

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	A cluster randomised trial of cloth masks compared to medical masks in healthcare workers
AUTHORS	MacIntyre, Raina; Seale, Holly; Dung, Tham; Hien, Nguyen; Nga, Phan; Chughtai, Abrar; Rahman, Bayzidur; Dwyer, Dominic; Wang, Quanyi

VERSION 1 - REVIEW

REVIEWER	Kathleen Harriman California Department of Public Health USA
REVIEW RETURNED	15-Sep-2014

GENERAL COMMENTS	<p>Although cloth masks are used by healthcare workers in some parts of the world, they have never been tested for efficacy in a RCT. The aim of this study was to compare the efficacy of cloth masks with medical masks and a control group (using masks per their routine). This study presents strong evidence demonstrating the lack of efficacy of cloth masks. This is important information for decision makers in countries where cloth masks are used.</p> <p>Specific comments</p> <p>Introduction section: It would be helpful if more information about the use of masks by Asian healthcare workers were provided, ie, masks are used more frequently by HCWs in Asia than by HCWs in other parts of the world. Page 4, paragraph 2, sentence 3: The word "wealth" should be "wealthy".</p> <p>Methods section: Page 6, paragraph 3, sentence 1 (Intervention): It would be helpful to add information about when in the year (season) this study took place. I assume that all hospitals participated in the study during the same time period, but this should be stated as well. Page 6, paragraph 3, sentence 3: What were the cleaning instructions that were provided for cloth masks? Were they to be cleaned each day they were used? Page 6, paragraph 3, sentence 5: It would be helpful to mention here that HCWs in the control group may have used either cloth masks or medical masks if they used masks.</p> <p>Page 7, paragraph 1, sentence 4: It would be helpful to provide some examples of aerosol-generating procedures for readers who may not be familiar with this term.</p>
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	<p>Page 9, paragraph 2, sentence 1: It would be helpful to state here that HCWs in the control arm may have used a cloth mask or a medical mask.</p> <p>Page 15, paragraph 1, sentence 3: It would be helpful to state here that medical masks were worn more often by HCWs in the control arm than were cloth masks.</p> <p>Page 16, paragraph 1, sentence 2: Add reference regarding airborne transmission of rhinovirus.</p> <p>Page 16, paragraph 2, sentence 2: This sentence should start with the word "This".</p> <p>Page 16, paragraph 2, sentence 4: I think that based upon the results of this study, it could be argued that cloth masks should not be used in even low-risk healthcare settings (it would be helpful to define "high-risk", I assume this means in a setting where a serious disease could be transmitted to HCWs).</p> <p>Page 16, paragraph 5, sentence 1: I would suggest changing the word "sterilisation" to "cleaning".</p> <p>Page 17, paragraph 1, sentence 3: I would suggest adding the word "some" before the word "reassurance".</p> <p>Page 17, paragraph 1, sentence 4: I would suggest editing the sentence to read, "...used to provide protection against droplet spread, and ...".</p> <p>Page 17, paragraph 1, sentence 5: Sentence should be edited to read, "...also recommend the use of medical masks to prevent transmission of...".</p> <p>Page 17, paragraph 1, sentence 7: Because medical masks do not offer optimal protection against pathogens transmitted by aerosols, I would suggest editing this sentence to read, "...cloth mask use to improve occupational...".</p>
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REVIEWER	Ronald Shaffer Centers for Disease Control and Prevention United States of America
REVIEW RETURNED	17-Oct-2014

GENERAL COMMENTS	<p>This manuscript describes a timely study given the current Ebola outbreak. The MacIntyre group has published a number of studies using similar methodology and statistical methods. I believe those methods are appropriate for studying cloth vs. medical masks, but a second opinion on the statistics would not be unreasonable (I'll defer to the editor on that issue). There are a number of limitations to the data (understandable given the challenges of RCT involving respirators or facemasks), but the authors have done a reasonable job of explaining them. The results are interesting, but not overwhelmingly compelling. I have made some suggestions in the remarks to the authors to downplay some of their more provocative recommendations in the abstract and discussion sections. Overall, I recommend publishing this paper with minor revisions. It will certainly add to the growing body of evidence relating to the use of masks in healthcare settings for prevention of infectious respiratory diseases</p> <p>Abstract: 2nd line in conclusion. I don't think the evidence is strong. Suggest changing to "present evidence against the use..."</p>
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Abstract: last sentence. I think the evidence provided, while interesting and indicating the need for further research, is not strong enough to justify the statement that cloth masks should not be recommended without context. I would be comfortable with that recommendation if some tempering language were added. I would suggest writing “However, as a precautionary measure, cloth masks should not be recommended at this time for HCWs, and guidelines need to be updated. Further research is needed to better validate these findings.”

Page 3. Article summary. 4th bullet. Delete “urgently” and insert “as a precautionary measure” after updated. Change “advice” to “advise”

Page 4. Introduction. The authors write that studies on cloth masks are outdated. I would disagree with that characterization. Reference #6 includes many studies from the past 10 years. In fact, there was a paper just published a few months back in Aerosol and Air Quality Research on filtration performance of cloth masks. I believe that the majority of the filter/respirator community has known for some time that cloth masks provide little, if any, protection against small particle aerosols. If worn and used properly, it has been thought by some that cloth masks could provide a convenient means of blocking direct sprays from reaching the mucous membranes and preventing the user touching their oronasal region. I think the data in this paper will certainly help us understand what role, if any, cloth masks can play in public health.

Page 5. Methods. Can the authors expand upon what they mean by “continuous use”? Does this include breaks for lunch or to take a drink of water or to use the rest room? What about non-patient activities such as staff meetings, typing up notes, etc.

Page 7. Data collection. I was very happy to see that the authors collected estimated number of patient contacts. However, I didn’t see that in the results or discussion section. Exposure assessment involves frequency and duration. This is very important data. I would strongly encourage this be reported in the final version of the manuscript. If the frequency of exposures was small, it would be suggestive that subjects became infected during exposures outside the workplace.

Page 9. Line 8. It says that a significance level of 0.25 was used. Is this a typo? I am used to seeing 0.05.

Page 13-14. Discussion of Table 6. While I appreciate the value of comparing the 3 studies there are significant differences that make generalization difficult. These are discussed in methods section of the manuscript, however, I also think the authors should note that the non-mask control group in ref #12 had a lab confirmed virus rate of 3.1% (15/481), which is less than the Vietnam trial (current paper).

Pages 15-16. Although the authors allude to this, it may be good to explicitly mention the possibility that improper doffing of a contaminated cloth mask may transfer pathogen from the mask to the bare hands of the wearer. This issue would be magnified with repeated reuses, especially if not cleaned properly. Some models have been developed to quantify contamination levels of masks that may be helpful to mention here in this context. Fisher et al, Validation and application of models to predict facemask influenza contamination in healthcare settings. Risk Anal. 2014 34(8):1423-34.

	<p>Page 16. I think the characterization that rhinovirus is an “airborne” disease could be misunderstood by the audience. CDC in its HICPAC guidance (http://www.cdc.gov/hicpac/2007ip/2007isolationprecautions.html) indicates that droplet precautions should be used for rhinovirus and contact precautions under certain conditions. There are multiple modes of disease transmission (contact, droplet sprays, small particle aerosol, etc.). I am concerned that airborne can be confused for aerosol transmitted disease (e.g., measles, TB, etc.). I think references are needed and some clarifying statements are needed to point out the different modes of transmission for rhinoviruses and how masks help block 2 of them (e.g., blocking direct sprays from reaching the mucous membranes and preventing the user touching their oronasal region).</p> <p>Page 16. Two other limitations that should be mentioned include the lack of data on exposures outside the workplace and lack of data on asymptomatic workers. This would be a much stronger study with those kinds of data. I recognize that they are not easy to obtain.</p> <p>Page 17. Last two sentences. Similar to my comments to the abstract: Insert “as a precautionary measure” and delete “urgently”.</p>
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REVIEWER	Lisa Casanova Georgia State University United States
REVIEW RETURNED	19-Oct-2014

GENERAL COMMENTS	<p>Suggest using a more precise term than "medical mask" in the title. What exactly a "medical mask" is needs to be more precisely described. Is this what is usually referred to as a surgical mask? Is there any use of N95 respirators in this setting? "In-vitro and experimental studies are sparse, inadequate and out-dated" (page 4, line 30). Briefly explain why.</p> <p>Was there any attempt to control for outside of work exposures? There are a large number of cases of rhinovirus, which may have been acquired outside of the occupational setting.</p> <p>Since there was only one laboratory confirmed influenza, influenza like illness does not seem like an appropriate endpoint here. What is its significance if there is no actual influenza found?</p> <p>On page 12, the discussion of compliance states "A post-hoc analysis adjusted for compliance and other potential confounders showed that the rate of ILI was significantly higher in cloth mask arm (RR 13.00, 95% CI 1.69 to 100.07), compared to the medical masks arm (Table 4). There was no significant difference between the medical mask and control arms." Is there a compliance-adjusted estimate for the difference between the cloth mask and control arm? What potential confounders are adjusted for? They should be stated.</p> <p>There is a lot of focus on influenza like illness and the significant results for ILI. There needs to be some further analysis of what is actually going on here, since the laboratory confirmed illness is mostly rhinovirus. What exactly is being prevented here? If most of</p>
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	<p>the detectable illness is rhinovirus, the significant effect of handwashing observed may be one of the more important things going on in this situation.</p> <p>The discussion is somewhat confusing. Although the authors state that this trial cannot determine if differences are due to efficacy of medical masks, there is a great deal of discussion of medical mask efficacy. Suggest taking this out. It seem that an important issue here is not efficacy of medical masks, but compliance. Is the difference between the cloth mask and control arm a difference in the mask itself or a difference in compliance? This seems like a significant issue that is under-explored in the discussion, since the compliance rates between the intervention and control arms are very different. Also, what does compliance look like in this population? How are masks worn? When? What triggers mask wearing? This needs more explanation.</p>
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REVIEWER	Adrian Barnett Queensland University of Technology, Australia
REVIEW RETURNED	04-Feb-2015

GENERAL COMMENTS	<p>This is an interesting paper with potentially important conclusions. The study appears to be well conducted. The results show a consistently higher risk of using a cloth mask in both the main and sensitivity analyses.</p> <p>What was the role of 3M? Did they provide any materials/masks? Did they have any input in the study results or control over the decision to publish?</p> <p>Recruitment was back in 2011, so why has it taken so long to publish the results? This seems particularly important given the authors' recommendation for 'urgently updated' guidelines.</p> <p>What time periods were the primary endpoints collected over?</p> <p>There were three primary endpoints, but the abstract only highlights the statistically significant one. It would be prudent to also mention the two other primary endpoints.</p> <p>Just because a variable is statistically significant that does not mean that it is a confounder (page 9 line 18). As this is a randomised design we should be surprised to find any confounders. Instead any other significant variables are likely to be independent predictors.</p> <p>It's not appropriate to use a statistical test to compare randomised groups at baseline (Table 1). See the CONSORT guidelines or papers by Doug Altman for details.</p> <p>Just because there was no difference between the results here and the previous two studies (page 13, line 42) that does not mean they were equivalent. Equivalence is usually determined by specifying a priori clinical important limits for the confidence interval.</p> <p>How were the previously published RCTs identified? From a systematic review?</p>
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	<p>Minor comments</p> <ul style="list-style-type: none"> - It would be nice to have a figure showing a photo of a typical cloth mask and medical mask. - page 4, line 25, typo 'wealthy' not 'wealth' - page 8, line 45, missing 'of' before 'sample size', and use 'participants' rather than 'subjects' for consistency - page 8, line 57, missing 'variables' after 'categorical' - page 9, lines 6-13, these two sentences are almost identical; I would delete one. - page 11, line 8 (and elsewhere) it's good practice to prefix every 'significant' with either 'statistically' or 'clinically' - page 12, line 38, 'In the control arm...' add 'the' - Table 5, change column heading from 'multivariate' to 'adjusted' to match table title - Table 6, the decimal places for the percents are inconsistent - Page 15, line 48, it's not clear what the 94 percent reduction refers to, is that absolute risk? - Page 15, line 51, is the virus isolation the lab confirmed results in table 6? - Page 16, line 16, 'They have been used in' rather than 'It has been reported in' - Page 17, line 18, 'provide some reassurance' add 'some' - Page 17, line 18, or ludicrously short expiry dates - Acknowledgements, first line, grant number needed - Is there any data or comments on comfort, and how this might effect compliance? Especially as you are looking at continuous use. - Is it worth mentioning that the follow-up period had the same calendar time?
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Introduction section:

1. It would be helpful if more information about the use of masks by Asian healthcare workers were provided, ie, masks are used more frequently by HCWs in Asia than by HCWs in other parts of the world.

Authors' reply: We have added a statement and supporting references about the common use of masks in Asian countries. Please see page 4, para 1 and references 8-11.

2. Page 4, paragraph 2, sentence 3: The word "wealth" should be "wealthy".

Authors' reply: This has been corrected, please see page 4, para 2.

Methods section:

3. Page 6, paragraph 3, sentence 1 (Intervention): It would be helpful to add information about when in the year (season) this study took place. I assume that all hospitals participated in the study during the same time period, but this should be stated as well.

Authors' reply: The detail about the timing of study was provided in the "methods section" (lines 2-3, para 1 of Methods). We have added the requested details. Please see Methods, page 5, para 1, lines 3 to 5.

4. Page 6, paragraph 3, sentence 3: What were the cleaning instructions that were provided for cloth masks? Were they to be cleaned each day they were used?

Authors' reply: The "Intervention" section has been revised and details have been added. Participants were asked to wash cloth masks with soap and water every day after finishing the work shift. Please see page 7, para 1.

5. Page 6, paragraph 3, sentence 5: It would be helpful to mention here that HCWs in the control group may have used either cloth masks or medical masks if they used masks.

Authors' reply: We have mentioned that, "the control group was asked to continue with their normal practices, which may or may not have included mask wearing" (Page 6, para 3). This could be any type of masks. The detail of the type used by control arm is provided on page 13, para 2. It states, "In control arm 170/458 (37%) used medical masks, 38/458 (8%) used cloth masks and 245/458 (53%) used a combination of both medical and cloth masks during the study period. The remaining 1% either reported using a N95 respirator (n=3) or did not use any masks (n=2)".

6. Page 7, paragraph 1, sentence 4: It would be helpful to provide some examples of aerosol-generating procedures for readers who may not be familiar with this term.

Authors' reply: We have added further detail on aerosol-generating procedures, i.e. "suctioning of airways, sputum induction, endotracheal Intubation and bronchoscopy". Please see page 7, para 2.

7. Page 9, paragraph 2, sentence 1: It would be helpful to state here that HCWs in the control arm may have used a cloth mask or a medical mask.

Authors' reply: We have revised the sentence. Please see page 9, para 2. Participants in the control arm were asked to go about their normal clinical practice, which may have involved use of any type of masks, including medical and cloth masks. The detail of the type used by the control arm is provided on page 13, directly below Table 4. It states, "In the control arm 170/458 (37%) used medical masks, 38/458 (8%) used cloth masks and 245/458 (53%) used a combination of both medical and cloth masks during the study period. The remaining 1% either reported using a N95 respirator (n=3) or did not use any masks (n=2)".

8. Page 15, paragraph 1, sentence 3: It would be helpful to state here that medical masks were worn more often by HCWs in the control arm than were cloth masks.

Authors' reply: We have added a sentence to the discussion. It states, "The control HCWs also used medical masks more often than cloth masks". Please see page 16, para 1.

9. Page 16, paragraph 1, sentence 2: Add reference regarding airborne transmission of rhinovirus.

Authors' reply: Two references have been added. Please see references 31 and 32.

32. Dick EC, Jennings LC, Mink KA, et al. Aerosol transmission of rhinovirus colds. *J Infect Dis.* 1987 Sep;156(3):442-448.

33. Bischoff WE. Transmission route of rhinovirus type 39 in a monodispersed airborne aerosol. *Infect Control Hosp Epidemiol.* 2010 Aug;31(8):857-859.

10. Page 16, paragraph 2, sentence 2: This sentence should start with the word "This".

Authors' reply: Revised accordingly, please see page 17, para 2.

11. Page 16, paragraph 2, sentence 4: I think that based upon the results of this study, it could be argued that cloth masks should not be used in even low-risk healthcare settings (it would be helpful to define "high-risk", I assume this means in a setting where a serious disease could be transmitted to HCWs).

Authors' reply: We have revised the text and added detail about high risk situations based on our previous research. Please see page 17, para 2.

12. Page 16, paragraph 5, sentence 1: I would suggest changing the word "sterilisation" to "cleaning".

Authors' reply: Revised accordingly, please see page 18, para 3.

13. Page 17, paragraph 1, sentence 3: I would suggest adding the word "some" before the word "reassurance".

Authors' reply: Revised accordingly, please see page 18, para 4.

14. Page 17, paragraph 1, sentence 4: I would suggest editing the sentence to read, "...used to provide protection against droplet spread, and ...".

Authors' reply: Revised accordingly, please see page 18, para 4.

15. Page 17, paragraph 1, sentence 5: Sentence should be edited to read, "...also recommend the use of medical masks to prevent transmission of...".

Authors' reply: Revised accordingly, please see page 18, para 4 and page 19, para 1. As CDC also updated its Ebola guidelines in October 2014, the text and reference have been updated.

16. Page 17, paragraph 1, sentence 7: Because medical masks do not offer optimal protection against pathogens transmitted by aerosols, I would suggest editing this sentence to read, "...cloth mask use to improve occupational...".

Authors' reply: Revised accordingly, please see page 19, para 1.

Reviewer: 2

1. Abstract 2nd line in conclusion. I don't think the evidence is strong. Suggest changing to "present evidence against the use..."

Authors' reply: Revised accordingly, please see page 2, conclusion of the abstract.

2. Last sentence. I think the evidence provided, while interesting and indicating the need for further research, is not strong enough to justify the statement that cloth masks should not be recommended without context. I would be comfortable with that recommendation if some tempering language were added. I would suggest writing "However, as a precautionary measure, cloth masks should not be recommended at this time for HCWs, and guidelines need to be updated. Further research is needed to better validate these findings."

Authors' reply: The abstract has been revised along the suggested lines, please see page 2, conclusion section of the abstract.

3. Page 3. Article summary. 4th bullet. Delete "urgently" and insert "as a precautionary measure" after updated. Change "advice" to "advise"

Authors' reply: The summary has been revised accordingly, please see page 3, article summary.

4. Page 4. Introduction. The authors write that studies on cloth masks are outdated. I would disagree with that characterization. Reference #6 includes many studies from the past 10 years. In fact, there was a paper just published a few months back in Aerosol and Air Quality Research on filtration performance of cloth masks. I believe that the majority of the filter/respirator community has known for some time that cloth masks provide little, if any, protection against small particle aerosols. If worn and used properly, it has been thought by some that cloth masks could provide a convenient means of blocking direct sprays from reaching the mucous membranes and preventing the user touching their oronasal region. I think the data in this paper will certainly help us understand what role, if any, cloth masks can play in public health.

Authors' reply: We have revised the introduction as per reviewer's suggestions, and specified that clinical effectiveness studies (rather than all studies) are lacking. Please see page 4, para 2.

5. Page 5. Methods. Can the authors expand upon what they mean by "continuous use"? Does this

include breaks for lunch or to take a drink of water or to use the rest room? What about non-patient activities such as staff meetings, typing up notes, etc.

Authors' reply: We have defined continuous use as wearing masks all the time during a work shift, except whilst in the toilet or during tea or lunch breaks. Please see page 5, para 4.

6. Page 7. Data collection. I was very happy to see that the authors collected estimated number of patient contacts. However, I didn't see that in the results or discussion section. Exposure assessment involves frequency and duration. This is very important data. I would strongly encourage this be reported in the final version of the manuscript. If the frequency of exposures was small, it would be suggestive that subjects became infected during exposures outside the workplace.

Authors' reply: Data on patient contact has been added. Please see page 11, para 1 and table 1.

7. Page 9. Line 8. It says that a significance level of 0.25 was used. Is this a typo? I am used to seeing 0.05.

Authors' reply: The level of 0.25 was taken as a threshold to identify variables suitable for multivariate analysis (not as an indicator of significance). For significance in multivariate analysis, the standard cut-off of <0.05 was used. We have updated text to make this clear. Please see page 9, para 1.

8. Page 13-14. Discussion of Table 6. While I appreciate the value of comparing the 3 studies there are significant differences that make generalization difficult. These are discussed in methods section of the manuscript, however, I also think the authors should note that the non-mask control group in ref #12 had a lab confirmed virus rate of 3.1% (15/481), which is less than the Vietnam trial (current paper).

Authors' reply: The rates vary due to different baseline levels of seasonal virus activity in the two countries at the different times of the three studies. We have acknowledged this limitation and mentioned in the method section that, "..... recognising that seasonal and geographic variation in virus activity affects the rates of exposure (and hence rates of infection outcomes) among HCWs". Please see page 10, para 1. We have also revised the discussion to add the point that the control group in the first Chinese RCT showed a rate of lab confirmed viral infection similar to all three medical mask arms. See page 17, para 1.

9. Pages 15-16. Although the authors allude to this, it may be good to explicitly mention the possibility that improper doffing of a contaminated cloth mask may transfer pathogen from the mask to the bare hands of the wearer. This issue would be magnified with repeated reuses, especially if not cleaned properly. Some models have been developed to quantify contamination levels of masks that may be helpful to mention here in this context. Fisher et al, Validation and application of models to predict facemask influenza contamination in healthcare settings. Risk Anal. 2014 34(8):1423-34.

Authors' reply: We have revised the discussion and added suggested reference. Please see page 16, para 2 and reference no 30.

10. Page 16. I think the characterization that rhinovirus is an "airborne" disease could be misunderstood by the audience. CDC in its HICPAC guidance (<http://www.cdc.gov/hicpac/2007ip/2007isolationprecautions.html>) indicates that droplet precautions should be used for rhinovirus and contact precautions under certain conditions. There are multiple modes of disease transmission (contact, droplet sprays, small particle aerosol, etc.). I am concerned that airborne can be confused for aerosol transmitted disease (e.g., measles, TB, etc.). I think references are needed and some clarifying statements are needed to point out the different modes of transmission for rhinoviruses and how masks help block 2 of them (e.g., blocking direct sprays from reaching the mucous membranes and preventing the user touching their oronasal region).

Authors' reply: We acknowledge that different guidelines vary in their classification of route of transmission of rhinovirus, and have revised this sentence to make it less definitive. Please see page 17, para 1. Please also note that the CDC guideline (referred by review) also states, "For certain other

respiratory infectious agents, such as influenza and rhinovirus and even some gastrointestinal viruses (e.g., norovirus and rotavirus) there is some evidence that the pathogen may be transmitted via small-particle aerosols, under natural and experimental conditions”.

11. Page 16. Two other limitations that should be mentioned include the lack of data on exposures outside the workplace and lack of data on asymptomatic workers. This would be a much stronger study with those kinds of data. I recognize that they are not easy to obtain.

Authors' reply: We have revised the discussion section and added some discussion of exposure to infection outside of the workplace. Please see page 18, para 1.

12. Page 17. Last two sentences. Similar to my comments to the abstract: Insert “as a precautionary measure” and delete “urgently”.

Authors' reply: Edited as per reviews' comments, please see page 19, para 1.

Reviewer: 3

1. Suggest using a more precise term than "medical mask" in the title What exactly a "medical mask" is needs to be more precisely described. Is this what is usually referred to as a surgical mask?

Authors' reply: We have revised the paper by clarifying the definition of “medical mask” in introduction section. Please see page 4 para 1.

Medical mask is most common terminology used by the WHO and other countries in various guidelines and other policy documents. Please see references below.

World Health Organization (WHO). Infection prevention and control of epidemic- and pandemic-prone acute respiratory infections in health care. 2014.

MacIntyre CR, Chughtai AA, Seale H, Richards GA, Davidson PM. Respiratory protection for healthcare workers treating Ebola virus disease (EVD): are facemasks sufficient to meet occupational health and safety obligations? *Int J Nurs Stud.* 2014;51(11):1421-6.

Chughtai AA, Seale H, MacIntyre CR. Availability, consistency and evidence-base of policies and guidelines on the use of mask and respirator to protect hospital health care workers: a global analysis. *BMC Res Notes.* 2013;6(216):1-9

2. Is there any use of N95 respirators in this setting?

Authors' reply: Hospital wards were randomised to one of three arms: medical masks, cloth masks or a control group. The control group followed standard practice, which may or may not include mask use. Our data showed that only 3 participants from control groups used N95 respirators. Please see page 13, para 2.

"In-vitro and experimental studies are sparse, inadequate and out-dated" (page 4, line 30). Briefly explain why.

Authors' reply: We have revised this section as per reviewers' comments. Please see page 4, para 2.

3. Was there any attempt to control for outside of work exposures? There are a large number of cases of rhinovirus, which may have been acquired outside of the occupational setting.

Authors' reply: Whilst we did not measure outside exposure to infection, the RCT design should theoretically equalise the effect of outside exposures between arms. We have revised the discussion section and added some discussion of exposure to infection outside of the workplace. Please see page 18, para 1.

4. Since there was only one laboratory confirmed influenza, influenza like illness does not seem like

an appropriate endpoint here. What is its significance if there is no actual influenza found?

Authors' reply: Influenza like illness (ILI) was a pre-specified endpoint in the trial registration and consort guidelines recommend that results are reported by pre-specified outcomes. The definition of ILI is generally more sensitive in children than adults for influenza, but being a clinical case definitions, captures many infections other than influenza.

5. On page 12, the discussion of compliance states "A post-hoc analysis adjusted for compliance and other potential confounders showed that the rate of ILI was significantly higher in cloth mask arm (RR 13.00, 95% CI 1.69 to 100.07), compared to the medical masks arm (Table 4).

There was no significant difference between the medical mask and control arms." Is there a compliance-adjusted estimate for the difference between the cloth mask and control arm?

What potential confounders are adjusted for? They should be stated.

Authors' reply: The potential confounders (vaccination, hand washing and compliance) are listed in Table 4. All variables listed in Table 1 with p values less than 0.25 were tested in the model, and only those which were significant or clinically important were included in the final model. The methods have been revised to clarify this. Please see page 9, para 1. Compared to the cloth masks arm, the rates of CRI, ILI and laboratory confirmed virus were low in the control arm, however the difference was not statistically significant. The rates of all outcomes were low in control arm due to a high rate of medical mask use by participants in the control arm.

6. There is a lot of focus on influenza like illness and the significant results for ILI. There needs to be some further analysis of what is actually going on here, since the laboratory confirmed illness is mostly rhinovirus. What exactly is being prevented here? If most of the detectable illness is rhinovirus, the significant effect of handwashing observed may be one of the more important things going on in this situation.

Authors' reply: We have added a discussion around the lack of specificity for influenza of the ILI definition 17, para 1; and on hand hygiene (Please see page 16, para 2.)

7. The discussion is somewhat confusing. Although the authors state that this trial cannot determine if differences are due to efficacy of medical masks, there is a great deal of discussion of medical mask efficacy. Suggest taking this out. It seem that an important issue here is not efficacy of medical masks, but compliance.

Is the difference between the cloth mask and control arm a difference in the mask itself or a difference in compliance? This seems like a significant issue that is under-explored in the discussion, since the compliance rates between the intervention and control arms are very different. Also, what does compliance look like in this population? How are masks worn? When? What triggers mask wearing? This needs more explanation.

Authors' reply: Masks were worn for the entire shift of work. The methods have been revised to clarify this (please see page 5, para 4, under "Randomisation"). As compliance rates were different between the arms, we adjusted for compliance in the multivariate models presented in table 3 and 4. The results, therefore, are independent of compliance. The finding of a high risk of infection with cloth masks is relative to medical masks, so the inverse explanation (of efficacy of medical masks) needs to be considered. The study was about cloth and medical masks, so we feel some discussion of the efficacy of both types of masks is needed. We have revised the discussion section in parts, also aligning this with suggestions from other reviewers. Please see page 16 para 1 & 2 and page 17 para 1-2 and page 18 para 1. We are conducting a separate study to examine the factors associated with compliance with the masks use.

Reviewer: 4

1. What was the role of 3M? Did they provide any materials/masks?

Authors' reply: 3M were the industry partner in the Australian Research Council Linkage Grant which

supported the study. 3M conducted testing of filtration of the facemasks. They did not provide any materials or masks, nor were their products used in the study. The statement of acknowledgments has been updated to make this clear. Please see page 20 para 1.

2. Did they have any input in the study results or control over the decision to publish?

Authors' reply: 3M did not have any input in the study results or control over the decision to publish. Please see response above and updated statement on page 20, para 1.

3. Recruitment was back in 2011, so why has it taken so long to publish the results? This seems particularly important given the authors' recommendation for 'urgently updated' guidelines.

The delay was due to the following reasons.

- Data were collected in Vietnamese language and there was a delay in waiting for translation of questionnaires into English.
- The grant funding did not cover the full study, so we had to wait for Vietnamese colleagues to be free to work on the study after recruitment (such as translation) and follow up was finished.
- Data cleaning.
- The preliminary data analysis was completed in 2012- 2013 and the Australian investigators travelled to Vietnam in July 2013 to check the data, discuss the preliminary results and plan publication. This included consultation with government stakeholders in Vietnam, as the National Institute of Hygiene and Epidemiology is a government institution.
- A long process of approvals for publication from the Vietnamese stakeholders
- The manuscript was submitted to BMJ Open in September 2014 and we did not receive feedback until February 2015.

4. What time periods were the primary endpoints collected over?

Authors' reply: Primary endpoints were collected over 4 weeks of mask wearing in March 2011 and for 1 week afterwards to account for the incubation period of common viruses. The methods have been updated to clarify the recruitment and follow up period (see page 5, para 1)

5. There were three primary endpoints, but the abstract only highlights the statistically significant one. It would be prudent to also mention the two other primary endpoints.

Authors' reply: A statement about the other outcomes being non-significant has been added to the abstract, raising the word count slightly above the limit.

6. Just because a variable is statistically significant that does not mean that it is a confounder (page 9 line 18). As this is a randomised design we should be surprised to find any confounders. Instead any other significant variables are likely to be independent predictors.

Authors' reply: We agree with this point. However, despite the RCT design, variables can still be unequally distributed between arms, as seen in Table 1. The standard approach to RCT analysis is intention-to-treat analysis, but if unequal distribution of variables is found between arms, they should be adjusted for and presented along with ITT results. As such we have presented both the ITT (Table 2) and adjusted analyses. We have revised the methods (page 9, para 1) to clarify this.

7. It's not appropriate to use a statistical test to compare randomised groups at baseline (Table 1).

See the CONSORT guidelines or papers by Doug Altman for details.

Authors' reply: As suggested by the reviewer, we have removed p-values from the table 1. Please see page table 1, page 11.

8. Just because there was no difference between the results here and the previous two studies (page 13, line 42) that does not mean they were equivalent. Equivalence is usually determined by specifying a priori clinical important limits for the confidence interval.

Authors' reply: We would like to clarify that we are not making any assumption of equivalence. We are saying that similar rates of laboratory confirmed viruses in previous trials, in which no efficacy of medical masks could be demonstrated, support that the difference we observed is not due to a protective effect of medical masks, but due to a detrimental effect of cloth masks. We felt this was an important additional analysis, because we did not have a no-mask control group. We have revised the method section (please see page 9 para 3 to beginning of page 10) and discussion (page 17, para 1).

9. How were the previously published RCTs identified? From a systematic review?

Authors' reply: We have recently conducted a systematic review on facemasks which is in press (Please see reference below). We identified 4 RCTs in healthcare setting, of which 2 (mentioned in table 6) were conducted by our group. We have revised the introduction section to add this reference. Please see page 4 para 2 and reference no 15.

MacIntyre CR, Chughtai AA. Facemasks for the prevention of infection in healthcare and community settings. *BMJ* (In press). 2015.

Minor comments

10. It would be nice to have a figure showing a photo of a typical cloth mask and medical mask.

Authors' reply: We are happy to provide photos if the editor agrees.

11. page 4, line 25, typo 'wealthy' not 'wealth'

Authors' reply: Revised, please see page 4 para 2.

12. page 8, line 45, missing 'of' before 'sample size', and use 'participants' rather than 'subjects' for consistency

Authors' reply: Revised accordingly, please see page 9 para 1.

13. page 8, line 57, missing 'variables' after 'categorical'

Authors' reply: This sentence has been deleted as suggested by other reviewer, please see page 9 para 2.

14. page 9, lines 6-13, these two sentences are almost identical; I would delete one.

Authors' reply: Two analyses were different. Table 4 was adjusted for clustering and table 5 was not adjusted for clustering. We have added that, "As we pooled data of participants from all 3 arms and analysed by mask type, not trial arm, we did not adjusted for clustering here". Please see page 9 para 2.

15. page 11, line 8 (and elsewhere) it's good practice to prefix every 'significant' with either 'statistically' or 'clinically'

Authors' reply: Revised accordingly, please see page 12 para 1.

16. page 12, line 38, 'In the control arm...' add 'the'

Authors' reply: Revised accordingly, please see page 13 para 2.

17. Table 5, change column heading from 'multivariate' to 'adjusted' to match table title

Authors' reply: Revised accordingly, please see table 5.

18. Table 6, the decimal places for the percents are inconsistent

Authors' reply: Revised accordingly, please see table 6.

19. Page 15, line 48, it's not clear what the 94 percent reduction refers to, is that absolute risk?

Authors' reply: The RR of ILI in cloth mask arm compared to the medical mask arm was 13, which is translated into 92% efficacy. The efficacy is 1-RR, and the RR of medical masks is the inverse of that for cloth masks. The figure should read 92% and has been revised. Please see page 17, para 1.

20. Page 15, line 51, is the virus isolation the lab confirmed results in table 6?

Authors' reply: Yes, virus isolation is lab confirmed results in table 6. We have changed the text to "laboratory confirmed viruses". Please see page 14 para 2.

21. Page 16, line 16, 'They have been used in' rather than 'It has been reported in'

Authors' reply: Revised accordingly, please see page 17 para 2.

22. Page 17, line 18, 'provide some reassurance' add 'some'

Authors' reply: Revised accordingly please see page 18 para 4.

23. Acknowledgements, first line, grant number needed

Authors' reply: Grant number added. Please see page 20.

24. Is there any data or comments on comfort, and how this might effect compliance? Especially as you are looking at continuous use.

Authors' reply: As compliance rates were different between the arms, we adjusted for compliance in both table 3 and 4. We have another detailed paper on comfort in preparation, but have added basic data on comfort.

"Adverse events associated with facemask use were reported in 40.4% (227/562) of HCWs in the medical mask arm and 42.6% (242/568) in the cloth mask arm (P-value 0.450). General discomfort (35.1%, 397/1130) and breathing problems (18.3%, 207/1130) were most frequently reported adverse events."

Please see page 15 para 1.

25. Is it worth mentioning that the follow-up period had the same calendar time?

Authors' reply: We have added this in the method sections. Please see page 5 para 1.

Reviewer 5: Statistical comments

1. They need to state what they mean by a ³medical mask² as surely a cloth mask is being used as a ³medical mask². Should they say disposable² or ³paper² for medical mask. Am I missing something here?

Authors' reply: We have revised the paper and defined "medical mask" and "cloth mask" in the introduction section. Please see page 4, para 1.

2. I agree with Barnett they should state the role of 3M.

Authors' reply: The role of 3M has been specified. Please see page 20 para 1.

3. How did they exclude the possibility of getting an infection from elsewhere (eg the journey to and from work?)

Authors' reply: We did not measure outside exposures. We have updated discussion section and added a commentary about the effect of infections acquired outside of work. Please see page 17, para 3 and page 18 para 1.

4. Why has this taken so long to write up? (conducted over 4 weeks>in March 2011)

The delay was due to the following reasons.

- Data were collected in Vietnamese language and there was a delay in waiting for translation of questionnaires into English.

- The grant funding did not cover the full study, so we had to wait for Vietnamese colleagues to be free to work on the study after recruitment (such as translation) and follow up was finished.
- Data cleaning.
- The preliminary data analysis was completed in 2012- 2013 and the Australian investigators travelled to Vietnam in July 2013 to check the data, discuss the preliminary results and plan publication. This included consultation with government stakeholders in Vietnam, as the National Institute of Hygiene and Epidemiology is a government institution.
- A long process of approvals for publication from the Vietnamese stakeholders
- The manuscript was submitted to BMJ Open in September 2014 and we did not receive feedback until February 2015.

5. Were the cloth masks ever changed?

Authors' reply: Participants in the cloth mask arm were provided with five masks in total for the study duration, which they were asked to wash and rotate over the study period. Cloth masks were not changed over the study period. Please see page 6 para 4.

6. Can they comment on whether there was any blinding of assessors?

Authors' reply: The laboratory results were blinded and laboratory testing was conducted in a blinded fashion. As facemask use is a visible intervention, clinical endpoints could not be blinded. The methods have been revised to clarify this (see page 6, para 1, line 1)

7. They need to tone down their conclusion - reviewers suggest this too as their findings are not definitive.

Authors' reply: We have revised the conclusion as per reviewers' comments. Please see page 2 conclusion section of the abstract, page 18 para 4 and page 19 para 1.

VERSION 2 – REVIEW

REVIEWER	Kathleen Hariman California Department of Public Health, USA.
REVIEW RETURNED	08-Mar-2015

GENERAL COMMENTS	This is a revised version of a manuscript that has already been reviewed. The authors have adequately addressed my comments and those of the other reviewers.
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REVIEWER	Lisa Casanova Georgia State University USA
REVIEW RETURNED	19-Mar-2015

GENERAL COMMENTS	The authors have provided comprehensive responses to most reviewer comments. The results suggest that there may be significant effects of both masks and handwashing, since rhinovirus played such an important role in this study. I would suggest some additional discussion on lack of handwashing measurement as a limitation.
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REVIEWER	Adrian Barnett Queensland University of Technology Australia
REVIEW RETURNED	05-Mar-2015

GENERAL COMMENTS	<p>The authors have answered all my previous queries. I have only a few minor comments. I still think a photo of the masks would be useful, the authors want the editors to decide this.</p> <ul style="list-style-type: none"> - 'statistically' in front of new 'significant' in the Results section of the abstract - page 7, line 25, what type of thermometer? - page 9, line 28, 'had' not 'have' - Table 1, decimal places vary for percents. Actually it may be best to use integers for the percents as there are a lot of numbers to take in - page 14, line 13, 'were remained' don't need the 'were' - page 15, line 38, 'were the most' added 'the' - page 17, line 44, I would imagine that the full-stop should come after the personal communication reference. - Figure 2, one decimal place should be fine
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VERSION 2 – AUTHOR RESPONSE

Reviewer: 1

1. I still think a photo of the masks would be useful, the authors want the editors to decide this.

Authors' reply: We are happy to provide photos if the editor agrees. Some examples are attached in supplementary file.

2. 'statistically' in front of new 'significant' in the Results section of the abstract

Authors' reply: Revised accordingly, please see page 2, result section of the abstract.

3. page 7, line 25, what type of thermometer?

Authors' reply: A traditional glass mercury thermometer was provided. We have added the relevant details, please see page 7, para 2.

4. page 9, line 28, 'had' not 'have'

Authors' reply: Revised accordingly, please see page 9, para 1.

5. Table 1, decimal places vary for percents. Actually it may be best to use integers for the percents as there are a lot of numbers to take in

Authors' reply: For consistency, we used integers for the continuous variables, such as age, number of hand wash and number of patients seen and we placed one decimal point for all rates in the table 1, please see page 11.

6. page 14, line 13, 'were remained' don't need the 'were'

Authors' reply: Revised accordingly, please see page 13, last para.

7- page 15, line 38, 'were the most' added 'the'

Authors' reply: Revised accordingly, please see page 15, para 1.

8- page 17, line 44, I would imagine that the full-stop should come after the personal communication reference.

Authors' reply: Revised accordingly, please see page 17, last para.

9- Figure 2, one decimal place should be fine

Authors' reply: We have edited figure 1 and placed one decimal point. Please see figure 1 in separate file.

Reviewer: 2

This is a revised version of a manuscript that has already been reviewed. The authors have adequately addressed my comments and those of the other reviewers.

Reviewer: 3

1. The results suggest that there may be significant effects of both masks and handwashing, since rhinovirus played such an important role in this study. I would suggest some additional discussion on lack of handwashing measurement as a limitation.

Authors' reply: We have added discussion around the limitations of self-report of hand washing measures, please see page 18, para 1.