Author's response to reviews

Title: Comparison of participants and non-participants to the ORISCAV-LUX population-based study on cardiovascular risk factors in Luxembourg

Authors:

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Author's response to reviews: see over
Dear Dr Diana Marshal

Dear Editors,

Reference: MS: 1492936804367602

We thank you for revising thoroughly our manuscript and giving us the opportunity to submit a revised version.

We are pleased to return you the new version revised in regard to the reviewers’ comments and suggestions.

We also provide a point-to-point response to all issues raised by the four referees. We hope that the revised version is now suitable for publication in your Journal.

Yours sincerely,

Ala’a ALKERWI
Point-by-Point Response

Reviewer: Pascal Bovet

Reviewer’s report:
The paper provides a useful account of the extent and meaning of participation rates in population-based surveys of cardiovascular risk factors in a high income country. Analysis and discussion for the results are valid and well done, overall. I have raised a few fairly minor issues.

1) The abstract is too long and could be shortened to main findings and messages.

Ok, the abstract was shortened as recommended by the reviewer.

2) I am not convinced of the pertinence of the aim “to descriptive strategies used to enhance response rates”. I think this aim, and much of the related discussion throughout the paper, should be dropped in the entire paper (and just a few words mentioned on what was done to increase participation as background information). Indeed, the strategies used in the survey are what is routinely expected from such surveys and, more importantly, the paper does not (and cannot) provide analysis of the impact of any of these strategies (what would be participation if X or Y was done or not done), so much of this discussion is conjectural.

The investigators do agree with the reviewer that within the context of this study, it is not possible to analyze the impact of applied strategies on increasing the response rate. However, it would be possible to compare this with another studies carried out in similar setting, but without such intensive enhancement strategies (vast media publicity, telephone recalls, successive postal reminders, multilingual trained personnel, 4-language questionnaire and others). Such analyses are important, not only to substantiate the high cost, necessary to carry out successful population-based studies, but also to stimulate the reflection about the alternative solutions. Though it is not the object of the present paper, this type of inter-studies comparison is fairly interesting, particularly in Western countries, to help decision-making as regards to appropriate allocation of human, financial and temporal resources.

The investigators understand not to considering this issue as an objective of the present paper (the text has been modified accordingly), but still believe that emphasizing on the applied pro-active strategies, to augment participation to ORISCAV-LUX study; the first national population-based study in Luxembourg is coherent with the topic of research. We consider that it is valuable to cite the traditional measures, as well as to add the own experience, such as “hiring multilingual personnel”, “translation to non-official languages” and “cardiologist’s feedback” as mentioned in the “Discussion” section. This could be considered as a lesson of good practice to be followed by other researchers. Moreover, these participation-enhancement strategies were applied as an approach to reduce potential selection bias, which is the central issue in this paper.
As seen in the revised text, the objectives of the paper were confined to investigate the sample representativeness and respondents-non respondent profile comparison.

3) In the abstract, only age-adjusted estimates (or possibly also age and sex adjusted estimates) should be given (i.e. no crude estimates) as what is of interest is only comparison when age of groups compared is accounted.

OK, the sentences concerning the crude estimates of prescribed medications, and the use of serum lipid reducing medication agents was removed from the abstract, but cited in details in the “Results” section.

4) Since several attempts (reminders) were made to contact eligible participants (as expected in such surveys), it would be useful to provide some analysis of the impact of sending repeated letters (since this info can be derived from the data).

OK, thanks for this comment. In fact, the two postal reminders and the repeated phone contacts enabled further recruitment of 323 and 37 subjects, respectively. Thus the participation rate was increased from 24% (1072/4452), then to 31.3% (1395/4452) and finally up to 32.2 (1432/4452) until the end of the study. Please see the table below, showing an increase in the final response rate of 7.3 % following the 2 reminders and of 0.8% following the repeated calls.

| Positive response after first invitation | 1072 | 24.1% |
| Positive response after 2 reminders | 323 | 7.3% |
| Positive response after repeated phone calls | 37 | 0.8% |
| Total participants | 1432 | 32.2% |
| Eligible participants | 4452 |

The increased percentages of participation rates were added to the text in “Discussion” section.

5) It would be useful to provide some estimate of the cost of the study, including when broken down by participant. Conducting such surveys is straightforward technically, but few appreciate the real (high) cost of such surveys and this information (cost) can help potential investigators to plan such surveys.

The investigators do agree and confirm the reviewer that such population-based, nationwide studies are quite expensive. Therefore, prior massive efforts were done to convince the research and public health authorities to co-finance this first of its
kind project in Luxembourg. In fact, ORISCAV-LUX study enables the decision-makers to respond to European and WHO demands for national surveillance of public health indicators and to address long-standing limitations in Luxembourg’s health information system. This study has dual significance. First, the collected ORISCAV-LUX database helped to establish national baseline statistics for a range of important pathologies and cardiovascular risk factors such as obesity, hypertension, diabetes, smoking, physical activity and metabolic syndrome. Second, it constitutes a worthy database attracting researchers to investigate thoroughly in various research-questions.

Concerning the suggestion of the reviewer to provide some estimate, of the cost of the study in this paper, the investigators believe that it is not suitable to quote just crude figures about the whole real cost of the study or per participant. The cost assessment of a population-based study is rather a complex matter and need further specific investigation, which is not the objective of the present work.

However, for reviewer’s interest, the total cost of ORISCAV-LUX study was 744,617€: 116,539 € for the preparation phase; 347,674 € for the recruitment phase; 194,403 € for data entry and analysis; and 86,001 € for data dissemination, publication and coordination for project implementation at cross-border level with the Lorraine in France and the Province of Liège in Belgium. The full cost by participant was 519.98 €, but, if we calculate this cost for the whole population residing in Luxembourg, it was 1.48 € by inhabitant.

6) A table well shows lower participation among youth, as expected. It would be useful to provide this data stratified for sex, as lower participation may be substantially different among men and women.

Ok, this analyze was done and showed a significant difference between participants and population source in terms of age groups for both genders. Table 1 has been modified accordingly.

7) Along the same line, the discussion could be extended, within 1 paragraph, about the future of population-based surveys in high income countries, including listing possible alternative options to get similar information (e.g. whole population surveillance mechanisms, etc). The fact that Luxemburg already has national mechanisms to routinely collect various data at a population level (e.g.IGSS) offers a good background to elaborate of such possible new ways to get such information.

Although there is a difference with respect to the target population (patient- versus population-based setting), the investigators appreciate the idea to beneficiate from the available IGSS “good-quality, official, regularly updated, medico-administrative database”, as an alternative option for expensive ongoing health surveillance system. However, this database leaks information about the socioeconomic and clinical characteristics.
In the context of this work, the IGSS database was used as a complementary source of information to investigate the demographic and cardiovascular-health related profiles of participants and non-participants to the ORISCAV-LUX survey, which is considered as a strong point in our study. This point was well indicated in the “Discussion” section and a related sentence has been added.

8) It would be useful to have one paragraph in the discussion to elaborate on the apparently discrepant notions that non participants did not differ from participants based on data from IGSS and the fact that non participants include substantially more “employees” and less “working class”, hence a strong SES difference. Considering that SES is a powerful predictors of CVD and many CVD risk factors (tobacco, obesity) this raises some questions.

Thanks for this relevant comment. A paragraph has been added to the “Discussion-strengths and limitations” section.
Reviewer: Lenoné Malan

The strength of this paper lies in its novelty representing confounding factors in recruitment and participation response of participants in Luxembourg for an epidemiological study regarding CVD risk. Avoiding bias in this field is an important factor and the authors exceeded themselves. Being a project leader I understand the hardship and participation bias. I am looking forward to the publication of results.

- Major Compulsory Revisions
1. Old versus young response concern: adequately addressed in discussion but add one-two sentences in your discussion regarding: ageing, decrease in health and need to be monitored opposed to young, healthy and no need for attention/monitoring.

In Luxembourg, notably during the academic period, the nonattendance of the young adults is obviously related to their study abroad, due to the limited possibilities inside the country. In addition, the authors have pointed out, in the discussion, that the cardiovascular topic of ORISCAV-LUX study might be not interesting to young age groups who usually enjoy a good health. Conversely, the over-representativeness of the older people might be reasonably due to their perception for the need to clinical check-up, especially when the cardiologist’s advices were provided freely.

These issues have been added to the revised text of the article.

- Minor Essential Revisions
1. Page 5: Description of methodology is been referred to but no reference is given. If you refer to your own results make it clear under which section please.

The reviewer is right in this comment. The methodology of ORISCAV-LUX study was detailed in a separated research article, submitted simultaneously to the same journal (BMC Public Health). The article follows the same scheme and under review for the moment. Meanwhile, the investigators suggest inserting the temporary ID reference number of the article to the “References” section.


OK, this paragraph has been modified to be more appropriate.

3. Page 6, paragraph 3: Refine wording: “chronic conditions, such as malignant neoplasm of the: colon, bronchus, lung, prostate, breast and thyroid; mental and behavioral disorders due to use of tobacco and alcohol, nutritional disorders……”

Thanks for this comment. The correction has been done.
4. Page 7: Statistical methods: All statistical analyses were carried out (last sentence) must be the first sentence of your section: statistical methods

Ok, this modification has been done.


OK, the word "regression" has been inserted.

6. Page 7: Replace sentence of statistical significance with the following suggested sentence: Statistical significance was a two-sided # level of 0.05 or less.

Ok, this modification has been done.

7. Page 8, paragraph 1: Other exclusions were pregnant women (N=21), severe mentally ill (N=5) …….etc.

OK. This modification has been done.
Reviewer: Dag Steinar Thelle

Reviewer's report:
Alkerwi et al’s analysis of participants and non-participants of the ORISCAV-LUX population-based study is addressing a phenomenon which has become increasingly important when planning and performing epidemiological studies. Population based studies in the 1970s managed to get high attendance around 80 percent, but the public’s enthusiasm for participation has dwindled all over the industrialized world during the last three decades. The obvious question of course is to what extent this matter for the validity of the results. This issue has been discussed in a number of papers, and the present study provides the possibility to assess some of the consequences. The paper is well written and adequately analysed, and this referee’s comments refer to the discussion which should go deeper into the issue of participation and representation.

Whether associations observed in epidemiological surveys are due to bias induced by low attendance “depend upon the (dis)-similarities of the fractions of the exposed and un-exposed as well as affected and un-affected of the source population actually included in the final study sample”. The quoted part of the above meaning is taken from: Elisabeth Strandhagen et al. Selection bias in a population survey with registry linkage: potential effect on socioeconomic gradient in cardiovascular risk EurJ Epidemiol (2010) 25:163–172, a paper which gives some insight on how to think about the consequences of biased participation.

So does also Anne Johanne Søgaard et al. The Oslo Health Study: The impact of self-selection in a large, population-based survey International Journal for Equity in Health 2004, 3:3. Both these quoted papers are based on analyses very similar to those performed by Alkerwi et al and are also supporting some of their conclusions.


This referee would therefore recommend the authors to consider including the two papers and the chapter from Rothman and Greenland in the discussion, and to lift the discussion up to a more principle level. The term used in the discussion that “literature provides paradoxical insights ..” does not help to understand why and how bias to non-attendance may occur. It all depends upon the dis-similarity between the fractions in study and source populations, such as referred to above.

Thanks for these relevant comments. The investigators went through the suggested references and considered them in the revised version of the paper, notably in the “Discussion” section. The investigators hope deeply that the added meaning to the revised version of the manuscript replies to the referee’s expectation.
Reviewer: Evangelos Polychronopoulos

Reviewer's report:

Minor essential revisions
Regarding the strategies to foster the response rate, do the Authors consider the option:
- to use a short non respondents Questionnaire ?

As cited in the “Strengths and limitations” section, it was not possible to apply a short version of the original self-reported health behaviors questionnaire, as an alternative approach to obtain information about the key outcome indicators (smoking, alcohol consumption, dietary habits and physical activity). For the reason that, after all enhanced efforts to contact and recruit the non-respondents and reluctant cases, it was irrational to re-contact them for an otherwise short questionnaire.

- to approach and persuade the non respondents by organizing Lectures and Workshops along with the Local Municipal Authorities , Teachers and Parents Associations, Religious Associations, women’s Clubs and other National or International Non profit Organizations and Clubs?

In fact, prior to kick-off phase of the ORISCAV-LUX study, about 5000 prospectus (brochures and posters) were widely distributed in all the hospitals; municipalities; private medical clinics of cardiologists, endocrinologists, internists and general practitioners; pharmacies; ministries; and other potential diffusion channels. In addition, a vast press campaign was organized to reach the general population.

Introduction
Second paragraph, Line 11 'by using multiple approaches' pls be more specific.

OK, the sentence has been modified.

Last paragraph Line 2 'selection bias', pls clarify how did you diminish selection and self selection bias?

In this paper, the term “non-response bias” was sometimes used alternatively to signify the “selection bias”.

As mentioned in the “Discussion” section, the investigators attempted to diminish selection bias by means of the following approaches: participation-enhancement strategies; well-planned sampling strategy and sample weighting. This issue has been pointed out in the “Discussion” section.

Concerning the “self-selection bias”, the study was based on selected representative random sample and there were no place for the volunteers.
Methods
First paragraph pls describe in more details the sampling districts of residence. Did you take into account, population border differences (France, Belgium, Germany), including rural urban and socio cultural differences? Comparison of participants and non-participants

The representative random sample, selected from the national insurance registry, was stratified according to gender, age groups, and district of residence. The three geographic districts in Grand-Duchy of Luxembourg are Luxembourg, Diekirch and Grevenmacher (see Figure below please). Luxembourg is relatively a very small homogenous country, i.e. there are no distinct urban-rural areas, nor real population neighbor country-related differences. Beside age and gender, the district-based sample stratification was opted for organizational and information availability raisons rather than characteristics population differences. Most of the preliminary analysis did not show significant district-related differences.

First Paragraph Line two, what was the educational level of participants and non-participants?

The education level was self-declared for the participants; however, the investigators do not have available information about the non-participants.
Would the **sampling procedures** be more successful, by approaching their Cultural Professional associations?

Excuse, the investigators do not understand well the meaning of this question! However, it has been indicated in the “Discussion” section that any investigation with respect to socio-economic status of the participants should be interpreted prudently.

Second paragraph, Line 3

Was the lower participation rate of Portuguese residents as compared to Luxembourgish, due to Citizen Status? Number of years living in Luxembourg? Gender Differences?

In fact, the investigators based on available information relating to the variable “nationality” to compare the two groups (participants versus non-participants) and found a significant difference in the participation rate in favor of Luxembourgish people. Further analyses showed that this difference still significant even after adjustment for age, gender and professional status. However, owing to the absence of information about the “country of birth”, or the “period of residence in Luxembourg” concerning the non-participants, we cannot assert this hypothesis.

It would be interesting a ‘follow up’ non respondents short questionnaire (North South differences of a Population of ‘Mediterranean’ Origin.)

Although the tiny size of Luxembourg made possible to organize the study at national level, conversely, the small sample size hampers a relevant sub-groups analysis.

Discussion

Paragraph 4, ‘Conventional level of response’. Pls be more specific

Ok, the term was replaced by “tolerable” level in the revised text.

Table 2, Nationalities 'Others' pls explain( Mediterranean Origin i.e. Greeks )?

“Others” included all other small proportions, other than Luxembourgish, Portuguese, French, Italians and Belgians. The global selected sample included 4 Greeks, from them only one accepted to take part in the ORISCAV-LUX study.