Author’s response to reviews

Title: Increasing prevalence of familial recurrence of multiple sclerosis in Iran: A population based study of Tehran registry 1999-2015

Authors:
Sharareh Eskandarieh (sh_eskandarieh@yahoo.com)
Narges Sistaniy Allahabadi (nickpier1990@gmail.com)
Malihe Sadeghi (sadeghimalih@gmail.com)
Mohammad Ali Sahraian (sahraian1350@yahoo.com)

Version: 1 Date: 04 Oct 2017

Author’s response to reviews:
BMC Neurology
ID: NURL-D-17-00204
Title: Increasing prevalence of familial recurrence of multiple sclerosis in Iran: A population based study of Tehran registry 1999-2015
Authors’ comments to the Editors of BMC Neurology
Thanks so much for the opportunity to revise our manuscript. We appreciate the reviewers for their nice comments to enrich the manuscript. Please find below a detailed response to the reviewers.

Reviewer reports:
Steve Simpson Jr (Reviewer 1): I note the authors have endeavored to action my comments from the original submission, which I appreciate. The article is much improved. I do have some various comments and suggestions as enumerated below. If the authors action these comments, it would be a further improvement.

Comments
- Since the authors state that the prevalence significantly increased during the study period, suggest the authors add the point prevalence of MS in Tehran in 1999.
Response: We add point prevalence of MS in Tehran in 1999 in the sentence according to reviewer comment. Line 32-33

- The authors' description of age standardisation seems incomplete. Needs to be specified to what population the prevalence estimates are being standardised to.
Response: Response: We changed the sentences according to reviewer comment (1st paragraph in Results). Line 129-130

- The whole of the paragraph running from lines 147-150 in the Results is incorrectly presenting analyses as though the outcome was the proportion of cases, but the table is actually comparing the proportions by sex. Suggest the table be moved.
Response: We changed the sentences according to reviewer comment. Line 142-149

- Also unclear why the reference age group differs between Table 1 and Table 2.
Response: We changed the reference age group in table 2, according to reviewer comment.

- The results in Table 2 for age & familial recurrence are not significant and they should be presented accordingly. You can say that the 18-27yo group had near-significantly greater proportions with familial recurrence compared to the 48+ age group, but you can't say it's different. Associated text in the Results and Discussion should be modified accordingly.
Response: We changed the sentences according to reviewer comment in Results and Discussion. Line 155-157 and 193-194

- I appreciate the authors effort to make use of my comment from the preceding review, but its present usage seems to miss the point. I propose that the fact you see a difference in familial recurrence by age is not a causal mechanism nor a risk factor but merely reflects a reality of your sample. I suggest you alter how these results are discussed to make better sense of what is happening.
Response: We changed a sentence and deleted another sentence in Discussion. Line 193-194
Response: We add a new sentence in Discussion. Line 177-178
- The sentence running from lines 208-210 does not make sense. Are you proposing that age of onset is a common characteristic between MS and schizophrenia? In any case, given as the preceding paper does not discuss non-MS conditions, I would suggest this topic not be broached in the Discussion without better substantiation.
Response: We deleted the sentences according to reviewer comment. (The association between familial recurrence and risk of MS incidence may be one of the causal factors such as schizophrenia). Line 205

- Much of the Discussion is almost like bullet points, rather than a coherent whole. Suggest the authors endeavour to restructure the Discussion so that it is more cohesive.
Response: We restructure the Discussion.

Minor comments

Introduction
- In line 45, I believe the authors mean MS is the second most common cause of disability.
Response: We changed the sentences according to reviewer comment. Line 45

- In line 48, resulted should be resulting.
Response: We changed the word according to reviewer comment. Line 48

- Suggest the sentence from line 52-53 should be restructured. Also era probably should be group.
Response: We changed the sentences according to reviewer comment. line 53-54

- Line 54, the "rank of" can be removed.
Response: We removed the rank of from sentences according to reviewer comment. Line 53

- In line 63, suggest authors replace "find out" with identifying.
Response: We changed the sentences according to reviewer comment. Line 64

- Line 65, suggest the word attached be replaced by associated.
Response: We changed the sentences according to reviewer comment. Line 66

- Line 71, suggest courses be replaced by types. Also the MS can just be written as MS.
Response: We changed the sentences according to reviewer comment. Line 72

Methods
- Line 96, remove the word, criteria, before Poser.
Response: We remove the word, criteria, before Poser according to reviewer comment. Line 96

- Suggest line 99 the word cod should be code.
Response: We changed the word according to reviewer comment. Line 99

- For line 99, suggest "their drugs" be replaced by treatment.
Response: We replaced the word according to reviewer comment. Line 99

- Suggest the sentence on line 101-102 should be rephrased.
Response: We changed the word according to reviewer comment. Line 100-102

- For line 109, into should be one word.
Response: We changed the word according to reviewer comment. Line 109

- For the sentence on lines 115-117, suggest the authors mean to say that because there is some number of participants who were not registered in their onset yet, the prevalence estimates calculated may be underestimates of the real values.
Response: We changed the sentences according to reviewer comment. Line 115-117

- For line 120, prevalence is not a rate.
Response: We changed the sentences according to reviewer comment. Line 120

- For line 126, analyses should be analyse.
Response: We changed the word according to reviewer comment. Line 127
Results
- For line 134, populations should be persons.
Response: We changed the word according to reviewer comment. Line 134

- For line 137, suggest all the text except the Figure citation can be omitted.
Response: We omitted the text according to reviewer comment. Line 137

- Please restructure the sentence from lines 142-143.
Response: We changed the sentences according to reviewer comment. Line 142-143

- The sentence running from lines 148-150 should be restructured.
Response: We changed the sentences according to reviewer comment. Line 147-149

- The sentence running from lines 157-159 should be restructured.
Response: We changed the sentences according to reviewer comment. Line 155-157

- The sentence on lines 168-169 is unclear and should be restructured.
Response: We omitted the text and moved the results in another sentences. Line 161-162

Discussion
- Suggest the bracketed mean ages of onset in lines 176-178 should add years to each.
Response: We changed the sentences according to reviewer comment. Line 173-175
- Further to the bracketed ages in lines 176-178, either present all ages with SD or none.
Response: We removed SD from the sentences, because some of our references did not report SD. Line 174-175
- On line 185-186, please provided the percentages with positive family histories of MS in Iran, Qatar and Azerbaijan.
Response: We add the percentages with positive family histories of MS in Iran, Qatar and Azerbaijan according to reviewer comment. Line 184-185
- On line 188, "Central America such as" can be removed.
Response: We removed the "Central America such as". Line 187
Eleonora Cocco (Reviewer 2): This is an epidemiological study focused on the frequency of multiple sclerosis in Teheran during the 1999-2015 period and the recurrence of the disease in families. The topic is not original but of interest. However, the article paper needs some major revisions:

- A detailed revision of the available literature should be done (references regarding both epidemiology and MS familial recurrence are inadequate).

Response: We revised the detailed in text and we add more references regarding epidemiology and familial recurrence of MS. We Add references number 13 and 36.

- The discussion is too simplistic and should be improved with a critical discussion regarding familial aggregation, factors (genetic, environmental, others) which can be explained the increasing prevalence of MS (etc.) in Iran. A comparison with previous studies in the same and with surrounding areas could be useful to explain the phenomenon. Moreover, the authors should explain which are the main characteristics of Iran and of the Iranian population which gives reason to the interest in respect to other population.

Response: We revised Discussion and we add more detail according to reviewer comments.