

Peer Review File

Article information: <http://dx.doi.org/10.21037/atm-20-6005>

Reviewer A

Comment 1: Line 127: Need to describe what the “Review Manager 5.3 software” does and how you are able to conclude that the frequency of handwashing included in the same range can be synthesized”. Also need to define “synthesized” for the reader that is new to / unfamiliar with that technique.

Reply 1: Thank you for your good comments and suggestions, which have enhanced the readability and clarity of our study. (1) We added some description of what the “Review Manager 5.3 software” does (see Page 7, line 148-156). (2) We concluded the frequency of handwashing in the same range according to the report of included studies (see Table 1). (3) “Synthesized” means “could be conducted meta-analysis”. We have revised “synthesize” to “conducted meta-analysis” to make the reader understand easily (see Page 6, line 132).

Comment 2: Lines 273-275: The “detailed educational plan” for healthcare workers has been developed by the World Health Organization and the CDC in their hand hygiene guidelines and website materials. They should be referenced at least and point out the need for the user (e.g. hospital) to adapt it to their culture and think of hand hygiene as a whole system (handwashing + alcohol-based hand sanitizer + gloving – used at different times and dependent on key variables, such as whether hands are visibly soiled). I think you should mention that in this section of the manuscript.

Reply 2: Thank you for this good suggestion. We have added mention in this section of the manuscript (see Page 14, line 317-319). The specific content is as follows “These can refer to the WHO and the CDC in their hand hygiene guidelines and website materials and the need for the user (e.g. hospital) to adapt it to their culture and think of hand hygiene as a whole system (41, 42).”

Comment 3: Lines 281-284: “Additionally, the impact of hand washing is influenced by many confounding factors (such as the standardization of hand washing methods, the cleaning agents used, religious culture, and the risk of disease exposure in the population), which may reduce the reliability of the results.” These limitations are

incomplete, overly simplified, and grossly understated. There are many other factors that impact hand washing efficacy (e.g. soap formulation, dose, delivery system, microbial contamination of open refillable soap systems, friction/force applied in the wash technique, how much of the hand is covered in the wash technique, wash time, skin condition, drying mechanism of hands – i.e. air dryers vs. paper towel, etc.). There are many other situational variables that likely impact the outcomes as well (e.g. use of other hand hygiene interventions such as alcohol-based hand sanitizer &/or gloving, air temperature and humidity, microbial bioburden/risks in the environment and most importantly compliance at highest risk moments to clean hands – not all hand hygiene opportunities and events are of equal risk!, etc.).

Reply 3: We have added some factors in the section of limitations (see Page 14, line 329, 330). We also want to adjust and analyze various confounding factors, but the information provided by the original studies (included studies) is limited, which is an objective limitation.

Reviewer B

Comment 1: (1) Please address the number of comments and suggestions in the text (as attached). (2) See what you can do to increase the impact for the reader. My take away is that increased handwashing reduces some diseases. This is NOT surprising. The major limitation of these reviewed papers is that they all deal with (hospital) patients. It's hard to believe there are no reports with hospitality or consumers. (3) Please use "reduced risk" do not use "prevents" that is simply not true.

Reply 1:

(1) Thank you for your good comments and suggestions, which have enhanced the readability and clarity of our study. We have made changes to the manuscript. The specific contents are as follows: ① We have revised based on the suggestions on sentence grammar and reasonable expression (see Page 1, line 20, 22; Page 2, line 24, 37-42; Page 3, line 48, 51; Page 4, line 74, 88; Page 5, line 95, 97, 107, 108; Page 6, line 112; Page 10, line 200; Page 10, line 217, 221; Page 11, line 240; Page 12, line 257, 258, Page 14, line 291). ② We have added the number of retrieval electronic databases (see Page 2, line 24). We have added the URL of electronic

databases to the reader (see Text S1). ③ We have revised and made it clear to the reader that our summary comment refers to the people with comprised immunity who need to wash their own hands more (see Page 3, line 63, 64) . ④ We have revised and made it clear to the reader (see Page 4, line 74-77). ⑤ The checklist of the Cochrane risk-of-bias tool can be seen in Table S1-S3. ⑥ We have added the explanation of the criteria of “High” (see Page 7, line 134-137). ⑦ The question on “L132--simple question--did you check the data that you were going to analyze to see if it was normally distributed? I think the mode or median may be a better description?”, we did not modify it, because two summary statistics are commonly used for meta-analysis of continuous data: the weighted mean difference and the standardized mean difference. The mean difference (more correctly, ‘difference in means’) is a standard statistic that measures the absolute difference between the mean value in two groups. It estimates the amount by which the experimental intervention changes the outcome on average compared with the comparator intervention. It can be used as a summary statistic in a meta-analysis when outcome measurements in all studies are made on the same scale. The standardized mean difference (SMD) is used as a summary statistic in a meta-analysis when the studies all assess the same outcome but measure it in a variety of ways. For our study, all included studies measure the frequency of handwashing using the same scale (times/day). So, it is appropriate to choose the mean difference. (<https://training.cochrane.org/cochrane-handbook-systematic-reviews-interventions>). ⑧ About the question “L 171 see what you can do to tell the reader much earlier than you are studying individuals washing their own hands vs hospital workers washing their hands before interacting with patients.” We have revised and made it clear on some similar confusing questions (see Page 5, line 104,105). ⑨ The reasons the quality of evidence was graded low were added (see Page 10, line 211, 220; Page 11, line 228, 234; Page 12, line 246, 255). ⑩ The question on “L197 pl put this is some kind of order--starting with the least frequent to most frequent HW”, we did not modify it, because we usually describe the results that are conducted the meta-analysis first, and then the results that cannot be conducted the meta-analysis.

(2) Although we didn't get the optimal handwashing frequency to reduce the risk of disease, our initial purpose was to explore the relationship between handwashing frequency and disease risk and to make more best practice recommendations on handwashing frequency. The intervention measures of studies we retrieved were on "handwashing frequency", and did not restrict the study subjects, but none of the study subjects that finally met the inclusion criteria were specifically targeted at hospitality or consumers. In addition, the participants of included studies are not only patients but also students, etc. (see Table 2).

(3) We have revised and used "risk reduction" instead of "prevention" in the revised manuscript.