Author's response to reviews

Title: Burden of traumatic spinal fracture in 2006 - 2007 in Tehran, Iran

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

Thanks for good comments. All comments of reviewers were answered one-by-one and relevant corrections were performed.

Kind regards,
V Rahimi-Movaghar MD

(1) Clear delimitation of the reference year of study is needed. Did the study cover 12 months or more or less? From when to when (e.g. March 2006 – March 2007).
Correct

(2) Page 9. “The study had several limitations. Data for the population of Tehran was available at 2006, but the data for incidence was from 2006 – 2007 and the data for sex, age, and associated injuries was related to 1999-2004. Different types of vertebral fractures have the same DW; therefore, different types did not separate.” Discuss how the limitations are believed not to hamper validity of the study results. What are the predictable overestimations or underestimations in different components of DALYs? We believe that annual incidence has not changed significantly in two consecutive years. The age-sex structure of people with spinal fx. is influenced by different risk factors among sex and age subgroups. During the recent decade, there is not any recognized change in the pattern of risk factors in sex-age subgroups (such change happened during the Iraq-Iran war which influenced men more than women). So the authors believe that these assumptions have not significant impact on our estimation for burden of spinal fractures. We do not expect to have different age-sex pattern of spinal fractures among large Iranian cities.

- Page 2. “The International Classification of Diseases, 10th revision (ICD-10) codes of S12.0, S12.1, S12.2, S12.7, S12.8, and S12.9 for cervical vertebral fractures, S22.0, and S22.1 for thoracic and S32.0 and S32.7, S32.8 for lumbar vertebral fractures were used to identify patients with TSF in the “National Trauma Data Bank (NTDB)”. " Page 2. “In brief, the NTDB is a database on more than 16,000 trauma patients that had been collected from 1999 to 2004 in 8 major cities of Iran including six hospitals in Tehran. Age and sex distribution of TSF patients (Table 1), outcome (death vs. survival), and associated injuries of TSF patients were also extracted from the databank.”
There are considerations regarding the place, time, and person (the injuries codes to be included or excluded).

(3) Place: Patient inflow of third-level hospitals in Tehran includes many patients from other cities. In the meantime, only six hospitals cannot include all the patient inflow from Tehran itself. So the patient population that is represented by six hospitals in Tehran does not exactly represent the population of Tehran.
We agree with the reviewer that it is not an exact calculation, but it is the best available estimate. Furthermore, we used just the age-sex pattern from that datum, not the incidence of fracture.

(4) Time: Where the study title mentions years 2006-2007 as the reference years, why the National Trauma Data Bank (NTDB) data from 2006-2007 was not used for? Where the data for 1999-2004 were used, how can this affect the study results? There is no mention of using average annual values for 1999-2004 data. Should average annual value be used for representing burden in one year, even though the mean value would refer to average for 1999-2004 time period. Unfortunately, the National trauma Data Bank was not continued after 2004 and we do not have more recent alternative estimate. So, we extracted age-sex pattern of spinal fractures from 1999-2004 dataset.

(5) Injury codes: Some of the codes that need to be included are not included and some of the codes that should not be included are included. S12.8 that is “Fracture of other parts of neck (Hyoid bone, Larynx, Thyroid cartilage, and Trachea)” should not be included but is included. This should not be included since it is not spinal fracture. S18 that is “Traumatic amputation at neck level (Decapitation)” is not included but should be included since it is traumatic spinal fracture. S19 that is “Other and unspecified injuries of neck” should be partly included but is not included. Parts of this code are traumatic spinal fracture and need special treatments like redistribution. S22.9 that is “Fracture of bony thorax, part unspecified” should be partly included but is not included. Parts of this code are traumatic spinal fracture and need special treatments like redistribution. S29.7 that is “Multiple injuries of thorax” should be partly included but is not included. Parts of this code are traumatic spinal fracture and need special treatments like redistribution. S29.9 that is “Unspecified injury of thorax” should be partly included but is not included. Parts of this code are traumatic spinal fracture and need special treatments like redistribution. S32.8 that is “Fracture of other and unspecified parts of lumbar spine and pelvis” is totally included whereas just a part of it is traumatic spinal fracture (that is “Fracture of lumbosacral spine NOS” – noted that lumbar is meant to be included in this study and sacral meant to be excluded) but the other part is not traumatic spinal fracture (that is “Fracture of ischium” and “Fracture of spine NOS”). This code needs special treatments like redistribution. S39.9 that is “Unspecified injury of abdomen, lower back and pelvis” should be partly included but is not included. Parts of this code are traumatic spinal fracture - lower back - and need special treatments like redistribution.

We accept to delete S12.8 from the list, however that was very rare and its deletion does not change the final estimate. We extracted all types of spinal fractures from our dataset. Not-stating ICD codes such as S22.9 or S29.7 does not mean that we have excluded such codes; we do not have such codes in our dataset which was the result of a research project and its non-clear and ill-defined codes were rare.
(6) Why the data on “outcome (death vs. survival)” are not provided. How were they used?
As written under title of “Relative risk of mortality (RRM)” we assumed that isolated spine fracture (iTsf) can not cause pre-hospital or in-hospital death (deaths are related to comorbid injuries such as spinal cord or brain injuries).
We provided an estimate of increased post-hospital mortality based on the Ioannidis (2009), Center (1999), Puisto(2009) and Leucht(2009) studies. So, we do not have real follow-up data of outcome of our patients.

(7) Provide data on all-cause death rates, cause-specific death rates, incidence, YLL, disability weights, YLD, and DALYs by age and sex in an appendix spread sheet.
Was attached – We accessed all cause death rates for 2006 through personal communication, but they have not published yet and we are not permitted to publish them.

(8) Pages 4-5. “In the study of Puisto and colleagues, a lifelong RRM of 1.33 for females and 1.43 for males following TSF was reported which was mainly due to cancers or respiratory diseases, even after exclusion of metastatic fractures at the time of TSF occurrence.(18) We considered post-hospital mortality based on these studies.” What was done to transform the lifelong relative risk of mortality to that during the reference year of study? We have estimated incidence-based DALYs, so all consequences (including life-long consequences) of incident cases of spinal fractures in the reference year, have been attributed to the reference year. It means that we estimated the number of increased mortalities in the future years after incidence of spinal fx in the reference year.

(9) Page 3. “For this purpose, the data on population structure and general mortality rates and at least three of the above mentioned epidemiological indices are necessary.” What was the source of data on general mortality rates and how was under-registration of deaths treated. More details needed on general mortality rates for Tehran in 2006-2007. Discuss the effects of cause of death misclassification on study results.
We used the Iranian Ministry of Health death registry which covers all provinces of Iran except Tehran; that was the best available evidence for estimating general mortality and cause-specific mortality rates. All mortality rates have been adjusted after correction of ill-defined causes of death and garbage codes.

(10) Page 3. “To estimate the incidence of TSF in 2006 and 2007, two population based studies were performed in September 2007 and 2008 in Tehran. The details of these studies have been described previously.(16)”
years that provided an incidence of 16.35 (95%CI: 3.4-48.0) per 100,000. TSF incidence was 21.29 and 11.17 per 100,000 for males and females, respectively. Citation to the second study is not mentioned here. Is there an interpretation of how the low number of cases in age and sex specific groups (essentially one case, each in one age-sex group, summing up to 3 cases) renders or not the estimates unreliable and how this affects the results? The second study has not been published yet; the study has been performed by the co-authors of the present study. We would agree that low number of cases decrease reliability of the study. It has been shown by wide 95% confidence interval of 3.4-48.0 per 100,000. However, the incidence of spinal cord injury (SCI) is almost half to one-third of traumatic spine fracture, which comparing with our previous publication of burden of SCI in Tehran seems reliable: Almost 7/100,000 SCI versus 16.35/100,000 spine fracture.

(11) Page 5. “The estimated sex-age specific incidence of 354 cases of iTSF has been demonstrated based on disease modeling in Table 2.” How does estimation of 354 cases of isolated Traumatic Spinal Fracture in 2006-2007 in Tehran with census-based population of 7,976,000 in 2006 (mentioned in page 2) relate to the estimated all-age incidence rates of 10.89 for males and 5.61 for females (mentioned in table 2), where 354 / 7,976,000 is 4.44 in 100,000? The estimated all-age incidence rates of 10.89 for males and 5.61 for females for isolated Traumatic Spinal Fracture (mentioned in table 2) multiplied by all-age population of 3,986,419 for males and 3,817,464 for females (mentioned in table 3) could produce about 434 and 214 cases respectively. How are these 648 cases related to “the estimated sex-age specific incidence of 354 cases of iTSF”? Why is the total population of Tehran in 2006-2007 mentioned in table 3 (i.e. 7,803,883) even less than the census-based population of Tehran in 2006 mentioned in page 2. i.e. 7,976,000? 354 cases of iTSF are not among Tehran population. These are patients from National Trauma Data Bank in Iran, 1999-2004. As we mentioned in previous paragraphs, we used this data just for age-sex distribution of TSF not for calculation of incidence. On the other hand, it is important not to mix it. There is small difference between Tehran urban population (7,803,883) in Table 3 and total rounded population of Tehran district (7,976,000 in page 2). There are small differences between delivered data of Iranian Statistical Centre in different times and the current version is a little different with our input population data (7,872,285 vs. 7,803,883).

(12) Page 9. “Regarding other associated injuries, we did not find a correlation between thoracoabdominal injuries and increased rate of mortality. Although the patients were severely injured, it was mainly due to increased incidence of associated thoracic injuries. No significant difference in mortality was observed (20).” Not ideal to present some results in the discussion section of the manuscript that have not been mentioned in the previous sections. Provide relevant details in methods and results sections and discuss the findings in discussion section. Reference number (20) is for DisMod II software. Is this a relevant reference for this paragraph?
"...we did not find a correlation between thoracoabdominal injuries and increased rate of mortality" in the literature (not in our study). Reference number 20 is "Rabinovici R, Ovadia P, Mathiak G, Abdullah F. Abdominal injuries associated with lumbar spine fractures in blunt trauma. Injury. 1999 Sep;30(7):471-4." The reference for DisMod is 2 not 20.

(13) The manuscript does not have an abstract.

The article has an abstract which has been submitted in the special field for manuscript submission. You can find it here:

Background: The Disability-Adjusted Life Year (DALY) was designed by the World Health Organization (WHO) to measure, compare, and analyze the burden of various diseases. To the best of our knowledge, this is the first study on the assessment of burden of traumatic spinal fracture (TSF) in an Iranian community. TSF includes both isolated (iTSF) and associated injuries related to traumatic spinal fractures (aTSF) in Tehran, the capital of Iran, for the year 2006-2007 using DALYs.

Methods: Burden of TSF was estimated based on information provided by the national data on Iranian trauma, data from the WHO, and literature data using disease modeling (DISMOD). Incidence of TSF and associated injuries were obtained from two population based studies and National Trauma Data Bank in Iran, while duration, and relative risk of mortality (RRM) were obtained from WHO data and the literature. The incidence, duration, and relative risk of mortality (RRM) were used to calculate DALY for TSF. To calculate DALY, the years of life lost because of premature mortality (YLL) were added to the number of years lost because of disability (YLD). DALY were calculated separately for both iTSF and aTSF. In-hospital YLD and post-hospital YLL for iTSF and in-hospital YLL and YLD were calculated for aTSFs.

Results: TSF incidence was 16.35 (95%CI: 3.4-48.0) per 100,000. The incidence of TSF in males was more than twice that of females. The largest DALY were seen in 15-29 years. The highest burden of associated injuries of TSF was related to spinal cord and head injury. DALY for aTSF were estimated to be 2496.9 years (32.0 DALY /100,000 population). The YLD and YLL was almost similar. Total DALY for iTSF and aTSF was 2568.9 years (32.92 DALY /100,000 population). Based on the literature, post-hospital increased risk of mortality was increased by 1318 DALY (16.89 DALY /100,000 population).

Conclusion: This study showed a considerable burden for TSFs mainly due to associated injuries and increased lifelong RRM in patients with TSF.

(B) Minor Essential Revisions
(1) Page 1. “To the best of our knowledge, there is no previous study on the assessment of burden of TSF in the Iranian community using the DALY.” The databases that were searched should be mentioned.
We searched PubMed and two Iranian database of Iranmedex and Scientific Information Database (SID).


(3) Page 3. “In the present study, among all associated injuries, we included only SCI, head, and extremity injuries in the calculation.” Why? We corrected the above-mentioned sentence in the article. "There were not any other combination between vertebral fractures and injuries other than SCI, head and extremity in non-fatal cases."

(4) Page 3. “Short-term mortality of iTSF was considered as zero.” Why is this assumption needed? Does it mean, for instance, that short-term mortality of head injury is zero? How does this assumption, if it holds true (that should not be the case here), affect the estimations?

Spine fracture does not kill anyone unless it is associated with other organs such as spinal cord injury. Head injury short-term mortality is not zero. This assumption was necessary, because it shows that there was no pre-hospital death in isolated cases (iTSF). Regarding head injury, there are many died patients before entry to the hospital (Pre-hospital). Thus, for calculation of burden of head injury, we need autopsy findings or literature based studies to show how many percents of patients died before hospital entry. In SCI, there were two studies in the literature one in Portugal and the other in Canada, which showed 16% SCI death pre-hospital which comprises the great burden.

(5) Page 4. “In brief, cluster random sampling was used and structured interviews were performed with participants to detect history of spine fracture. All cases with positive history were evaluated by a specialist to document the spine fracture.” Was this evaluation a review of medical documents held by patient and/or examination? More details needed. What about the fatal cases? What about cases that have migrated out of Tehran? How the validity and reliability of these measurements can be judged about?

All suspected cases of spinal fractures had been evaluated by their medical records and documents and some of them have been examined by neurosurgeon. We had a list of died people among household survey, but none of them were suspected for a spine fx.

The other concerns (such as migration of household) are common shortages of estimating incidence based on cross-sectional surveys and interview with current residents. As overall, underestimation of incident cases in a population-based survey is lower than hospital-based data (according to problems such as access and cost of treatment)
(6) Page 5. “Post-hospital YLD was estimated to be zero, because there was no definite evidence for continuous pain or disability after 51 days.” Is this an empirical finding or a clinical impression? It is based on the assumptions of the first round of GBD. In that study, just a short-term 51 days disability was considered for isolated spinal fractures.

(7) Table 5. Where the long-term YLD for “Open wounds” is zero (in the second row of data - if dash is meant to represent zero), how can that for “Open wound plus skull Fx” that is 8.409 be greater than that for “Skull Fracture” that is 8.408? How can long-term YLD for “Brain [injury??] + Limb Fx” be marked with “-” (second last row of data) where “Brain Injury” has the second highest long-term YLD of 10.362? Why it is not correct if one interprets these figures as if a limb fracture on the top of one’s brain injury prevents long-term disability that would otherwise ensue if there were no limb fracture?

We used detailed case-by-case data to calculate YLDs. Some of the injuries to head are not expected to produce long-term disabilities.

(8) Page 6. “In 25 died patients with aTSF, 9 patients presented with intracranial hemorrhage, 2 with skull fractures, 6 with spinal cord injuries (SCI), 4 TSF and associated dislocation, 1 tracheolaryngeal crush, 1 open wound, and 2 unknown injuries.” What does “presented” mean here? Is it the main clinical presentation or cause of death? How are these categories mutually exclusive? Was not there any patient with two of these conditions together?

“Presented with” means "had …" and it is "cause of death" here. We did not have any combination of associated injuries in the dataset.

(C) Discretionary Revisions
(1) Provide ICD-10 codes for associated injuries in an appendix file. This can be useful for other researchers and readers.

Level of interest: An article of importance in its field
Quality of written English: Needs some language corrections before being published
An American native scientist is one of the co-authors of the article and corrected the language.
Reviewer: Farid Abolhassani
Reviewer’s report:
General Points:
The main ideas behind burden of disease calculation are to compare the burden of intended disease with other diseases or injuries or using the results in economic evaluations. It is only emphasized in the text that it is for the first time that burden of TSF is calculated using DALYs, but it has not been mentioned why it was found necessary or at least appropriate to spend so many time on estimating burden of TSF.

TSF does not have a considerable quota on total burden of injuries and diseases, but there are special groups (both health care providers and patients) which have special interests on it.

It seems that isolated TSF and associated TSF are different entities. In isolated TSF the problem seems to be with the spine itself, but in associated TSF the trauma is the main causal factor. The underlying predisposing factors in isolated TSF seem to play significant roles in increased lifelong mortality observed in these cases. Therefore TSF is a presentation of either a predisposing factor like osteoporosis or metastasis or a component of a severe injury accompanied by other presentations like ICH. Based on this classification of TSF, on which the study is based, it is not justifiable to calculate burden of TSF as an entity. It is more plausible to estimate burden of TSF as one of non-fatal outcomes of underlying conditions or one of a number of problems resulting from an injury.

In burden of disease studies, we can quantify burden of determinants of health, risk factors, diseases/injuries and complications; we chose the traumatic spinal fracture as a specific entity and like many other diseases (such as diabetes mellitus or hypertension), TSF can be considered as a factor that increases mortality in the following years. It is another view to burden of injuries, to estimate burden of a specific anatomical injury (such as spine fracture) instead of estimating burden of external causes of injury.

The authors have assumed that aTSF is the major injury that is accompanied by other co-incident injuries. In this way the burden of ICH, when accompanied by TSF, is categorized as aTSF. Base on such an approach, it is also possible to assume that ICH is the major injury and ascribe the burden of co-incident TSF to it. Therefore even if we are trying to estimate burden of aTSF as an entity, including the burden of co-incident injuries does not seem neither reasonable nor necessary.

This is correct and we considered it by splitting the results by isolated/associated TSF. Whenever a researcher wants to estimate burden for other injuries associated, it should be considered to avoid duplication of data.

There are four major value concerns in calculating DALYs: Disability weight, lost years due to premature death, discounting and age weighting. Disability weights and discount rate have been discussed in the text, but nothing has been mentioned regarding the other two value concerns.

In Figure 1, we explained that how we considered YLL (Years Lost due to premature deaths) in estimation. An explanation about age-weighting was
added to the article: "We used standard age-weights with $\beta=0.04$ and $c=0.1658$ for estimation of DALYs; so, the DALY(0.03, 1) was estimated."

The data used for estimating DALYs have been acquired from two major sources, a rather long registration (NTDB) and two population surveys. These sources of data are acceptable as minimum required local data for estimating DALYs.

The numbers included in the text are not consistent and also not compatible with those presented in tables. For example sum of male and female aTSF DALYs ($843.69+1725.1=2568.79$) is greater than 2496.9 that is mentioned as the total aTSF DALYs. In the second paragraph under "Results", 2568.9 is mentioned as the total DALYs of TSF, including both iTSF and aTSF.

Thanks for the reviewer's attention. However, 2568.9 in the paragraph (total burden of TSF) denotes total burden of pre-hospital and in-hospital stages of both iTSF and aTSF. 2496.9 is the total of DALYs for aTSF.

We added an explanation to this paragraph: "To calculate burden of spine fracture, DALYs for iTSF was added to the calculated DALY for aTSF which provided a total DALY of 2568.9 years for pre-hospital and in-hospital stages".

While "identifying key opportunities for health gain", "policy implications" and "research implications" are mentioned as the main purposes of conducting this study, these topics are not covered under the discussion.

The limitations of the study are pointed out in the text. Although data sources do not belong to the same period, but type of information provided by each source and closeness of data gathering periods make these sources quite acceptable for such a study. Therefore I think that this point could not be considered as one of major limitations of the study. Using values from literature for duration of disability, which depends on local quality of care, could be considered as one of limitations of this study.

We added it to limitations.

The topic chosen for the paper is quite informative, but unfortunately the abstract is not included in the text. The text is not fully acceptable from writing style point of view and should be edited.

The article has an abstract which has been submitted in the special field for manuscript submission.

An American native scientist is one of the co-authors of the article and corrected the language.