Author's response to reviews

Title: Keep Cool: Effectiveness of a web-based education program to improve vaccine storage conditions in primary care: study protocol for a randomized controlled trial

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Author's response to reviews: see over
Reply to the reviewer’s comments:

Keep Cool: Effectiveness of a web-based education program to improve vaccine storage conditions in primary care: study protocol for a randomized controlled trial

Dear editors,
dear Dr. Baker,

We would like to express our gratitude for your kind review and the very helpful suggestions. Please find our answers and revisions enclosed and in the revised manuscript.

Best regards, Anika Thielmann and Birgitta Weltermann

Reviewer’s comments and authors’ answers:

1. The terms ‘practice assistants’ and ‘practice personnel’ are used along with physicians to describe the target population. It is not clear what professional group these personnel belong to, are they qualified nurses, unqualified health care assistants, clerical staff or all of these? This should be specified as it has implications for the utility of the intervention for training purposes and for the target readership.

   **Answer:** Thank you. The text in the section “Study population” was revised.

   **Revised text:**
   “The target population of this randomized controlled trial are primary care physicians and their practice personnel. The majority of these personnel completed a 3-year vocational training with a degree (practice assistants). Few practices also employ secretaries, nurses, or personnel without a degree but with on-the-job training. The intervention will address all staff members handling vaccines irrespective of their prior training.”

2. Page 8, line 33- There is no explanation as to why the refrigerator closest to the reception desk will be selected in those practices that have more than one refrigerator.

   **Answer:** The text was clarified. These criteria were used in a prior study.

   **Revised text on page 9 (Section” Measurement instruments):**
   “In practices using more than one refrigerator for vaccine storage, the refrigerator most frequently used and closest to the reception desk will be selected.”

3. Page 11, lines 5 and 6- The citations are sequenced wrongly and do not correlate with the reference numbers.

   **Revised text:**
   “This percentage is derived from the above-mentioned prospective feasibility study in 17 primary care practices with 21 vaccine refrigerators and similar results reported by Bell et al. (2001), Jeremijenko et al. (1996) and Lewis et al. (2001) [14,18,20].”

4. Editing- The paper would benefit from additional editing before publication as a few grammatical errors are present for example:

   - page 6, line 19: “To set up a comprehensive temperature monitoring”. Additional word required: “To set up a comprehensive temperature monitoring system”.
   - Page 4, line 34 “…vaccine storage manager and backup is documented by the study assistant already during recruitment”. Re-wording required: “…vaccine storage manager and backup will have already been documented by the study assistant during recruitment”.
   - The consistent use of the word ‘breech’ rather than ‘breach’ needs correction (page 2, line 15; page 6, line 13).

   **Answer/Revised text:**
   The text was reviewed and edited by a native speaker. Please find the corrections in the full document enclosed.

Discretionary Revisions/Suggestions
1. Safety issues are not addressed and the actions to be taken by research staff on discovery of breaches in the cold chain that are potentially harmful to patients should be described.

**Answer:** Thank you for this comment. A new section “Safety issues” was included in the methods section.

**Revised text in Methods/Design:**

“Safety issues

All practices will be informed in detail about their vaccine refrigerator temperature. The tailored education and the download material will address the issue of how to deal with temperature breaches. Practices with temperature readings outside the target range will receive additional information after t2. The following safety regulations will be followed:

1. Practices with any temperature beyond the target range will receive detailed information on the date and duration of the incident.
2. They will also receive detailed information recommending that the manufacturer’s hotline(s) be contacted for information on how to deal with vaccines exposed to inadequate temperatures, and if additional vaccinations of patients are required to assure patient immunity.
3. In addition, practices will receive the contact data of the Paul Ehrlich Institute, the Federal German agency responsible for vaccines and appropriate management thereof.

2. Many of the studies discussed in the background section are relatively dated (11, 12, 13, 18 and 19) with publication dates ranging from 1996-2002. Best practice guidelines for vaccine storage cited by the authors post-date these studies. More up-to-date studies should be referenced if available, though a cursory search does reveal a dearth of literature in this area. If this is indeed the case, it could be addressed in the discussion section.

**Answer:** Although millions of vaccines are applied yearly, the issue of vaccine storage has been studied surprisingly little. Our current PubMed search using the terms (((storage OR cold chain OR coldchain) AND (vaccine OR immuni*ation)) [Title/Abstract]) yielded 1157 results. A review of the abstracts showed one further relevant publication (Yakum, Ateudjieu, Walter & Watcho, 2015). The article was included as reference number 11.

**Revised text in the section “Background”:**

“These results are in line with studies worldwide, which discuss the following key problems related to vaccine storage: 1) temperatures outside target range [10,11], 2) lack of adequate temperature measurement devices [12–14], 3) lack of continuous temperature documentation [4,12–14], 4) use of inadequate refrigerators [9,10,12], 5) lack of separate refrigerators [13–15], 6) inadequate storage practices [2,12,14,15], 7) lack of designated personnel [14], 8) insufficient staff training and guidance [12,14,16–18].”

3. The rationale for the sample size could be clarified. As previously noted, studies cited to support the assumption that 60% of refrigerators will be outside the target temperature range are dated (1996-2001), again more up-to-date studies should be referenced if available. The sample size calculation estimates a dropout rate of 20%; a reference could be added to support this choice.
Answer: We recently finished a feasibility study of 21 vaccine refrigerators from 17 practices of our primary care research network: 33.3% of the 21 refrigerators failed to consistently maintain the correct temperature range between 2°C and 8°C. This corresponds well with the results from the literature. We updated the sample size calculation.

Revised text in the Methods/Design:
“As the intervention will only be conducted in practices with suboptimal temperatures, a total of 174 practices will have to be recruited for t0. This is based on the assumption that 33.3% of refrigerators will be outside the target range (n=58). This percentage is derived from the above-mentioned prospective feasibility study in 17 primary care practices with 21 vaccine refrigerators and similar results reported by Bell et al. (2001), Jeremijenko et al. (1996) and Lewis et al. (2001) [14,18,20]. Our calculation takes into account a dropout rate of 20%. This dropout rate is based on our experience and corresponds to reports from other cluster randomized trials [24]. Using an adaptive design, baseline temperature measurements for t0 will be stopped as soon as the anticipated total sample of n=58 is reached.”