Author's response to reviews

Title: Inequalities in mortality among refugees and immigrants compared to native Danes - a historical prospective cohort study

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Author's response to reviews: see over
Dear editor,

We have now revised the manuscript according to the reviewers’ comments, which are addressed point-by-point below.

Kind regards,

Marie Norredam

Reviewer # 1:

Major compulsory reviews:

1. Abstract: (1) There was no abstract in the text for review.
   RESPONSE: We apologise. By default the abstract was apparently not uploaded during the submission process. This has now been done.

2. Methods: (1) Although it may be a little difficult to establish a complete and unequivocal correlation of ICD-8 and ICD-10, classification based on ICD-8 should not preclude determination of the frequency of neoplastic and cardiovascular causes of death, as groups. If possible, these deaths should be added accordingly in cause-specific analyses.
   RESPONSE: We understand the reviewer’s point. Initially, we meant to make analyses of more refined neoplastic and cardiovascular diagnostic categories, which is why diagnose specific validity was important to us. We therefore only obtained data according to ICD-10 from Statistics Denmark from 1.1.1994. However, due to small numbers we were not able to make these detailed analyses. Obtaining data for 1993 at this stage is unfortunately not financially and practically possible.

3. Results: (1) It is desirable to make a brief commentary on baseline characteristics, to clarify to the reader what the sample is like and to assure that matchmaking was successful.
   RESPONSE: To outline the matchmaking process more clearly and to show baseline characteristics of the cohort we have now inserted the following paragraph in the methods section on p.4-5:
   “We matched 4:1 on an individual level on age and sex using a random sampling procedure. We were able to make a matching for all refugees resulting in 145 870 individuals: 29 174 refugees and 116 696 controls. Four of the family-reunited immigrants were missing a total of five controls due to difficulties
with age matching because of outlying ages; accordingly, there were 33,287 family-reunited immigrants and 133,143 controls. The study cohort and matching procedure has previously been described in more detail [14]. Baseline characteristics of the cohort on 31.12.1999 when inclusion was ended showed more males (55.6%) among refugees and conversely more females (64%) among immigrants'. Refugees and their Danish-born comparisons controls were 32.9 years old and immigrants and their Danish-born comparisons 27.5 years (see table 1 stratified by sex). Refugees and their controls had been followed for a mean of about 8 years and immigrants and their comparisons for a mean of about 6 years”.

4. Discussion: (1) Are there any estimates on the rate of remigration? As these individuals are more prone to be considered alive, high rates could markedly influence the results. A sensitivity analysis using reasonable estimates, considering these individuals dead (or, at least, with a mortality rate similar to the adjusted number of those who remained in Denmark), would add more value to the article.

RESPONSE: Table 1 shows the percentage of remigration in the cohort according to migrant status and sex. Thus, among all refugees about 14% had a first time remigration during the period and among immigrants about 20%. We do not know how many among these have returned. Also we do not know the distribution of death and alive in this population as we discuss on p.9. In the analysis, the individuals that remigrate are treated as censored observations at the time of remigration. This means that they contribute to the analysis as alive until remigration. The subsequent censoring implies an explicit assumption that the remigrated individuals have the same mortality as those that remained in Denmark.

We are currently analyzing the morbidity patterns of the refugees and family-reunited immigrants, and this research might give an idea of the magnitudes of possible differences in mortality between the remigrated and remaining individuals. For now, we feel that it is premature to conjecture about reasonable input parameters for a sensitivity analysis.

Minor compulsory reviews
1. Methods: (1) How the income database works, and how data is uploaded in this system? Are there any biases this information may be susceptible to?

RESPONSE: We have inserted the following sentence on p. 6 to clarify background for income data: “We also adjusted for data on income using annual personal income based on wages from earnings and social transfers. Statistics Denmark obtains all income information from tax authorities”.

Moreover, we have adjusted the following paragraph on p.11 in the discussion to discuss bias regarding income information:
“However, personal income may inadequately reflect SES especially among elderly and family reunified individuals. Education would have been a more stable indicator of SES, but education is
not registered in a valid and consistent way for migrants in Denmark”.

2. Discussion: (1) in “the healthy migrant effect’(x)”, what does (x) stand for? Is it just a typo?
RESPONSE: We apologise. This is indeed a typo. It has been changed as part of the general proof reading.

3. Conclusion: (1) The text “Moreover, to prevent ethnic inequalities in mortality becoming more disadvantageous in the future, public health authorities should discourage the further adoption of unhealthy risk behaviour. Preventive strategies could extend to screening for diabetes and cancer-related infectious diseases among risk groups upon arrival.” Although
RESPONSE: We apologise. This is a typo. It has been changed as part of the general proof reading.

Review #2:
Title: Is all-cause and cause-specific mortality lower among refugees and immigrants than among native Danes? - a historical prospective cohort study
Version: 2 Date: 8 May 2012
Reviewer: Augusto Hasiak Santo
Reviewer's report:
Comments about the manuscript "Is all-cause and cause-specific mortality lower among refugees and immigrants than among native Danes? – a historical prospective cohort study.

Title: the title of the manuscript is too long, includes a question and even its answer, and might be improved. (discretionary revision).
RESPONSE: We do agree that the title includes a question and is long. We have now abbreviated the title as follows: “Inequalities in mortality among refugees and immigrants compared to native Danes – a historical prospective cohort study”.

On page 3, Study cohort, the phrase "Danish-born comparisons were used once only" should have its meaning clarified.
RESPONSE: It has been clarified. The following sentence replaces the original sentence: “Each of the family-reunited immigrant or refugee was age and sex matched with four Danish-born controls. Each control was selected randomly from all eligible controls without replacement, so each control was a control only once for a family-reunited immigrant or refugee”.

Also, the authors inform that 6,188 migrants born in Western Countries were
excluded. This information might be clarified. We see that there are migrants from Former Yugoslavia included in the studied cohort and this is a point of confusion. Is Former Yugoslavia considered a Western country? (minor revision)

**RESPONSE:** We understand this may create confusion. We have inserted the following in order to clarify on p.4: “Western countries does not include refugee producing areas like Former Yugoslavia, which was separated out due to their large numbers”

On page 4, Data collection, the authors mention "death causes"; what sounds strange; maybe "causes of death" would be better (discretionary revision).

**RESPONSE:** This has now been changed accordingly throughout the text.

Also on page 4, it would be necessary to inform that the deaths due to cancer (malignant neoplasms) and cardiovascular diseases (CVD) are qualified as underlying causes of death. (compulsory revision)

**RESPONSE:** We fully agree with the reviewer and have adjusted the following sentence on on p.4 to clarify: “All deaths in the cohort, which had cancer (C00-D09) and CVDs (I00-I25;I27,I30-I52) as the underlying death cause were identified”.

It would be interesting the have the methods of data standardization better specified: direct of indirect standardization, standard population, standardization of the Danish mortality data (?). (compulsory revision)

**RESPONSE:** The matching allows the unadjusted mortality rates to be interpreted as direct standardised mortality rates of the controls (and family-reunited immigrants and refugees). The mortality rates are in this way standardized with the family reunited immigrants and refugees and respective standard populations.

On the last line of page 4, "cause-specific" instead of "case-specific".

**RESPONSE:** We have changed this typo to “cause-specific”.

On page 5, Statistical analysis, it is supposed that the relative risk (RR) is estimated by means of comparison between migrants and reference Danish death rates. Nevertheless, the word "rate" appears in the manuscript once only. In Results and Discussion, lower and higher risks variations would receive correct meaning and connotation when described by means of rates (compulsory revision)

**RESPONSE:** We agree and have changed accordingly to rates in the analysis, results and discussion section.

It would be interesting to show death rates on Tables (discretionary revision).

**RESPONSE:** We think we understand the comment and agree it would be interesting. But, have
refrained from enlarging the tables, which we think already are quite explanatory. We hope the reviewer understands.

On page 7, Results, in the first line of the paragraph beginning with "Table 4 shows", "cardiovascular" instead of "cardiovascular".
RESPONSE: We have changed this typo to "cause-specific".

On page 8, Methodological strengths and limitations, it is mentioned that 1.7% of all death certificates had "unknown" causes of death, which might be qualified as "ill-defined causes-of-death" or be referred to the specific chapter of the International Classification of Diseases. (minor revision)
RESPONSE: We agree with the reviewer that terminology is difficult here. We chose ‘not known’ because this is the wording on the death certificate which Danish doctors fill out and send to the Register of Causes of Death at the National Board of Health and thus the terminology used in a Danish context. We are therefore reluctant to change it in the text.

On page 9, All-cause mortality, there is a reference to "the healthy migrant effect (x)" whose meaning might be clarified (minor revision)
RESPONSE: This is a mistake which has now been changed.

On Table 1, please confirm the "Emigrations" values for Danes. Is it correct so many people leaving Denmark?
RESPONSE: Yes it is correct that this is the number of first time emigrations registered by the authorities, however, many later return to Denmark again. As such some migrants have many emigration and immigration dates in the register.

On Table 1, it is supposed that the values between parentheses related to median ages refer to confidence intervals.
RESPONSE: No they refer to the lower and upper quartile. This has now been clarified with a note to the table.

Additional editorial requirements:

(1) Please document within your manuscript whether the data retrieved for your study is openly available.
RESPONSE: We have inserted the following sentence on p. 8 to clarify this: “According to the Danish Act on Processing of Personal Data all data subjects must be guaranteed confidentiality and anonymity. Therefore, individual level data is not as we used
are not openly available. Instead datasets and linkages between datasets are constructed at Statistics Denmark. Researchers may then access data using remote online access”.

(2) Please include the email addresses of all authors in the title page.
RESPONSE: This has been done.

(3a) Please ensure that you include an abstract in the manuscript file, and that the abstract is identical in the manuscript file and on the submission system. Abstracts should not cite references, nor refer to figures or tables. Please check the instructions for authors to ensure that your abstract follows the correct structure for this journal and article type.
RESPONSE: This has been done.

(3b) Background section of the Abstract needs context info.
RESPONSE: This has been inserted.

(4) After reading through your manuscript, we feel that the quality of written English needs to be improved before the manuscript can be considered further.
RESPONSE: The manuscript including abstract has now been revised by a professional editing service.

(5) Competing interests:
RESPONSE: We have now inserted a competing interest sentence in the manuscript

(6) Please include an Authors' Contributions section after Competing interests.
RESPONSE: This has been changed.

(7) Please note that we are unable to display vertical lines nor display merged cells, please re-layout your table without these elements.
RESPONSE: The tables have been re-layouted accordingly.