## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (see an example) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below. Some articles will have been accepted based in part or entirely on reviews undertaken for other BMJ Group journals. These will be reproduced where possible.

## ARTICLE DETAILS

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| **TITLE (PROVISIONAL)** | Reporting of lifetime fractures: methodological considerations and results from the Thai Cohort Study |
| **AUTHORS** | Berecki-Gisolf, Jannek e; McClure, Rod; Seubsman, Sam-ang; Sleigh, Adrian |

## VERSION 1 - REVIEW

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| **REVIEWER** | Professor CM Court-Brown<br>Professor of Orthopaedic Trauma<br>Royal Infirmary of Edinburgh<br>Edinburgh<br>EH16 4SU<br>UK |
| **REVIEW RETURNED** | 24-Apr-2012 |

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| **THE STUDY** | The main problem with the paper is the methodology. The authors have sought to define fracture epidemiology in Thailand by looking at a very select group and simply asking them if they have had a fracture. The group is taken from adult Open University students and will simply not be representative of the Thai population. We know that fracture epidemiology varies with many factors including age, gender, residence and deprivation and these will simply not be covered fully in this cohort. The authors point out the differences between their group and the Thai population and this effectively negates their results. They have also simply asked if their group have had a fracture quoting the work of Donaldson. He wrote 2 papers one of which relied on proper diagnosis in a defined population with the second study merely relying on the patients replying to a letter asking them if they had ever had a fracture. The 2nd study had 3 times the fracture incidence of the first. Many para-medical personnel will diagnose fractures and it is common for patients to be told by general practitioners, physiotherapists, osteopaths etc that there pain is secondary to a fracture. thus simply asking the patient, and having no proof of a fracture, is pointless. It is also important that the whole population is examined as fractures vary considerably with age and social circumstances and the educated Open University population will not be representative of the whole population.<br><br>There are more modern references and it does not look as if the more recent orthopaedic literature has been consulted. |
| **RESULTS & CONCLUSIONS** | With inadequate methodology the message is questionable. In fact the main message is that there is a increase in fracture incidence in post-menopausal Thai women. This increase has been known about for many years and Buhr and Cooke drew attention to it in the 1950s. Post-menopausal fracture incidence is what has caused the interest in fragility fractures. Proving that Thai women also have this problem is not sufficient to merit publication. The other point is that |

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| | the fractures are merely lumped together in crude body areas. So in the leg it is ankle or the rest of the leg. That really is not much use to orthopaedic surgeons who might wish to study fracture incidence in Thailand. |

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| **REVIEWER** | Samkaew Wanvarie<br>Associate Professor<br>Faculty of Medicine, Ramathibodi Hospital<br>Mahidol University<br>Thailand<br><br>Conflicts of interest: None |
| **REVIEW RETURNED** | 11-May-2012 |

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| **THE STUDY** | Multi-stage sampling of eligible voters nationwide in the list of Ministry of Interior would be more representative sample |

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| **REVIEWER** | Pritaporn Kingkaew, Researcher,<br>Health Intervention and Technology Assessment Program (HITAP), Thailand.<br><br>Please see the attached ICMJE Conflicts of Interests form. |
| **REVIEW RETURNED** | 29-May-2012 |

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| **THE STUDY** | As mentioned by the authors, there is a selection bias of younger population and those relatively healthy and active older persons. However, the authors stated that they omit the results that affected from such bias. |
| **GENERAL COMMENTS** | This is a cross-sectional study of incidence and prevalence of established fractures among Thai adults from the Thai Cohort Study. A structured questionnaire was sent to study samples asking about the past experience of fractures. The strength of this paper is to illustrate a method to manage recall bias that is usually unavoidable in this type of research. There are some minor comments as follows:<br>• Given this is a questionnaire-based study, the authors should comment on the effect of the low respond rate (44%).<br>• The authors should use the term “establish fracture” instead of “fracture” throughout the manuscript since respondents can only recognise the clinical fractures.<br>• Given in Thailand, traffic accident is one of the leading causes of morbidity and mortality among Thai adults.[1] I found the discussion on the prevalence of osteoporosis is quite irrelevant as it is not stemming from the findings. It might be the case that many fractures in this study samples caused by accidents. Therefore, the discussion on such issue may mislead the readers.<br>• The questionnaire did not ask respondents about the causes of fractures. For future research, the authors should include the causes of fractures in order to gain a comprehensive understanding of age and sex patterns in fracture incidences.<br>• Since Thailand has achieved Universal Health Coverage in 2002, large hospital dataset started to become available, especially from the public hospitals. Therefore, it is now possible to analyse the fracture incidence from hospital data, based on individual patient records. |

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| | • It should be noted that the morphometric fractures[2] (not a self recognised fracture) are also important from the public health perspective, the author should discuss on how to improve the findings by cooperating the survey information with data from the national database.<br><br>References<br>1. Porapakkham Y et al. Estimated causes of death in Thailand, 2005: implications for health policy. Popul Health Metr. 2010 May 18;8:14.<br><br>2. Incidence of vertebral fracture in europe: results from the European Prospective Osteoporosis Study (EPOS).J Bone Miner Res. 2002 Apr;17(4):716-24. |

**VERSION 1 – AUTHOR RESPONSE**

Reviewer: Professor CM Court-Brown

The main problem with the paper is the methodology. The authors have sought to define fracture epidemiology in Thailand by looking at a very select group and simply asking them if they have had a fracture. The group is taken from adult Open University students and will simply not be representative of the Thai population. We know that fracture epidemiology varies with many factors including age, gender, residence and deprivation and these will simply not be covered fully in this cohort. The authors point out the differences between their group and the Thai population and this effectively negates their results.

We acknowledge that the fracture incidence derived from the Thai Cohort Study 2009 survey is not representative of the general Thai population, and we have revised the manuscript accordingly. However the Thai Cohort Study is a very large nation-wide study and the participants represent well the socioeconomic status of the young Thai population. The variations in fracture rates by age and gender observed by internal comparisons in the Thai Cohort Study participants are therefore likely to reflect fracture rate patterns in the general young Thai population.

They have also simply asked if their group have had a fracture quoting the work of Donaldson. He wrote 2 papers one of which relied on proper diagnosis in a defined population with the second study merely relying on the patients replying to a letter asking them if they had ever had a fracture. The 2nd study had 3 times the fracture incidence of the first. Many para-medical personnel will diagnose fractures and it is common for patients to be told by general practitioners, physiotherapists, osteopaths etc that there pain is secondary to a fracture. Thus simply asking the patient, and having no proof of a fracture, is pointless. It is also important that the whole population is examined as fractures vary considerably with age and social circumstances and the educated Open University population will not be representative of the whole population.

The difference in fracture incidence per study methodology (i.e. self-report vs. 'proper diagnosis') is not likely to confound the observed associations between fractures and age, gender and other potential exposure variables. Although we acknowledge that the overall Thai Cohort Study fracture incidence may not reflect the general Thai population doctor-diagnosed fracture incidence, the associations within the cohort (i.e. the internal validity) need not be affected. Furthermore the findings of the current study can also be used for (i) comparisons with other studies where a similar methodology was used, and (ii) to track changes in, and determinants of, fracture rates of the cohort over time.

With inadequate methodology the message is questionable. In fact the main message is that there is a increase in fracture incidence in post-menopausal Thai women. This increase has been known about for many years and Buhr and Cooke drew attention to it in the 1950s. Post-menopausal fracture incidence is what has caused the interest in fragility fractures. Proving that Thai women also have this problem is not sufficient to merit publication. The other point is that the fractures are merely lumped together in crude body areas. So in the leg it is ankle or the rest of the leg. That really is not much use

to orthopaedic surgeons who might wish to study fracture incidence in Thailand.
We acknowledge that this study may not be of practical use to orthopaedic surgeons who wish to study the overall Thai fracture incidence and concentrate on the age-related effects of osteoporosis. But it is a study to help grow knowledge on population-level effects in Thailand and form a foundation for future longitudinal analyses.

Reviewer: Samkaew Wanvarie
Multi-stage sampling of eligible voters nationwide in the list of Ministry of Interior would be more representative sample

Reviewer: Pritaporn Kingkaew, Researcher
Are the patients representative of actual patients the evidence might affect? As mentioned by the authors, there is a selection bias of younger population and those relatively healthy and active older persons. However, the authors stated that they omit the results that affected from such bias.
The age range of the study participants is limited (i.e. the majority of participants are between 20 and 50 years) but the study population represents well the age distribution in the young adult age band as well as the socioeconomic status of the Thai population. Older persons are not well represented and older study participants are likely to be a relatively healthy selection of their population age group. Although results for participants over 50 are presented in some of the tables and figures, the main study findings apply to young Thais, as stated throughout the manuscript.
This is a cross-sectional study of incidence and prevalence of established fractures among Thai adults from the Thai Cohort Study. A structured questionnaire was sent to study samples asking about the past experience of fractures. The strength of this paper is to illustrate a method to manage recall bias that is usually unavoidable in this type of research. There are some minor comments as follows:
• Given this is a questionnaire-based study, the authors should comment on the effect of the low respond rate (44%).
A 44% response rate to the baseline questionnaire can be considered a high initial response rate. The TCS cohort is embedded in the Thai population and has a very similar socio-economic status.
• The authors should use the term “establish fracture” instead of “fracture” throughout the manuscript since respondents can only recognise the clinical fractures.
The study participants will only be able to report established fractures, and given the survey nature of the study this will be clear to the reader. Fractures that are visible on X-ray but not recognised by the patient (such as vertebral fractures) are more likely to be a health concern for an older population.
• Given in Thailand, traffic accident is one of the leading causes of morbidity and mortality among Thai adults.[1] I found the discussion on the prevalence of osteoporosis is quite irrelevant as it is not stemming from the findings. It might be the case that many fractures in this study samples caused by accidents. Therefore, the discussion on such issue may mislead the readers.
Yes we agree that among young Thais, accidents are the leading cause of fractures, and osteoporosis is not likely to play a role in this age group. We have removed the discussion of osteoporosis accordingly.
• The questionnaire did not ask respondents about the causes of fractures. For future research, the authors should include the causes of fractures in order to gain a comprehensive understanding of age and sex patterns in fracture incidences.
Recognising the impact of accidents on the young Thai population, a section of each Thai Cohort Study survey is dedicated to recent injuries; this includes questions about setting (workplace, traffic), mechanism and nature of the injury. This has resulted in several publications (listed below). The fracture questions analysed in the current study are not linked to the accident research questions but are intended to capture lifetime fractures as part of the participants’ medical history. We have demonstrated that fracture self-report is possible and we plan further analyses of fracture and its determinants in the future.
1: Yiengprugsawan V, Stephan K, McClure R, Kelly M, Seubsman S, Bain C, Sleigh AC; Thai Cohort

Study Team. Risk factors for injury in a national cohort of 87,134 Thai adults. Public Health. 2012 Jan;126(1):33-9.
2: Stephan K, Kelly M, McClure R, Seubsman SA, Yiengprugsawan V, Bain C, Sleigh A; Thai Cohort Study Team. Distribution of transport injury and related risk behaviours in a large national cohort of Thai adults. Accid Anal Prev. 2011 May;43(3):1062-7.
3: Stephan K, McClure R, Seubsman SA, Kelly M, Yiengprugsawan V, Bain C, Sleigh A; Thai Cohort Study Team. Review of injuries over a one year period among 87,134 adults studying at an open university in Thailand. Southeast Asian J Trop Med Public Health. 2010 Sep;41(5):1220-30.
• Since Thailand has achieved Universal Health Coverage in 2002, large hospital dataset started to become available, especially from the public hospitals. Therefore, it is now possible to analyse the fracture incidence from hospital data, based on individual patient records.
These data are not available yet. When they do become available there will still be difficulty in establishing true fracture incidence as this depends on accuracy in determining hospital catchment areas. Often these are indeterminate. Survey data still holds an important place alongside administrative datasets in providing sociodemographic information as well as outcomes. Longitudinal studies also provide information on exposures prior to the outcome. Such analyses will be possible with the Thai Cohort Study in the future.

• It should be noted that the morphometric fractures[2] (not a self recognised fracture) are also important from the public health perspective, the author should discuss on how to improve the findings by cooperating the survey information with data from the national database.
Osteoporotic vertebral fractures could be studied better in a slightly older cohort.
References
1. Porapakkham Y et al. Estimated causes of death in Thailand, 2005: implications for health policy. Popul Health Metr. 2010 May 18;8:14.
2. Incidence of vertebral fracture in europe: results from the European Prospective Osteoporosis Study (EPOS).J Bone Miner Res. 2002 Apr;17(4):716-24.

**VERSION 2 – REVIEW**

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| **REVIEWER** | CM Court-Brown<br>Professor of Orthopaedic Trauma<br>Edinburgh<br>UK<br><br>There are no conflicting interests |
| **REVIEW RETURNED** | 18-Jun-2012 |

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| **THE STUDY** | The methodology is inappropriate. |
| **RESULTS & CONCLUSIONS** | As I said previously the two main problems with the study are the fact that a particular subset of the Thai population has been used and that the population has simply been asked if they have ever had a fracture - with no proof.<br><br>The methodology is equivalent to asking shoppers in Tesco or Waitrose if they have ever had a fracture. You will get information which is unlikely to be representative of the whole population. The Americans often analyse fractures in Insured groups or their armed forces. Both produce results but there are no elderly or uninsured and the results are meaningless. The Thai open university population will not represent the whole population and therefore the results are not likely to be accurate.<br><br>The authors are correct when they say that it is more difficult to use a better retrieval system. However that is what they must do. |

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| **REVIEWER** | Pritaporn Kingkaew<br>Health Intervention and Technology Assessment Program<br>6 th Floor, 6 th Building, Department of Health, Ministry of Public Health, Tiwanon Rd., Muang, Nonthaburi 11000, Thailand<br><br>I declare that I have no competing interests. |
| **REVIEW RETURNED** | 16-Jul-2012 |

- The reviewer completed the checklist but made no further comments.