Author's response to reviews

Title: Risk Factors for Ischemic Stroke; Results from 9 Years of Follow-up in a population based cohort of Iran

Authors:

Nooshin Fahimfar (nfahimfar@gmail.com)
Davood Khalili (dkhalili@endocrine.ac.ir)
Reza Mohebi (reza.mohebi@gmail.com)
fereidoun Azizi (azizi@endocrine.ac.ir)
Farzad Hadaegh (fzhadaegh@endocrine.ac.ir)

Version: 2 **Date:** 4 September 2012

Author's response to reviews: see over

Reviewer's report (1)

Title: Risk Factors for Ischemic Stroke; Results of 9 Years Follow-up in a Middle East cohort

Version: 1 **Date:** 13 July 2012

Reviewer: J Ivan Ivan Lopez

Reviewer's report:

Major Compulsory Revisions

- The purpose of the study is not stated in the abstract. This needs to be clearly

stated.

Agreed, done. In the current study, we aimed to determine the potential risk factors and their population-attributable fraction (PAF) for stroke in an Iranian population. (The related statement was added to the abstract.)

- It is not clear what interventions were done in these patients. Changes in diet?

Exercise? What type of exercise? Were medications given to patients?

An educational intervention was carried out to modify lifestyle through primary preventions for non-communicable disease by improving nutrition and dietary pattern, increasing physical activity levels, and reducing cigarette smoking.

Nutrition educational classes were held 4 days of the week. Twelve adults on average participated in these educational sessions. Methods of education included face-to-face consultation, educational videos and slides, and nutritional education and consultation, which involved demonstrations of healthy food preparation. Participation in religious ceremonies; sessions in mosques, particularly in the holy month of Ramadan; and lectures given to participants about the main topics of intervention were also used as a strategy to educate study subjects. Public conferences on occasions such as the World Diabetes Day or World No-Tobacco Day were held to promote the importance of healthy lifestyle behaviors. Courier of Health, 12 published every 3 months, contained health messages in lay language.

The school based lifestyle modification program was designed as a multidisciplinary health promotion program using a population approach, which has its underpinnings in the Health

Promoting Schools philosophy. The program was intended to influence anti-tobacco, healthy nutrition, and physical activity practices. These explanations have been published elsewhere and the related article was referenced in the text (page no. 5,"study population" section).

- Furthermore, why does it matter which, if any, interventions were implemented?

Intervention might affect the outcome of stroke, thus it was included in the model as a possible confounder. (Of course it did not influence the outcome and did not remain in the model)

- The definition of TIA need to be revised. Most TIAs last no more than 1-3 hours. TIAs defined as symptoms that last less than 24 hours is not longer used by stroke neurologists.

The TLGS has been started more than 10 years ago; we did not change the stroke definition during follow-up for consistency. However it does not matter which definition is used because we included all cases, regardless of definite or possible stroke or TIA description.

Minor Essential Revisions

- This paper contains numerous errors of grammar, punctuation and syntax that distract the reader from its content and obscure its message. The paper would benefit greatly from careful proofreading and revision by an individual proficient in idiomatic and medical English.

Agreed, done.

- The authors mention that "the Tehran Lipid and Glucose Study is a prospective population-based study carried out on 15005 people aged 3 years..." 15005 people? 3 year-old patients, toddlers? It seems very difficult and futile to study glucose and lipid levels in patients at this age. Please clarify this.

This study has been considered to be continued for 20 years. The rational and design of the Tehran Lipid and Glucose Study has been published before (Ref. no. 10 of the manuscript). Current study was just carried out on participants aged 50 y and over.

- In the Discussion section, authors go from strengths one to three, without mention of strength two. This needs to be corrected also.

Agreed, done.

Reviewer's report (2)

Title: Risk Factors for Ischemic Stroke; Results of 9 Years Follow-up in a Middle East cohort

Version: 1 **Date:** 19 July 2012

Reviewer: M. Arfan Ikram

This is an important manuscript that investigates stroke risk factors in an Iranian population. Given the scarce data on this topic, I believe the data are an important contribution to the literature. The authors have performed a well-designed study with proper statistics.

There are a few comments, though, that I invite the authors to consider:

Major Compulsory Revisions:

- The authors should specify how they diagnosed the subtype of ischemic stroke.

We classified strokes as ischemic or hemorrhagic according to all available information from informant interviews, medical records, and brain imaging studies (Computed Tomography and Magnetic Resonance Imaging). (This point was added in the text, page 8)

- The presentation of Tables need to be optimized. Table 1 in its current format implies that the study was a case-cohort, which it is not. The authors should present the characteristics of the whole population together, or if anything for men and women separately.

Agreed, done. We added the incidence rate of stroke in exposure-positive and exposure-negative groups instead of frequency in cases and controls.

- In Tables 2 and 3, the associations for non-significant risk factors should also be shown.

Other variables did not remain in the model because of stepwise method with the criteria of p<0.2 for entry or p>0.1 for removal, thus the output did not contain any HR and consequently PAF for these variables to show. Results of univarate analysis for these variables can be seen in Table 1 based on Log Rank test.

- I gather that the source study was designed as a trial. What was the intervention? How many people in the current analysis were in the intervention group? The authors should state more clearly the trial-origin of this sample.

Yes. An educational intervention has been carried out to modify lifestyle through primary preventions for non-communicable diseases by improving nutrition and dietary pattern, increasing physical activity levels, and reducing cigarette smoking.

Nutrition educational classes were held 4 days of the week. Twelve adults on average participated in these educational sessions. Methods of education included face-to-face consultation, educational videos and slides, and nutritional education and consultation, which involved demonstrations of healthy food preparation. Participation in religious ceremonies; sessions in mosques, particularly in the holy month of Ramadan; and lectures given to participants about the main topics of intervention were also used as a strategy to educate study subjects. Public conferences on occasions such as the World Diabetes Day or World No-Tobacco Day were held to promote the importance of healthy lifestyle behaviors. Courier of Health, 12 published every 3 months, contained health messages in lay language.

The school based lifestyle modification program was designed as a multidisciplinary health promotion program using a population approach, which has its underpinnings in the Health Promoting Schools philosophy. The program was intended to influence anti-tobacco, healthy nutrition, and physical activity practices. These explanations have been published elsewhere and the related article was referenced in the text (page no. 5,"study population" section). In the current study, all participants including 953 individuals of intervention group and 1425 individuals of cohort group were pooled to improve the power of the study, however intervention was considered as a possible confounder in analysis. (this statement was added to the text, page 5)

- I understand the use of categorization in the various variables to calculate PAR. However, to fully appreciate the data (also from a public health perspective) the authors should also provide associations using the continuous variables.

Agreed, done. These results were added to the tables 2 and 3 with a description in the material and method (page 9)

Minor Essential Revisions:

- The authors present there sample as Middle Eastern, which is true; however, even in the Middle East there are many ethnicities. It is best to be even more accurate and mention Iranian throughout the paper.

Agreed, done.

- On page 7, the authors mention "incident CKD". This should be "prevalent CKD".

Agreed, done

- The authors should explain what they mean with "verbal autopsy"?

Verbal autopsy is a method of obtaining as much information as possible about a deceased person by asking questions of the immediate family and others who can define the mode of death and situations preceding death. This method is used especially in developing countries and in settings and situations in which postmortem pathologic examination is not feasible. (The related explanation was inserted in the text, page 8)

- In the limitations, I miss the "second" limitation.

It was corrected.

- 69 cases of stroke/minor stroke/TIA is rather low for 9 years follow-up. The authors should expand more on what could be possible explanations.

We explained this matter in the discussion (Page 14   Line 12-15).

Discretionary Revisions:

-   Are there data on atrial fibrillation?

There were not ECG data for all participants.

Reviewer's report (3)

Title: Risk Factors for Ischemic Stroke; Results of 9 Years Follow-up in a Middle East cohort

Version: 1 **Date:** 2 August 2012

Reviewer: Masoud Mirzaei

Reviewer's report:

<mark>Major Compulsory Revisions</mark>

-   Introduction, risk factors of ischemic and hemorrhagic strokes are different and should be mentioned.

Agreed, done. (page4 line9).

Minor Essential Revisions

-   Page 2- the type of study should be mentioned.

Agreed, done.(It was mentioned in the title, abstract and methods)

-   Page 2- abstract- Please report PAF for modifiable and non-modifiable risk factors separately and report the numbers from high to low.

Agreed, done.

-   Page 2- conclusion of the abstract. The Middle East instead of Middle East.

We replaced Middle East with Iran based on the other reviewer comment.

- Page 4- line 3 dramatic instead of dramatically.

Agreed, done.

- Page 4- line 4.Burden of disability.

Agreed, done.

- Page 4- Second para. It is better to divide risk factors to modifiable and non-modifiable.

We reported the results of PAF based on modifiable and non-modifiable risk factors in the result section (page 11).

- Page 4 line 14- The study instead of they

Agreed, done.

- Page 4 last line. Regional incidence rates and measure of association need to be...

Agreed, done.

- Page 6 line one. You defined the studied variables as following...

Agreed, done.

- Page 6 last line of last para, please explain the education to change the life style or give ref.

Agreed, done. We referred to reference 10 and 11.

- Page 7 line 7, lower than instead of below than

Agreed, done.

- Page 7 line 15. at the hospital

Agreed, done.

- page 7 line 16. please explain how the mortality data recorded in the hospital

Agreed, done. (page 7 line no.16)

- Page 8 line 8 need reference

Agreed, done.

- Page 9 line 11 draw the K-M line?

The sentence changed to "We compared the Kaplan-Meier failure rates of these categories".

- Page 10- Discussion line 2- population attributable risk or fraction?

It was corrected as population attributable fraction.

- Page 11- line 2. the study showed.

Agreed, done.

- Page 11- line8 goes more.

Agreed, done.

- Page 11 line 8- Please

We cannot find anything.

- Page 11- para two. results and tables should come in the result section.

Agreed, done.

- Page 11 line 15 patients

Agreed, done.

- Pge 11 last line. Than

Agreed, done.

- Page 12 1st line independently associated

Agreed, done.

- Page 13 line 6. take out IN

Agreed, done.

- Page 13 last para. difference of two types of stroke should be mentioned in Intro

Agreed, done.

- Page 13 last line. a substantial number... is not true. please give reference

The sentence was corrected.(page14 line 12-15)

- Page 14 end of the 1st para. What do you mean by ME Caucasian, please give Reference

We change the term of Middle East by Iran based on the comment of one of reviewers.

- Reference 14 and 15 need correction

Agreed, done.

- Reference 17 Ed or edition

Agreed, done.

- Reference 21 Page range?

Agreed, done.

- Table 1. title should be stand alone.

Agreed, done. We revised the title with more explanation.

- Table 2 stroke

Agreed, done.

Discretionary Revisions

- table 3 Please sort the variables according to the HR values (descending)

It was preferred that more general variables were the first ones in the table.

Level of interest: An article of importance in its field

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