective equipment.

*of acquiring Ebola disease or Marburg Disease;

**Methodological issues: refers to gaps in standardized methods and patterns for IPC research related to EBOD/MARD

Data analysis

For the first round, the cut-off point proposed was >50% agreement among participants to exclude or include a given question. If >50% of participants agreed to the relevance of question (whether with modifications or not), that question was retained in the list. The minimum possible score was 108, and the maximum possible score was 540.

For the second round, the responses were organized in a single Excel® file to facilitate the synthesis of the results. The sum of each research question's total score and individual criteria score was calculated. Finally, the percentile distribution of the sum of the scores was used to stratify the scores based on pre-determined cut-offs (Table 2).

Table 2. Classification of priority level for the research questions on Ebola Disease/Marburg Disease Infection Prevention and Control for health care facilities according to the distribution of percentile of scores attributed by the participants. January—March 2023.

Priority level	Percentile distribution of scores
Higher priority	≥ 75
Intermediate priority	≥25 and <75
Lower priority	<25

4. Results

First round
In the first round, 17 out of 41 (41.5%) participants completed the survey. All participants considered all questions (n=45) were relevant and should remain in the exercise for the second round, with revision of the language in several questions. Some questions were combined and others were modified to cover broader themes that may assist with future reviews on IPC recommendations for EBOD or MARD, resulting in 36 research questions that entered the second round. The results of the first round are detailed in Annex 1, Table A.1.1.

Notably, the question Q21 related to the occupational risk of EBOD/MARD (*What are the risk factors for health and care workers' occupational acquisition of EBOD/MARD*?) received unanimous agreement for inclusion in this first round. Some questions related to PPE and disinfection received above 80% approval for inclusion without changes and, for those, none of the participants voted for exclusion. These questions were: Q11*: Are there novel alternatives (e.g. methylene blue) as hand hygiene products for disinfecting gloved hands?;* Q22: *What are the human factors, usability and safety aspects related to use of multiple pieces for long periods?;* Q42*: What is the efficacy and usability of new PPE designs for eye and face protection?*

Second round
A total of 18 out of 41 (43.9%) participants completed the second round. Nine out of the 36 (above percentile 75) research questions were ranked as *higher priority*, 18 (between percentile 25 and 75) ranked as *intermediate priority* and the remaining nine (below the percentile 25) ranked as *lower priority*. One participant each did not score research questions Q04, Q08, and Q12, and two participants did not score research question Q25, which might have created inaccuracies in the scores for these questions.

The total score for each research question ranged from 323 to 445. The criterion C1: "likelihood of improving IPC practices and reducing EBOD/MARD transmission" had a higher weight in the overall score for each research question (Figure 1). The criterion C6: "ability to reduce the environmental impact" received the lowest median score and largest interquartile range. The dispersion of scores was high as well for the criterion C2: "implementation feasibility for LMIC" and C3: "access considerations – whether the solutions match the needs of the poor population and whether they will be able to afford it and readily implement."

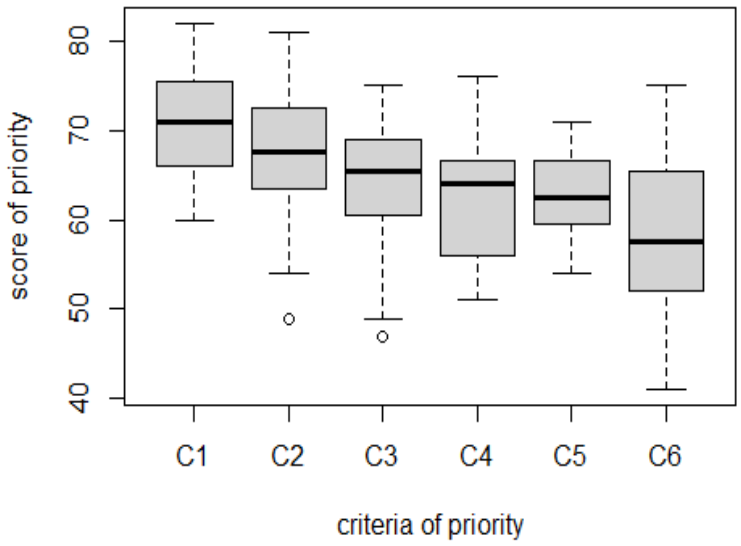

Figure 1. Distribution of the research questions' total scores for each of the six criteria (C1: likelihood of improving IPC practices and reducing EBOD/MARD transmission; C2: implementation feasibility for low- and middle-income countries; C3: access considerations–whether the solution matches the needs of the poor population and whether they will be able to afford it and readily implement it; C4: the potential cost-effectiveness of preventing EBOD/MARD transmission; C5: ability to strengthen the local research capacity; C6: ability to reduce the environmental impact).

A table presenting the total score for each research question is available in Annex 1, Table A.1.2. The eight research questions that scored as higher priority belonged to the following categories:

- **glove disinfection:** Q11, score 408: *Are there alternative agents for gloves disinfection that are equal or superior to chlorine related to germicidal effect (log reduction) on EBOV/MARV, but that are less toxic for humans, less of an environmental hazard, better cost-effectiveness, and better acceptability*?
- **health and care workers' EBOD/MARD occupational risk:** Q15, score 404: *What are the risk factors for HCW (health and care worker) occupational acquisition of EBOD/MARD? Are the risk factors significantly different for different EBOV/MARV strains*?; Q16, score 433: *What are the human factors, usability and safety aspects related to use of a full set of PPE for long periods*?; Q17, score 411: *Does the full set of PPE (full body suit including head and neck) significantly reduce the risk of transmission of EBOD/MARD to health and care workers OR burial teams compared to set of PPE that allow exposure of some parts of contact skin (e.g. neck, head)?*
- **methodological issues: Q26, score 428:** *What is the Impact of different methods of IPC training programmes (virtual, face-to-face, practical sessions) in the containment of EBOD/MARD outbreaks?*
- **putting on and taking off PPE:** Q29, score 432: *Does spraying OR wiping chlorine on the fully PPE dressed HCW before the doffing reduce the risk of HCW contamination with EBOV/MARV compared to no PPE disinfection before removing?*
- **PPE indication for use:** Q31, score 430: *Is the risk of EBOD/MARD reinfection among survivors low enough to preclude the need for a full set of PPE and use only standard precautions PPE*?;

Q32, score 445: *Is the risk of EBOV infection among vaccinated people low enough to preclude the need of full set of PPE and use only standard precautions PPE?*

- **PPE reuse:** Q33, score 439: *Does the decontamination process of reusable PPE (e.g. boots, plastic apron) by using chlorine solution OR alternative method provide sufficient log reduction of EBOV/MARV to make the PPE safe for reuse and maintain the integrity characteristics for the subsequent use compared to a new PPE? How many times can an item of PPE be decontaminated and maintain its integrity compared to a new PPE?*

The summaries of higher, intermediate and lower priorities are available in the Annex 2, Box A.2.1, A.2.2, A.2.3.

5. Discussion

During the development of the *Infection prevention and control guideline for Ebola and Marburg Disease (9*), a systematic literature review was undertaken as part of the guideline development process. The results of the review highlighted the fact that the evidence base for IPC practices for EBOD and MARD was generally limited to low-certainty or very low-certainty evidence (*10*).

The themes categories of research related to PPE and disinfection had been pointed out as relevant since the phase of questions generation; they remained as relevant until the second round, which reflects the importance of both categories for IPC intervention. PPE is of particular importance since adherence to PPE guidelines is a critical element to preventing EBOV/MARV infections among health and care workers, while many measures are currently based more on traditional practices than on scientific evidence. Of note, the adherence to proper use of PPE in health care is complex and influenced by many factors, including the PPE design (*11*).

Furthermore, outbreaks of EBOD and MARD more frequently affect people in LMICs, where inequalities in health care facilities' environmental conditions (*12*) represent an additional challenge in implementing IPC measures. Therefore, in addition to being culturally acceptable, measures for disinfection, linen management and other IPC measures should be feasible, with low costs.

Additionally, there are aspects related to the occupational risk of EBOD/MARD that need further scientific investigation. Despite the fact that much information has been gathered from outbreaks, the evidence about risk factors for EBOD/MARD among health and care workers is still lacking. Therefore, it is essential that the medical community develop well-designed and validated research protocols that can be performed during outbreaks to clarify how health and care workers can best protect themselves.

This exercise had limitations. The participants were restricted to those belonging to the groups mentioned in the methods section; therefore, it is possible that other participants might have generated a different set of questions to be prioritized. Additionally, not all of the invited individuals actively participated in this exercise. However, those participants who were involved had strong experience in IPC and EBOD/MARD in both academic and health care settings.

Working in various areas of health care, WHO has performed prioritization exercises (*13-16*) that share the goal of aligning scientific efforts to foster the implementation of evidence-based practices. As was the case with other exercises, the list of research questions herein presented is not exhaustive and the priorities cited can be changed as new evidence appears. Furthermore, these questions can be explored by using a variety of research methods, including basic studies, implementation, clinical care and public health research.

6. Conclusion

The results of this exercise demonstrate participants' concerns about the uncertainty of the evidence base supporting protection recommendations for health and care workers as well as supporting PPE use in EBOD/MARD outbreaks. Additionally, higher priority was given to research questions focusing on the evidence related to the impact of different IPC training programme methods (virtual, face-to-face, practical sessions) in the containment of EBOD/MARD outbreaks. Researchers and funding bodies weighing whether to support future initiatives to provide evidence for IPC related to EBOD/MARD should be aware of the results of this exercise.

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Annexes

Annex 1. Results from first and second round of prioritization exercise

Table A.1.1. Results of first round of the prioritization exercise on Ebola Disease/Marburg Disease Infection Prevention and Control for health care facilities: research questions proposed, percentage of answers for inclusion, exclusion or inclusion with modifications.

N	Research question	Percentage of answers (total of answers = 17)		
		Inclusion	Exclusion	Inclusion with modification
Q1	What is the concentration of EBOV/MARV on skin surface of dead bodies?	64	24	12
Q2	What is the concentration of EBOV/MARV on the body bags' exterior, after the body is prepared to be given to families?	47	35	18
Q3	Is the concentration of EBOV/MARV on body surfaces and body bags reduced by spraying OR wiping the dead body with chlorine?	53	20	27
Q4	Where are the highest concentrations of EBOV/MARV on the Ebola disease treatment units surfaces?	52	24	24
Q5	What is the reduction of EBOV/MARV on surfaces with body fluids after chlorine spraying OR wiping?	47	24	29
Q6	What are alternative disinfection products other than chlorine solutions?	76	12	12
Q7	What is the EBOV/MARV transmission risk reduction after chlorine spraying OR wiping on surfaces?	58	24	18
Q8	What is the concentration of EBOV/MARV on exterior gloves of health and care workers between EBOD/MARD patients in a care setting?	59	35	6
Q9	If double-gloved hands are washed with chlorine, what is the final EBOV/MARV concentration on the exterior gloves, and is it reduced enough that it can be used to provide care to the next patients?	70	24	6
Q10	What is the final concentration of EBOV/MARV on exterior gloves after a four-step procedure? (current WHO recommended procedure is: (1). Double-gloved hands are washed with chlorine, then (2) exterior glove removed, (3) interior gloves washed with chlorine, and (4) a new exterior glove is put on)	65	29	6
Q11	Are there novel alternatives (e.g. methylene blue) as hand hygiene products for disinfecting gloved hands?	88	0	12
Q12	Have the alternative disinfectants equal or non-inferior efficacy in disinfecting gloved hands compared to chlorine solution?	70	12	18

Q13	What is the cost-effectiveness of the alternative product for disinfecting gloved hands?	59	29	12
Q14	What are the adverse effects of the alternative product for disinfecting gloved hands?	70	12	18
Q15	What is the efficacy of immersing various types of linens in chlorine solution to inactivate EBOV/MARV?	70	6	24
Q16	What is the efficacy of boiling various types of linens to inactivate EBOV/MARV?	64	24	12
Q17	What is the efficacy of immersing various types of linens in different products to inactivate EBOV/MARV?	64	18	18
Q18	What is the feasibility and acceptability in the community of leaving linens in the environment for virus desiccation rather than incinerating them?	58	18	24
Q19	What is the feasibility and acceptability in the community of linens that are disinfected by heat (boiling/washing machine with hot water) rather than linen incineration?	76	18	6
Q20	What are the risks of EBOD/MARD transmission to staff/persons handling the linens (washing manually OR by machine)?	53	29	18
Q21	What are the risk factors for health and care workers' occupational acquisition of EBOD/MARD?	100	0	0
Q22	What are the human factors, usability and safety aspects related to use of multiple pieces of PPE for long periods?	82	0	18
Q23	What is the risk of contamination of neck skin by EBOV/MARV during health care assistance?	58	18	24
Q24	What is the risk of EBOV/MARV transmission through intact skin?	82	12	6
Q25	What is the best definition for health care associated infections caused by EBOV/MARV during outbreaks?	76	6	18
Q26	What are the health care associated infections rates (for inpatients/outpatients) during outbreaks?	70	6	24
Q27	What are the health care associated infections rates of other epidemiologically relevant pathogens (e.g. methicillin resistant Staphylococcus aureus) during EBOD/MARD outbreaks?	64	18	18
Q28	What are the mortality rates among inpatients (both EBOD/MARD and non-EBOD/MARD) during EBOD/MARD outbreaks?	70	18	12
Q29	Is the use of fluorescent tracing with synthetic blood, vomit, diarrhoea in simulated situations equivalent or non-inferior to the use of actual organic material?	59	12	29
Q30	What is the best method to assess the impact of IPC interventions (e.g. the IPC ring approach) during EBOD/MARD outbreaks?	76	6	18
Q 31	Is Phi6 an appropriate surrogate to simulate EBOV/MARV contamination and transmission patterns in lab settings?	58	24	18

Q32	What is the Impact of training programmes in the containment of EBOD/MARD outbreaks?	71	0	29
Q33	How to assess the impact of IPC interventions in rural versus urban settings?	58	24	18
Q34	What is the concentration of EBOV/MARV on surface of PPE before they are removed?	58	24	18
Q35	Does spraying health and care workers using PPE with chlorine before removal reduce the concentration of EBOV/MARV to ensure safety of health and care workers?	59	29	12
Q36	What is the safety rating of different procedures for putting on and removing the ensemble of PPE?	70	24	6
Q37	What is the risk of reinfection of survivors of EBOD/MARD?	65	29	6
Q38	What is the risk of infection among individuals with complete vaccination scheme for EBOD?	70	18	12
Q39	What is the efficacy of the PPE disinfection process using chlorine solution OR other products (e.g. methylene blue + sunlight) against EBOV/MARV?	71	12	18
Q40	What is the cost-benefit of different technical specifications of PPE?	70	12	18
Q41	What is the efficacy AND usability of new PPE designs with full body protection, including head and neck?	76	0	24
Q42	What is the efficacy AND usability of new PPE designs for eye and face protection?	82	0	18
Q43	What is the cost-effectiveness of new PPE?	76	6	18
Q44	What is the environmental impact of new PPE compared to the currently used PPE?	88	12	0
Q45	How many times can a biodegradable apron be used before the integrity of its material is compromised compared to that of a non-biodegradable apron?	58	24	18

EBOD: Ebola disease; EBOV: Ebola virus; MARD: Marburg disease; MARV: Marburg virus; PPE: Personal protective equipment

Table A.1.2. Results of second round of the prioritization exercise on Ebola Disease/Marburg Disease Infection Prevention and Control for health care facilities: research questions, total score and percentile rank of the score distribution.

N	Research Question	Total score[(a)]	Percentile rank
Q1	What is the concentration of EBOV/MARV on skin surface and on orifices of dead bodies, duration of persistence of viable infective concentrations?	366	0.25
Q2	Does disinfection of the external body bag after the body preparation reduce the concentration of EBOV/MARV enough to safely handle compared to no disinfection?	390	0.51
Q3	Does wiping with chlorine (compared with spraying of chlorine or with an alternative disinfectant) result in a significant log reduction in the concentration of EBOV/MARV on body surfaces and the external surfaces of body bags?	370	0.31
Q4*	What is the survival time of EBOV/MARV on different surfaces (e.g. porous and non-porous) if desiccated in organic material?	375	0.34
Q5	What are the relative concentrations of EBOV/MARV across the various Ebola disease treatment units environment surfaces and how do these concentrations relate to the types of activities performed?	366	0.25
Q6	What is the germicidal efficacy (log reduction) of EBOV/MARV on different surfaces (e.g. wood materials, ceramics) comparing the methods of spraying OR wiping with chlorine and other disinfectants?	392	0.54
Q7	Are there alternative disinfectants that are equal or superior to chlorine regarding their germicidal efficacy (log reduction), but that are less toxic to humans and the environment?	393	0.57
Q8*	What is the EBOV/MARD risk of transmission by using the wiping method versus the spraying method for routine surface disinfection?	362	0.22
Q9	What is viral load range on external surfaces of gloves of health care providers immediately after they provide care to EBOD/MARD patients?	352	0.11
Q10	What is the difference in efficacy (log reduction) of EBOV/MARV on exterior gloves by washing with chlorine compared to alcohol handrub after a four-step procedure? [Current WHO-recommended procedure is: (1) double-gloved hands are washed with chlorine, then (2) exterior gloves removed, (3) interior gloves washed with chlorine, and (4) a new exterior glove is put on.]	405	0.74
Q11 §	Are there alternative agents for glove disinfection that are equal or superior to chlorine in terms of their germicidal effect (log reduction) on EBOV/MARV, but that are less toxic for humans, less of an environmental hazard, more cost-effective and better accepted?	408	0.77

Q12*	What is the germicidal efficacy (log reduction) of EBOV/MARV of immersing various types of linens in different concentrations of chlorine solution compared with alternative disinfection methods?	349	0.08
Q13	What is the feasibility and acceptability within the community of processing EBOV/MARV-contaminated linen by boiling it versus machine-washing it in hot water versus incinerating it?	396	0.62
Q14	What are the risks of EBOV/MARV transmission to staff/persons handling the contaminated linens by washing manually compared to machine washing?	394	0.60
Q15 §	What are the risk factors for health and care workers' occupational acquisition of EBOD/MARD? Are the risk factors significantly different for different EBOV/MARV strains?	414	0.82
Q16 §	What are the human factors, usability and safety aspects related to use of a full set of PPE for long periods?	423	0.85
Q17 §	Does use of a full set of PPE (full body suit including head and neck) significantly reduce the risk of transmission of EBOD/MARD to health care personnel OR burial teams compared to use of a set of PPE that allows exposure of some parts of contact skin (e.g. neck, head)?	411	0.80
Q18	What is the risk of EBOV/MARV transmission through intact skin?	379	0.42
Q19	What is the most accurate definition of HAI caused by EBOV/MARV during community outbreaks?	353	0.14
Q20	What are the incidence and prevalence rates of HAI caused by EBOD/MARD (for inpatients/outpatients) during community EBOD/MARD outbreaks?	398	0.65
Q21	What are the incidence and prevalence rates of other epidemiologically relevant pathogens (e.g. methicillin resistant Staphylococcus aureus) in Ebola disease treatment units?	356	0.20
Q22	Is there a significant difference between mortality rates among patients who acquired health care associated infections caused by EBOV/MARV compared to overall mortality of EBOD/MARD?	336	0.05
Q23	Is the lab simulation with fluorescent marking equivalent OR non-inferior to actual organic material (blood and body fluids) and real world to identify the risk of contamination by EBOV/MARV during health care assistance procedures?	331	0.02
Q24	How to measure the impact of IPC ring approach during EBOD/MARD outbreaks compared to not using the IPC ring approach?	377	0.4
Q25**	Is Phi6 an appropriate surrogate in lab settings to simulate EBOV/MARV contamination patterns for different surfaces (e.g. wood, skin) compared to the actual EBOV/MARV?	323	0
Q26 §	What is the Impact of different methods of IPC training programs (virtual, face-to-face, practical sessions) in the containment of EBOD/MARD outbreaks?	428	0.88

Q27	What are the methods to assess the impact of IPC interventions in different settings (e.g. rural versus urban areas, primary care, Ebola disease treatment units to reduce the risk of EBOD/MARD transmission?	401	0.71
Q28	What are the concentrations of EBOV/MARV on different pieces of PPE (e.g. gowns, gloves, face shield) before the removal procedure?	355	0.17
Q29 §	Does spraying OR wiping chlorine on the fully PPE-dressed HCW before the removal procedure reduce the risk of health and care worker contamination with EBOV/MARV compared to no PPE disinfection before removing the PPE?	432	0.94
Q30	Is there a significant difference in the risk of health and care worker contamination by EBOV/MARV between different procedures for putting on and taking off the full set of PPE?	398	0.65
Q31 §	Is the risk of EBOV/MARV reinfection among survivors low enough to preclude the need for a full set of PPE and use only standard-precautions PPE?	430	0.91
Q32 §	Is the risk of EBOD among vaccinated people low enough to preclude the need for a full set of PPE and use only standard-precautions PPE?	445	1
Q33 §	Does the decontamination process for reusable PPE (e.g. boots, plastic apron) by using chlorine solution OR an alternative method provide sufficient log reduction of EBOV/MARV to make the PPE safe for reuse and maintain its integrity characteristics for the subsequent use compared to a new set of PPE? How many times can an item of PPE be decontaminated and maintain its integrity compared to a new PPE?	439	0.97
Q34	Are any future designs for full body protection equivalent or superior to the current set of PPE for EBOD/MARD health care regarding the safety, usability, reduced environmental impact and cost saving?	376	0.37
Q35	Are any future designs for face protection equivalent or superior to the current set of masks and face shield for EBOD/MARD health care, regarding the safety, usability, reduced environmental impact and cost saving?	379	0.42
Q36	How many times can a reusable biodegradable apron be used before the integrity of its material is compromised compared to that of a non-biodegradable apron?	385	0.48

(a) Total score: the sum of score attributed for the research question by all participants (minimum possible score was 108, and the maximum possible score was 540).
*question was not scored by one participant.
**question was not scored by two participants.
§: higher priority score.
EBOD: Ebola disease; EBOV: Ebola virus; MARD: Marburg disease; MARV: Marburg virus; PPE: Personal protective equipment

Annex 2. Research priorities

Box A.2.1. Higher priorities research questions for infection prevention and control related to Ebola Disease and Marburg Disease.

- Is the risk of EBOV infection among vaccinated people low enough to preclude the need for a full set of PPE and use only standard precautions PPE?
- Does the decontamination process for reusable PPE (e.g. boots, plastic apron) make the PPE safe for reuse and maintain the integrity characteristics for the subsequent use compared to a new PPE? How many times can an item of PPE be decontaminated and maintain its integrity compared to a new PPE?
- Does spraying OR wiping chlorine on the fully PPE-dressed health and care worker before the PPE removal reduce the risk of health and care worker contamination with EBOV/MARV compared to no PPE disinfection before removal?
- Is the risk of EBOD/MARD reinfection among survivors low enough to preclude the need for a full set of PPE and allow the use of only standard precautions PPE?
- What is the Impact of different methods of IPC training programmes (virtual, face-to-face, practical sessions) in the containment of EBOD/MARD outbreaks?
- What are the human factors, usability and safety aspects related to use of a full set of PPE for long periods?
- What are the risk factors for health and care workers' occupational acquisition of EBOD/MARD? Are the risk factors significantly different for different EBOV/MARV strains?
- Does use of the full set of PPE (full body suit, including head and neck) significantly reduce the risk of transmission of EBOD/MARD to health and care workers OR burial teams compared to use of the set of PPE that allows exposure of some parts of contact skin (e.g. neck, head)?
- Are there alternative agents for glove disinfection that are equal or superior to chlorine in terms of their germicidal effect (log reduction) on EBOV/MARV, but that are less toxic for humans, less of an environmental hazard, better in terms of cost-effectiveness and acceptability?

Box A.2.2. Intermediate priorities research questions for infection prevention and control related to Ebola Disease and Marburg Disease.

- What is the difference in efficacy (log reduction) of EBOV/MARV on exterior gloves by washing with chlorine compared to alcohol hand rub after a four-step procedure*? [Current WHO-recommended procedure is: (1) double-gloved hands are washed with chlorine, then (2) exterior gloves removed, (3) interior gloves washed with chlorine, and (4) a new exterior glove is put on.]*
- What are the methods to assess the impact of IPC interventions in different settings (e.g. rural versus urban areas, primary care, Ebola disease treatment units to reduce the risk of EBOD/MARD transmission?
- What are the incidence and prevalence rates of health care-associated infections caused by EBOD/MARD (for inpatients/outpatients) during community EBOD/MARD outbreaks?
- Is there a significant difference in the risk of health and care worker contamination by EBOV/MARV between different procedures for putting on and taking off the full set of PPE?
- What is the feasibility and acceptability within the community of processing EBOV/MARV-contaminated linen by boiling it versus machine-washing it in hot water versus incinerating it?
- What are the risks of EBOD/MARD transmission to staff/persons handling contaminated linens by washing manually compared to machine washing?
- Are there alternative disinfectants that are equal to or superior to chlorine in terms of their germicidal efficacy (log reduction), but that are less toxic to humans and the environment?
- What is the germicidal efficacy (log reduction) of EBOV/MARV on different surfaces (e.g. wood materials, ceramics) comparing the methods of spraying OR wiping with chlorine and alternative disinfectants?
- Does disinfection of the external body bag after the body preparation reduce the concentration of EBOV/MARV enough to safely handle compared to no disinfection?
- How many times can a reusable biodegradable apron be used until the integrity of the apron's material is compromised compared to that of a non-biodegradable apron?
- What is the risk of EBOD/MARD transmission through intact skin?
- Are any future designs for face protection equivalent or superior to the current set of masks and face shield for EBOD/MARD health care, regarding the safety, usability, reduced environmental impact and cost saving?
- How to measure the impact of the IPC ring approach during EBOD/MARD outbreaks compared to not using the IPC ring approach?
- Are any future designs for full body protection equivalent or superior to the current set of PPE for EBOD/MARD health care, regarding the safety, usability, reduced environment impact, and cost saving?
- How long does EBOV/MARV survive on different surfaces (e.g. porous and non-porous) if desiccated in organic material?
- Does wiping with chlorine (compared with spraying with chlorine or an alternative disinfectant) result in a significant log reduction in the concentration of EBOV/MARV on body surfaces and the external surfaces of body bags?
- What is the concentration of EBOV/MARV on skin surfaces and orifices of dead bodies, duration of persistence of viable infective concentrations?
- What are the relative concentrations of EBOV/MARV across the various Ebola disease treatment unit environment surfaces and how do these concentrations relate to the types of activities performed?

Box A.2.3. Lower priorities research questions for infection prevention and control related to Ebola Disease and Marburg Disease.

- What is the EBOD/MARD risk of transmission by using the wiping method versus the spraying method for routine surface disinfection?
- What are the incidence and prevalence rates of other epidemiologically relevant pathogens (e.g. methicillin-resistant *Staphylococcus aureus*) in Ebola disease treatment units?
- What are the concentrations of EBOV/MARV on different pieces of PPE (e.g. gowns, gloves, face shield) before the removal procedure?
- What is the most accurate definition of health care-associated infections caused by EBOV/MARV during community outbreaks?
- What is viral load range on external surfaces of gloves of health and care workers immediately after they care for EBOD/MARD patients?
- What is the germicidal efficacy (log reduction) of EBOV/MARV associated with immersing various types of linens in different concentration of chlorine solution compared with alternative disinfection methods?
- Is there a significant difference between mortality rates among patients with health care associated infections caused by EBOV/MARV compared to overall mortality caused by EBOV/MARV?
- Is the lab simulation with fluorescent marker equivalent OR non-inferior to the use in the real world of actual organic materials (blood and body fluids) in identifying the risk of contamination by EBOV/MARV during health care assistance procedures?
- Is Phi6 an appropriate surrogate in lab settings to simulate EBOV/MARV contamination patterns for different surfaces (e.g. wood, skin) compared to the actual EBOV/MARV?

For further information, please contact:
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