Author's response to reviews

Title: Hand hygiene instruction decreases illness-related absenteeism in elementary schools: a prospective cohort study

Authors:

Claudia H Lau (clau@u.northwestern.edu)
Elizabeth E Springston (e-springston@fsm.northwestern.edu)
Iyana Mason (imason@lungchicago.org)
Emily Gadola (egadola@lungchicago.org)
Maureen Damitz (mdamitz@ccbhs.org)
Ruchi S Gupta (RUgupta@childrensmemorial.org)

Version: 2 Date: 4 December 2011

Author's response to reviews: see over
We sincerely thank the reviewers and editor for their helpful comments. Please find our responses to each reviewer comment below. While we were unable to incorporate every suggestion into the revised manuscript due to the nature of the data collected, we believe the changes made have strengthened the text and are happy to work with the editorial office to ensure its dissemination.

Editorial requests
Please include the ages of the children in the abstract, as well as the grades.

Distribution of children by grade was added to the demographic table, as well as school cut-off ages per grade. Unfortunately, we do not have ages of participating children but feel distribution by grade does give a sense of child age.

Referee 1

ABSTRACT

1. Readers who are not from the northern hemisphere could be given in a few words why October to May were chosen (includes your influenza season, no long student breaks or whatever).
   Thank you for this suggestion. We have clarified in the abstract and methods that the study period occurred during the academic year and included peak flu season.

2. Inform the reader of the illnesses included in the rate (6th line of methodology change to something like ‘All absences were collected and only absences related to diarrhea and influenza or ILI illness were used to establish rates’).
   Changed to “Only absences as a result of respiratory or gastrointestinal illness were used to establish absenteeism rates.”

BACKGROUND

3. Hands are one mode of transmitting infectious diseases others include saliva, droplet and airborne particle transmission (the latter two are especially important for respiratory disease transmission). Replace ‘the primary’ with ‘an important’.
   Replaced.

4. Paragraph 2, sentence 2. provide references.
   Provided.

5. Paragraph 2, 3rd-4th sentence – “suggested to reduce” is not entirely informative given Nandruo-Bus found a significant (P=0.002) reduction (but not by gender) while Master et al results could not reach significance.
   We appreciate this observation but feel a detailed introduction to discrepancies in hand washing studies is beyond the scope of our paper. Our objective is not to demonstrate the utility of hand hygiene per se, but rather to demonstrate the utility of instruction in hand hygiene. We did, however, change the language to be more clear about the findings we cite as follows: ‘Hand washing interventions have been shown to significantly reduce illness-related absences in elementary school students by as much as 26%,9 and significantly reduce a subset of illness-related absences (i.e. gastrointestinal illnesses) by as much as 32%.10”

The success or failure of interventions may be complex related to confounding as well as the intervention itself; we know it’s the alcohol in the ABHR that is the active agent that kills microorganisms and that some ABHR have a long acting action. In the 4th sentence studies using alcohol based hand rub (ABHR) have been lumped with handwashing (Guinan et al) and non alcohol based sanitizer (Dyer et al) without informing the readers of possible cause for the effect (i.e. non alcohol based sanitizer may be less effective in a larger trial than the action of washing with soap and water; there is strong evidence that ABHR is more effective than nonABHR). An important confounder is the incorrect use of ABHR when hands are visibly dirty or sticky as organic material on soiled hands prevents the active agent of the ABHR to penetrate and kill microorganisms.

We agree that there are many complexities in hygiene interventions and appreciate your concern for the accuracy of our statement. We only wish to convey that both hand washing and hand sanitizer
have been shown to be effective but that the role of instruction in use is less clear. If you feel we are misleading to this end, we are happy revise the statement per your suggestions.

6. Paragraph 2, 2nd last line. Please modify as ABHR/sanitizers are not an alternative to handwashing when hands are soiled or sticky.
   Added “when hands are not visibly dirty”.

METHODS

7. Move reference to Table 1 into Results.
   Moved.

8. In 1994 FDA reclassified benzalkonium chloride as tentatively safe and effective – has this changed? Can the authors give a brief explanation why ABHR was not used?
   ABHR was not used per the request of school administration, as there were concerns on having alcohol-based hand sanitizer in preschool classrooms. This was added to the limitations for clarification.

9. Figure 1 shows “When to Use Hand Sanitizers:” and illustrates ‘after using the bathroom’ which is in contradiction to the Methods on Page 5 last paragraph sentence in parenthesis) but importantly this is contraindication of correct use (sanitizers will not actively kill microorganism on dirty hands.
   Removed from the previous Figure 1 (now Figure 2).

10. Were children instructed that it was not to be used on sticky/visibly soiled hands?
    Yes, thank you for pointing this out. We added for clarification that “Children were instructed to use soap and water en lieu of hand sanitizer when hands were visibly dirty.

11. Figure 2 could be given as dot points in Methods or in a box in the Methods.
    Thank you for this suggestion. We are happy to change previous Figure 2 (now Figure 3) if necessary.

STATISTICAL ANALYSIS

13. Incidence density: the rate of absenteeism is given as % of students. This assumes that at any one observation period (such as a month) the denominator is stable (which it may be with exception of influenza season). A superior method that adjusts for changes in the denominator (if there was a change by month) is to use incidence density for each reporting period using number of exposed days (ie total student days) to give a rate= number of absentees for the month/ total number of student days for the month.
    Thank you for this helpful suggestion. However, due to the way in which the data were collected (absences not linked to specific children/participant identifiers), we are not able to use the Poisson regression or NBreg.

RESULTS

14. Participant characteristics, 2nd and 4th sentences please reword “Data from grades... were not used in analysis...for a final sample of..” as this was not clear and the wording was unusual. Change “for a final” to “giving a final sample of”
   Changed.

15. The removal of 109 absences is a total of 12% which indicates a possible internal validity issue (possible selection bias is based on a rough rule of thumb of 2% loss). Please mention in the Methods if you examine these children to determine whether they are no different for potential biases such as English, ethnicity, length of absence, month of absence? If not please mention in the Conclusion this was a limitation.
    Thank you for this suggestion. However, due to the way in which data were collected (demographic data not linked to absences), we are not able to determine whether excluded children were different from included children. Instead, we acknowledge that our sample is convenience based in the limitations.
16. Demographics are usually given to indicate potential confounders and generalizability. A variable is only a confounder when it fulfills 3 rules (roughly: not equally distributed between exposure groups; not part of the hypothesis; proxy or direct cause of the outcome). If you do not wish to control for confounding but wish to present the findings as being applicable to diverse schools then remove the totals in the Results (Table 2a/2b). Otherwise to aggregate the schools and present total (Both schools) you will first need to test for confounding and if it exists then controlled for it by simple stratification (and you cannot give a total rate but leave as 2 distinct schools) or use a MLR (controlling for whichever is an important confounder e.g. ethnicity, low income and limited English) then you can present the results as a total. In addition, when comparing results within Walsh School across intervention/control arms limited English (21.2%) may be a confounder (not distributed between active/passive arms). Did you examine this variable as a potential confounder across the grades (this can be done using stratification by each potential confounders)? Did you check if ethnicity is a potential confounder within Alcott School.

Thank you for this helpful suggestion. However, due to the way in which data were collected (data points were not linked to demographic data) we cannot control for confounders. The totals in the results were needed to demonstrate statistical significance, as sample size was not large enough which presented by school. We acknowledge our small sample size in the limitations section.

17. Another important confounder is vaccination rate for influenza. Can you give vaccination coverage for the intervention/control arms and by school.

No, unfortunately we do not have this data.

18. Figure 3 needs a legend.

Also per journal request, we placed the previous Figure 3 (now Figure 1) legend under the corresponding figure title at the end of the text.

CONCLUSION

19. Mention should be made of important limitation of the study; non alcohol based product used; students may have siblings at home who may be a source of infection. The antimicrobial action of non alcohol based sanitizers and ABHR are severely affected by the presence of organic material – could children with soiled/sticky hands have used the product.

We clarify in the limitations that non-alcohol based hand sanitizer was used instead of ABHR. We also clarified that “Children were instructed to use soap and water en lieu of hand sanitizer when hands were visibly dirty.” While we appreciate your concern regarding siblings as a source of infection, we believe this influence should be random as we did not include or exclude students according to number of siblings.

20. In 1994 FDA benzalkonium chloride was tentatively classified as safe and effective – has this changed?

To our knowledge, no. However, per the requests of the school, we chose to use non-alcohol based hand sanitizer.
to intervention, even grades to control), we did not feel a CONSORT flowchart was necessary. We also do not have the level of detail needed to create the flowchart (i.e. number of children in each classroom). In addition, we excluded absences due to missing data, not children, which would be difficult to report in the CONSORT flowchart of number of participants.

3. If an intervention is allocated at cluster level (classroom) then the analysis MUST take this clustering into account. Get expert statistical help for this. Almost inevitably, the p values will increase, which may impact on the interpretation of the findings. This is a major flaw that must be addressed. Otherwise this article would be unsuitable for publication.

Thank you for this helpful suggestion. However, due to the way in which the data were collected (absences not linked to specific children/participant identifiers nor demographic data), we are not able to take clustering into account.

4. When dealing with count data and incidence rates, you should use Poisson regression, not the t-test, unless you analyse classroom level rates. How exactly was absence rate defined? How were multiple absence episodes in a child treated? Why do tables 2a and b report a percentage (a risk), and not a rate (e.g. incidence per person time, or mean number of episodes per individual)?

Thank you for this suggestion. However, due to the way in which the data was collected (absences not linked to specific children/participant identifiers), we are not able to use the Poisson regression or NBreg. As a result, we do not know whether there are multiple absences per child, nor can we report results ‘per person.’

5. What was the primary outcome of this study as specified in the protocol prior to the study? If it was not the difference of absence during the influenza season, then this finding should not be the main conclusion, and not emphasised in the abstract.

It was our goal to reduce illness-related absences in peak flu season through use of hand hygiene instruction. Added “particularly during influenza season when illness-related absences are at a peak” to the study goal in the abstract and background.

MINOR

1. For non US readers the term “Bimonthly” may not be easy to understand. Does it mean every two months? Or twice per month?

   Bimonthly means every 2 months, changed in the text.

2. Please explain for non-US readers the acronym “IL”.

   IL stands for Illinois, changed in the text.

3. „As hands are the primary mode of transmission of infectious disease among schoolaged children,“ I would disagree that this is as clear cut as this. There is an ongoing debate on the relative importance of droplet, airborne or contact transmission for the transmission for example of respiratory pathogens, especially influenza.

   Changed to “an important mode of transmission”.

4. “evidence-based curriculum was used“ what evidence?

   “Evidence-based” was removed. The curriculum was developed by educators and presents well-established methods in hand hygiene in grade-appropriate formats.

Referee 3

MAJOR COMMENTS:

BACKGROUND

The described problem of absenteeism in schools, universities or day care centers due to colds and gastrointestinal diseases has been widely described in the literature. This includes studies that have examined
the effect of educational programs on hand hygiene and illness rates. (For example: White, C. et al., The impact of a health campaign on hand hygiene and upper respiratory illness among college students living in residence halls, J Am Coll Health. 2005 Jan-Feb;53(4):175-81.)
The aim of the study and the extent to which this approach differs from the existing literature should be worked out better.

We appreciate your suggestion to differentiate our study from past work. We have taken care to clarify in the goals that the aim of our study was to examine the effect of instruction in hand hygiene on illness-related absences specifically among school-aged children, who behave differently from college students and also encounter different microbial exposures. We apologize if it was not clear previously.

**METHODS**

The methodology described leaves some important questions open:

1. How was the randomization of the intervention and controls performed?
   
   **Randomization was not performed and was not mentioned in the manuscript.** We apologize if this was not clear previously. We clarified the method of sampling by adding “Systematic sampling was used to assign odd grades to the intervention group (n=15) and even grades to the control group (n=16) (cluster design)” and also acknowledge that a convenience sample was used.

2. How was it ensured that only students in the intervention group received the instructions? What if information were passed among the children, for example in cross-class activities? Especially as it is added in the discussion that the study was conducted at a time of heightened hand hygiene awareness.
   
   We agree that this is a potential limitation but did not feel it was in the students’ best interest to instruct them from sharing information on hand hygiene. We now acknowledge this in the limitations.

3. How exactly were the relevant diseases defined in advance? Who controlled the self-reporting by parents? Did other, noninfectious reasons contribute to the collapsed absenteeism rate (e.g. asthma?)? If yes, to a relevant extend? These questions should be addressed and answered in the text.

   **Statistical analysis now reads:**
   
   “Per school policy, data were collected documenting each student absence as reported by parents. If reason for absence was not submitted, study personnel called parents to determine reason for absence. For the purposes of this study, study personnel classified a respiratory or gastrointestinal illness as an illness-related absence. Other illnesses or excuses were documented as non-illness-related.”
   
   Unfortunately, we did not collect data on other non-infectious reasons.

**RESULTS**

The demographic characteristics could be supplemented with information on sex and age.

**Distribution of children by grade was added to the demographic table, as well as school cut-off ages per grade.** Unfortunately, we do not have ages of participating children but believe grade does give a sense of distribution by age.

As in described the methods section, the intervention was implemented from October 2009 to May 2010. However, evaluations are also be done for September 2009 as part of the influenza season (e.g. Figure 3), please explain.

**September is included only to show a baseline absentee rate prior to the start of the intervention and before peak flu season.** A bracket has been added to the previous Figure 3 (now Figure 1) to indicate the intervention period, and a phrase has been added to the limitations to remind the reader that the significant outcome is conservative.

According to Tables 2a and 2b, the total absence in the “non-influenza months” was higher on average per month in comparison to “influenza months”. Unfortunately this is not further broken down graphically. Furthermore the corresponding graph is not divided for both schools. One idea could be another graph complementary to Figure 3 showing the rates over the entire course (October - May). **Previous Figure 3 (now Figure 1) was expanded to show non-influenza months while highlighting**
influenza months. We felt that further dividing the graph of overall numbers into the two schools would be confusing for the reader and would not add to the main message.

Without a breakdown of absences to reasons, this sub-analysis of the “influenza season” of a (yet short intervention) is not very conclusive. What is the extra information provided? I would recommend to omit this section or to break it down more deeply.

**Our focus was on changes in absentee rates during influenza season, which is why we analyzed gastrointestinal and respiratory-related absences only. We stated this in the methods and apologize if it was not clear. We have taken care to make this clarification in the methods.**

**DISCUSSION**

During the influenza season, the rate in intervention group at Alcott School was 65.9%, but over the course of the study it is 78.6%. Therefore, the rate must much higher in the other months, right? What are possible causes for this? And if so, the sub-analysis is more than just misleading. Please explain.

Thank you for pointing this out! We double-checked the results in Table 2a and amended the table. Table 2a now shows significant results.

**MINOR COMMENTS:** none

**RECOMMENDATION:** The study confirms previous results from several other groups (“9-14”). The extra information provided is quite small, the more, as the design has several limitations as rightly stated by the authors. The sub-analysis is misleading and should be extended or, preferably, omitted.

Please see point-by-point responses above.

---

**Referee 4**

**MAJOR**

1. Teacher’s perceptions paragraph 1: With only 30 teachers in their sample, the authors should have made a bigger effort to get everyone 76% response is low in this instance. It is unclear of the relevance of reporting by school. This should be revised to report by control and intervention. It may even be possible that there is a statistically significant result in this data.

   Teacher’s perceptions were collected prior to intervention and therefore cannot be reported as intervention vs. control. Instead, per your suggestion, we collapsed most data from the two schools to report general perceptions overall.

2. Teacher’s perceptions paragraph 2: I am concerned that there was no effort to determine usage. The discussion should be control vs. intervention, not by school.

   Weekly ‘spot checks’ were done to refill hand sanitizer and ensure hand sanitizer was being used (mentioned in original methods).

3. DISCUSSION/conclusions: What is the implication of the fact that the differences on absenteeism didn’t persist beyond flu season. This should be discussed.

   After double-checking results for Referee 3’s comment regarding the discussion, we found that the differences in absenteeism did persist beyond flu season and were incorrectly reported in the first draft. We have revised the data accordingly and appreciate the reviewers’ attention to this detail.

**MINOR**

1. Abstract METHODS: It says here that classrooms were assigned randomly by grade to intervention or control within the same school. This information is not repeated in the paper itself. Why wasn’t this assignment done by school to avoid cross contamination between classrooms in the same school. It’s possible that students in one class learned about hand washing from other students in their grade.

   Classrooms were not assigned randomly – they were systematically assigned to an intervention or control group by grade, now described in more detail in the methods. We apologize if it was not clear
previously. The assignment was not done by school because the two schools were very different demographically (see Table 1). Cross-contamination of educational information was added to the limitations.

2. Study Design paragraph 2: Why was alcohol based hand sanitizer not used? It has been shown to be the most effective hand sanitizer and used successfully in schools without incident. ABHR was not used based on school administration requests, as there were concerns on having alcohol-based hand sanitizer in preschool classrooms. This was added to the limitations.

3. Study design paragraph 2: No evidence is presented on hand sanitizer or soap use. How do we know if students used these, and what was the extent of use. A better design would have measured use during some period, and looked at differences in use. Weekly ‘spot checks’ were done to refill hand sanitizer and ensure hand sanitizer was being used (mentioned in the original methods).

4. Statistical Analysis paragraph 2: The authors fail to mention the presence of H1N1. This was a very special flu season and very unusual in its timing. The activity around H1N1 would have an influence on the schools. This is a significant confounder that is not discussed. This is not mentioned until the section on study limitations. We agree that H1N1 made our study period unique and also believe its presence likely contributed to the conservative nature of our results, which is why we chose to mention it in the limitations. Per your suggestion, we now also discuss H1N1 in the results where we present teacher perceptions on hand hygiene.

5. Results: Absentee Rates: The authors failed to note that October was the peak of H1N1 activity. The authors fail to discuss their statistical results. It is odd that there is no statistical significance in either school, but just in the sample as a whole. This doesn’t invalidate the result, but the statistical implications should be further analyzed and discussed. The authors need to dig a little deeper. Also, figure 3 needs to be titled, and the lines labeled. I assume that one is control and one intervention, but it doesn’t say.

We appreciate your concern about the role of H1N1 and hope that our revisions above are sufficient. We also hope that our revisions on the whole have addressed your concern about our discussion of the statistical results. Specifically, in the first paragraph of the discussion we interpret out findings to indicate that instruction in use reduces illness-related absences more than access to hand hygiene facilities alone, particularly during peak flu season. We also acknowledge in the results that “The peak in illness-related absenteeism rates matched the peak in number of influenza-like illnesses in 2009 (both regular and pandemic i.e. H1N1) reported by the City of Chicago” in order to provide the reader a framework to interpret our findings.

We believe the reason that correct directionality without statistical significance was observed prior to analyzing the sample as a whole was a result of small sample size as well as limitations in study design, which we now discuss thoroughly in the limitations section.

Per journal request, we placed figure titles at the end of the text. Titles include: Figure 1 - Illness-related absenteeism rates during the 2009-2010 academic year. Figure 2 - Hand sanitizer use protocol, distributed and implemented in all classrooms. Figure 3 - Overview of hand hygiene curriculum administered in intervention classrooms. Also per journal request, we placed the previous Figure 3 (now Figure 1) legend under the corresponding figure title at the end of the text.