Author's response to reviews

Title: Strategy for recruitment and factors associated with motivation and satisfaction in an interventional study with 210 healthy volunteers without financial compensation

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Version: 5 Date: 26 August 2014

Author's response to reviews: see over
Title: Feasibility, recruitment and factors associated with motivation and satisfaction in an interventional study with 210 healthy volunteers without financial compensation

New title: Strategy for recruitment and factors associated with motivation and satisfaction in an interventional study with 210 healthy volunteers without financial compensation

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Author’s response to review: see below
Reviewer's report

Title: Feasibility, recruitment and factors associated with motivation and satisfaction in an interventional study with 210 healthy volunteers without financial compensation.

Version: 3
Date: 11 June 2014

Reviewer: Benjamin Kasenda

Reviewer's report:

The authors investigated recruitment of healthy volunteers into an interventional study without financial compensation at a single centre in France. The investigators also mention a randomized trial, but, unfortunately, it is absolutely not clear to me what the authors wanted to investigate with the randomized trial. Probably, the present study was a sub-study of the mentioned randomized trial.

Overall the manuscript has an average level of wording – I recommend that a native speaker should review it before re-submission. According to the reviewer’s suggestion, the manuscript has been thoroughly checked once again by a native English speaker in terms of grammar, spelling and in order to enhance the overall level of language.

Regarding the content, I think it is an interesting topic to investigate recruitment of healthy volunteers without direct financial incentives; therefore I think the value this study adds to the topic is good.

However, there are several major issues that have to be revised:

Abstract
1. Why do you use the term biomedical in this setting?
   The term “biomedical research study” has been replaced by “interventional study”.

2. The objective of the study is not clear to the reader when only reading the abstract! In accordance with the above comment, the objective has now been changed as follows:
   “The aim was to describe a strategy for recruitment of healthy volunteers (HV) into an interventional study without financial compensation, and to identify factors associated with the motivation and satisfaction of these HV.”

3. This is a randomized trial, but I cannot see that from the abstract!
   In fact, this is not a randomized trial but rather a sub-study survey of a randomized trial which required 210 HV. We have now corrected the abstract to clarify this point:
   “Our study is ancillary to the randomized trial conducted at the Clinical Investigation Centre (CIC) of Rouen University Hospital in 2013.”

4. Who are managers? You have to give a contrast; otherwise it is difficult to understand if you only have the abstract.
Thank you for this helpful comment. The Clinical Investigation Centre of Rouen University Hospital managed the strategy for recruitment and assessed the motivation and satisfaction of the 210 HV. The abstract has been changed as follows:
“Strategy for recruitment was managed by the CIC using our HV database and a communication campaign which included posters and media advertisements.”

Methods – interventional study
1. Please drop the term biomedical; it does not suit here.
In accordance with the reviewer’s suggestion, the term “biomedical research study” has now been replaced by “randomized trial” throughout the manuscript.

2. I do not really understand the objective of the randomized trial. When were the patients randomized?
Information on the baseline randomized trial has been added as follows:
“One the same day, the HV first signed the informed consent document, was then randomized and after performed the intervention (no follow up).”

a. What was the intervention / control group? How long did the intervention take?
In answer to the reviewer’s questions, information on the baseline randomized trial has now been added:
“Randomization was performed by sealed envelopes and HVs were allocated into one of the three tested arms: 1- telephone assistance with the order to perform cardiac massage then hang up (control group); 2- continuous telephone assistance with an emergency regulating doctor; 3- telephone assistance with the order to perform cardiac massage then continuous guidance by a sound pace. Then the HV performed continuum cardiac massage on a manikin during 5 minutes.”

b. How long did the intervention take?
Information on the baseline randomized trial has been added as follows:
“Then the HV performed continuum cardiac massage on a manikin during 5 minutes.”

c. What was the primary endpoint of the study?
In answer to the reviewer’s question, we have added information on the baseline randomized trial:
“The end-point of the baseline randomized trial was the effectiveness of the cardiac massage (frequency and depth).”

d. How long was the follow-up?
We now mention absence of follow-up in the manuscript:
“On the same day, the HV first signed the informed consent document, was then randomized and after performed the intervention (no follow up).”

3. You mention 210 HV were needed, how did you come up with this number?
Any power calculation, please report details about this!!
As our study was ancillary to the randomized trial, we have not detailed the number of subjects calculated to be necessary for the randomized trial: we studied all 210 healthy volunteers required for the randomized trial. The number of subjects required was calculated: the calculation was made effective for a pre-tailed test at a
significance level of 2.5% and a power test of 80% relative to such a difference that the proportions of success are respectively 6% and 24% with one order to perform and continuous audioguide. The proportion of 24% was estimated in a pilot study with the continuous audio guide strategy. This study also found a success ratio of 6% with the strategy of single point. Given these data, a total of 210 healthy volunteers (70 per group) was deemed necessary.

The reference has been added as follows:
“The number of subjects required was calculated for the randomized trial (significance level of 2.5% and a power test of 80%) (34).”

Methods – selection criteria
1. Selection criteria, why do you say “patients”, should be HV, isn’t it?
We thank the reviewer for this keen observation and subsequently the term “patients” has been removed and replaced with “HV”.

2. I would change “selection” to “eligibility” criteria.
The term “selection” has now been replaced by “eligibility” as per the reviewer’s suggestion.

3. Why did you exclude pregnant women?
Pregnancy was a non-inclusion criterion of the baseline randomized trial. Pregnant women were not included due to the intense physical activity required (cardiac massage for 5 minutes). Generally pregnant women are not required to participate in randomized trials except for interventions concerning pregnancy.

Methods - recruitment
1. You mention a database (Logic CIC), have you chosen HVs randomly or did you contact all of them? Please clarify this.
We extracted the coordinates of all HVs aged 18 to 60 years registered in the database Logic CIC, then we attempted to contact all HVs extracted (no random draw) by telephone.
This has been clarified in the manuscript:
“Recruitment for the baseline randomized trial was based on extraction of mobile and land line telephone numbers of all HV aged 18 to 60 years registered in Logic CIC on August 27, 2013. We attempted to contact by telephone all HV extracted from Logic CIC and proposed participation in the study to those HV successfully contacted.”

2. How were the HVs selected for this existing database? Are the contacts updated regularly? How many variables do collect in this database? Please provide more information or references for this database.
More details on this database have been added to the manuscript:
“Logic CIC is a software programme which was specially designed by the French National Institute of Health and Medical Research (INSERM) to assist CICs in France in managing their own HV database. Healthy volunteers wishing to participate in medical research protocols are registered in this database with their demographic characteristics (family name, first name, gender, date of birth, place of birth, profession), life-style characteristics (contraception, smoking, alcoholism) and their contacts(address, telephone numbers). Our registration of HV began in January 2000
for our database and included an overall 1500 HV at time of extraction. The database is updated when HVs self report any changes and when participating in a study.”

Methods – data collection
1. What do you mean by “was sought”?
The verbal phrase “was sought” has been replaced by “was collected” or “was asked”.

Methods – statistical analysis
1. Why did you choose the age cut-offs? Making cut-offs has several limitations regarding statistical analysis.
   We chose to form three age groups because of the small number of HV. This categorization limits the interpretation of results and seemed the most appropriate.
   Further explanation has been added to the manuscript: “The age cut-offs were chosen to form approximately equal periods of time (about 15 years for each age group) with a similar number of HV in each age group (compromise between the two arguments).”

2. Why did you choose the median of the satisfaction scores? Did you have an idea about a minimal important difference for this satisfaction score?
The satisfaction scores are very high in our study (as reported in the literature for other French CIC) and the variability is low. So we split the score by the median to differentiate between two groups and not according to satisfaction as a continuous variable.
   We conceived the satisfaction score so there was no minimally important difference as previously described in the literature. However, we believe that those HV who were not completely satisfied might refuse future participation and also discourage their relatives from participating. Any improvement in the score (even 1 point) seemed important to us. So splitting by the median and analysing completely satisfied HV versus those not completely satisfied seemed relevant.

3. What was the dependent variable in your logistic regression? You use a logistic regression, so it must by a binary variable. I assume you build a cut-off again. Please report that clearly! Please also report the motivation and rationale about the cut-off.
The dependent variable was satisfaction score (binary variable: not fully satisfied and fully satisfied HV, according to median cut-off).
   This has been further clarified in the manuscript: “Two multivariate analyses to identify factors associated with full satisfaction were performed using logistic regression for each of the two satisfaction scores (Overall welcome satisfaction and protocol management satisfaction) as dependent variable (two groups: not fully satisfied or fully satisfied HV). Factors with a p value lower than 0.30 (sex, age, socio-professional category and registration status in Logic CIC database) were included in the multivariate analysis and p value lower than 0.05 was considered to be significant.”
The rationale of the cut-off is described in the previous point (2).

4. Why did you choose the listed variables? Why did you not include whether HVs were recruited by the database or the other media strategy?
   Factors with a p value lower in univariate analysis than 0.30 were included in the multivariate analysis.
This had been added to the manuscript:
“Factors with a p value lower than 0.30 (sex, age, socio-professional category and registration status in Logic CIC database) were included in the multivariate analysis and p value lower than 0.05 was considered to be significant.”
We have included whether HVs were recruited by the database (“Registered HV”) or other media strategies (“Unregistered HV”).
This had been specified in the manuscript and in table 4:
“HV's unregistered in Logic CIC database were those recruited by other communication strategies.”

Results – recruitment process
1. What do you mean by “cognizance”? The term “source of cognizance” has now been replaced by “source of information”.

2. Please be clearer in describing your findings, e.g. “Younger age of HV was associated with word-of-mouth” can be changed to “Younger HVs were more often recruited to the study by word-of-mouth….” The sentences had been modified as suggested above.

3. In ALL tables: Please provide frequencies and proportions in all rows not only the columns.
The number of responses has been added to Table 2 for each source of information (in the “Overall” column). All HV reported at least one source of information in the questionnaire. However there were some missing data (on gender, age, socio-professional category, motivation, satisfaction, participation outlook). Thus we have indicated the maximal number of respondents in each column head in Table 3 (for example 135 women in Table 3) but not the number of respondents for each row (for example, one woman did not respond to participation in a new research study, Table 3). Furthermore, adding the number of respondents to each cell lowered the readability of the table. For example, for the item “Participation in a new research study”, 134 women out of an overall 135 responded to the question. And among the 134 respondent women, 132 agreed, 98.5%. Indicating “132 /134 (98.5%)” in the cell is less readable than the proportion “98.5%”). Indicating the number of missing data is also difficult because this is different for each cell.

Results – in general
1. Please always provide absolute frequencies, denominators, and proportions for all findings you report in the text. These have now been added accordingly.

2. Please don’t report medians and ranges in the text, put them all into the tables. The median of the satisfaction scores was used to dichotomize HV into two groups: not fully satisfied (score lower or equal to the median) and fully satisfied HV (score above the median). Thus we consider that the median was an important piece of data (cut-off) and wish to report it in the text. Moreover, no table shows the overall scores as quantitative and indicating these data is difficult (tables 3 and 4 present the scores as dichotomized).
Discussion

1. Please shorten the discussion section by about one page; it is too long.
The length of the discussion has now been shortened as suggested.

2. The fact that you don’t have mobile numbers or emails in your database should be discussed as a weakness of your study.
Not using e-mail addresses was an aspect of the recruitment strategy described. We only used mobile and land line telephone numbers to contact HV.
This has been clearly stated in the text (methods section):
“Recruitment for the baseline randomized trial was based on extraction of the mobile and land line telephone numbers of all HV aged 18 to 60 years registered in Logic CIC”

This limitation has been clearly stated in the discussion section:
“However the means used to contact the HV (mobile or land line telephone) could be different according to age and limits the interpretation of our results. This possible confounder is minimized because the telephone numbers provided by HV for Logic CIC database registration were the numbers which were the most easily reachable.”

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
I declare that I have no competing interests
Reviewer's report

Title: Feasibility, recruitment and factors associated with motivation and satisfaction in an interventional study with 210 healthy volunteers without financial compensation.

Version: 3 Date: 19 June 2014

Reviewer: Jane Kim

Reviewer's report:

Thank you for the opportunity to review this paper. A better understanding of the incentives and barriers is essential for many stakeholders involved in clinical research, investigators and IRB members alike. Scientific advancement after all, rests on the participation of such volunteers and the topic is high salience in the research community.

Strengths of the paper:
1. Methods are appropriate and well described.
2. Authors found some interesting results, for example – it is surprising that social networking and radio were not found to useful methods of recruitment.

Major Compulsory Revisions:
1. The title of the paper suggests that feasibility of recruitment without the reliance financial incentives will be addressed. Authors should clarify exactly how feasibility was assessed, beyond the simple stating the low participation rate.
   We thank the reviewer for this helpful comment. Indeed, as feasibility only concerned the recruitment strategy, that has been removed from the title.
   The title has been changed as follows:
   “Strategy for recruitment and factors associated with motivation and satisfaction in an interventional study with 210 healthy volunteers without financial compensation.”
   The objective has also been modified as follows:
   “The aim was to describe a strategy for recruitment of healthy volunteers (HV) to an interventional study without financial compensation, and to identify factors associated with the motivation and satisfaction of these HV.”

2. The major study flaw seems to be that there may be a large sampling bias. As mentioned in the discussion – greater age was associated with easier contact by telephone. If this is indeed true then the sampling has missed a younger population who may be swayed less by financial incentives in making decisions to participate. I think this is a major drawback and at the very least the limitations need to be further bolstered to include this.
   Indeed greater age of HV was associated with easier contact by telephone (Table 1) and this is interesting for future recruitment of HV. However agreement to participate was not associated with age among those HV successfully contacted (Table 1: agreement proportions were 51.4% of under 30 year old HVs, 59.8% of 31 to 45 year old HVs and 58.8% of 46 to 60 year old HVs; p= 0.07). Thus we consider that the telephone reachability of the HV was not a major bias in their decision to participate in a study without financial compensation.
3. Were the outcomes dichotomized at the sample median. This seems problematic if outcomes were categorized according to empirical median – cut-offs will vary by type of question and there is no a priori logic that governs the cut-off – furthermore the results will not be very interpretable.

The satisfaction scores are very high in our study (as reported in the literature for other French CIC) and the variability is low. So we split the score by the median to differentiate between 2 classes and not according to satisfaction as a continuous variable.

As we conceived the satisfaction score, there was no minimally important difference as already described in the literature. However, we believe that HV who were not completely satisfied might refuse future participation. Any improvement in the score (even 1 point) seemed important to us. So split by the median and analysis of the completely satisfied HV versus those not completely satisfied seemed relevant to us.

4. Final recruitment was 10.1% – with such low recruitment rates, I doubt whether this sample is representative of the target population in this study. It is reasonable to then think that a highly interested group of volunteers were selected and are thus more likely to report high satisfaction and a different set of motivating factors.

We studied factors influencing satisfaction and motivation among HV accepting to participate in an interventional study then HVs who agreed to participate represented the target population of our study.

Moreover, there was no difference in either gender or age for the 210 HV who agreed to participate in the interventional study (Table 1: “HV accepted participation” and “HV attended the inclusion visit”; p> 0.05).

Minor essential revisions:

p.5 L 108: What is meant by “not rescuer” – can the authors provide a more detailed explanation or precise definition

“Not rescuer” is the term employed in the protocol of the baseline randomized trial. This term concerns people whose profession requires implementation of first-aid (fire fighters, ambulance attendants, first-aid volunteers).

This has now been clearly stated in the manuscript:

“Only healthy volunteers and not rescuers (fire fighters, ambulance attendants or first-aid volunteers) were eligible for inclusion.”

p.5 L123 One may wonder whether the choices available in the reasons listed may have biased the respondent to respond in a certain manner; for example, if “no time” was a reason, perhaps this would be more likely to be chosen.

The question "why do you not wish to participate?" was asked. Categorization ("not available", "no financial compensation", "other" or "reason not given") was defined retrospectively according to the reasons given spontaneously by the HV.

This has been clearly stated in the methods section:

“In cases of refusal to participate, the reason for refusal was requested by an open-ended question and the answer was retrospectively categorized as “HV not available”, “no financial compensation”, “other” or “reason not given”.

We are aware of the potential misclassification of these reasons, which we point out as a limitation in the discussion section:

“Moreover refusal to participate due to absence of financial compensation was little reported in our study (4.6% by the 323 HV contacted by telephone who refused to
participate) but under-reporting of this reason is likely, especially among those who gave no reason for refusal (38.7%)."

Discretionary Revisions:

p.4 L87: I would doublecheck the accuracy of the statement..

We did not find any topics in the literature which were related to HV specifically without financial compensation.

We performed requests in several search engines (PubMed, Embase and Google Scholar), with different terms (simple, Mesh, EMTREE: “motivation”, “satisfaction”, “healthy volunteers”, “demography”, “recruitment”, “financial incentives” etc.) but we did not find any studies on motivation or satisfaction of HV which were not financially compensated.

We would be most grateful to receive any relevant information you might have on the subject, so that we might change the sentence accordingly.

p.4 L98: It would be helpful to have further clarification on the randomized trial – what is the control or were the 3 different strategies compared to each other.

We have added more information on the baseline randomized trial as follows:

“On the same day, the HV first signed the informed consent document, was then randomized and after performed the intervention (no follow up). Randomization was performed by sealed envelopes and HVs were allocated into one of the three tested arms: 1- telephone assistance with the order to perform cardiac massage then hang up (control group); 2- continuous telephone assistance with an emergency regulating doctor; 3- telephone assistance with the order to perform cardiac massage then continuous guidance by a sound pacer. Then the HV performed continuum cardiac massage on a manikin during 5 minutes. The end-point of the baseline randomized trial was the effectiveness of the cardiac massage (frequency and depth).”

p.5 L115 Some restating would make this clearer.

The sentence has now been reformulated for clarity:

“The first stage in the recruitment process of HV was our CIC database.”

Additional details on the database have been added:

“Logic CIC is a software programme which is specially designed by the French National Institute of Health and Medical Research (INSERM) to assist CICs in France in managing their own of HV database. Healthy volunteers wishing to participate in medical research protocols are registered in this database with their demographic characteristics (last name, first name, gender, date of birth, place of birth, profession), life-style characteristics (contraception, smoking, alcoholism) and their contacts (address, telephone numbers). Registration of HV began in January 2000 for our database and included an overall 1500 HV at time of extraction. The database is updated when HVs self reports any changes and when participating in a study.”

p.11 L 275 Omit the sentence “It would be interesting…” This seems like a casual thought or better placed at the end of the discussion

As recommended, this sentence has now been removed.

p.12 L283 I would suggest reducing the examples in the literature. There should be greater emphasis on the actual data collected in the current study

References to other articles have been reduced and citations have been simplified.
**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**
I declare that I have no competing interests.