Author’s response to reviews

Title: Comparison of Screening Strategies for Prevalent Vertebral Fractures in South Korea: Vertebral Fracture Assessment vs. Spine Radiography

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Response to reviewers

Reviewer 1: This is an interesting study comparing VFA and X-ray for the detection of prevalent fractures regarding clinical and cost-effectiveness as well as radiation dose.

The following are some questions/suggestions:

- From the title and abstract it is not clear that actually only a prediction model was calculated based on data from the literature and no "real" patient data were evaluated
Response

We appreciate the kind words and helpful comment. As pointed out by the reviewer, only a prediction model was calculated based on data from the literature; however we also used transition probabilities from real patient data that linked hospital cohorts and Korean National Health Insurance claims data to capture hospital healthcare usage, since VFA is not widely used in clinical practice. Therefore, we have corrected the sentences as below.

Title:

Comparison of Screening Strategies for Prevalent Vertebral Fractures in South Korea: Vertebral Fracture Assessment vs. Spine Radiography

Abstract

Three screening strategies: 1) Spine radiography (X-ray) following Vertebral Fracture Assessment (VFA), 2) VFA only, and 3) X-ray only, for every two years were compared using a Markov model based on administrative data from South Korea over a 10-year period in a population aged ≥50 years.

- Maybe also refer to the fact that having analyzed Korean data in abstract and title?

Response

In the Markov model, some important input parameters such as prevalence, incidence, and cost of VFs were obtained from claims database of South Korea. We have presented this information as below.

Title:

Comparison of Screening Strategies for Prevalent Vertebral Fractures in South Korea: Vertebral Fracture Assessment vs. Spine Radiography
Abstract

Three screening strategies: 1) Spine radiography (X-ray) following Vertebral Fracture Assessment (VFA), 2) VFA only, and 3) X-ray only, for every two years were compared using a Markov model based on administrative data from South Korea over a 10-year period in a population aged ≥50 years.

Response

We have corrected the sentence.

Page 4, Last paragraph, Introduction

There has been one study of the cost-effectiveness of VFA versus X-ray in postmenopausal women with osteopenia [14] but none assessing the clinical benefits and disadvantages of X-ray and VFA as a screening tool in the general population.

- Authors should explain briefly in the introduction why not only VFA and X-Ray were compared, but also X-Ray following VFA (false negative i.e. upper thoracic vertebra)

Response

We have added the reason for using X-ray following VFA in the introduction.

Page 4, 2nd and 3rd paragraphs, Introduction

Until now, lateral thoracic and lumbar X-rays have been used as the gold standard for VF identification [6], because of the potential false negative rate of VF due to the poor image quality of the upper thoracic vertebrae in VFA [10, 11]. Therefore, in this study, we aimed to compare estimate the clinical effectiveness, cost-effectiveness, and radiation exposures of VF screening strategies in adults aged 50 years and older using X-ray following VFA, VFA only and X-ray only, as performed to detect prevalent VFs early and to prevent new VFs.

- The sensitivity and specificity of new DXA devices (i.e., iDXA) might be much higher - This would change the results regarding VFs reduction and has to be discussed
Response

We agree to and have added the following comment about iDXA in the discussion section.

Page 13, 1st paragraph, Discussion

Although the new DXA devices such as iDXA are not widely used in the clinical field, the results of this study would be different if we used such a device because of its high sensitivity and specificity [31].

- In daily clinical routine it is very convenient to perform VFA at the same time as BMD measurements; once a fracture is detected, normally no additional X-ray has to be performed (on iDXA)

Response

We agree with the reviewer’s comment, and many recent practice guidelines recommend VFA rather than X-ray for screening vertebral fractures. However, not all DXA devices are up-to-date and there is not enough information about the availability of iDXA in the real world. Therefore, we defined the gold standard for VF detection as X-ray, and compared effectiveness and radiation exposure between X-ray only, X-ray following VFA and VFA only. We have added a comment about the use of iDXA in the discussion section.

Page 13, 1st paragraph, Discussion

Although the new DXA devices such as iDXA are not widely used in the clinical field, the results of this study would be different if we used such a device because of its high sensitivity and specificity [31].

- Why did "VFA only" have the highest costs? Just because of unnecessary treatment? Otherwise I would expect this to have lower costs than X-Ray following VFA

Response

The differences in cost of the three strategies derive from the cost of each screening test and treatment of the VF. The X-ray following VFA strategy had the lowest cost, since the X-ray,
which has 100% sensitivity and specificity, is performed after the VFA screening, which has half the cost of X-ray; only patients diagnosed as VF by X-ray are treated, and the others are screened after 2 years. On the other hand, in the VFA only strategy, again patients diagnosed as VF by VFA are treated and the other patients are screened after 2 years but because VFA is less specific than X-ray, more patients are treated with anti-osteoporotic agents in the VFA only strategy than in the X-ray following VFA strategy.

Reviewer 2: Interesting paper, the authors present the research on new screening strategies for detecting vertebral fractures. Based on the results showed by authors, the conclusions are reasonable and objective. However, I have several issues that need to be addressed:

1. As the authors stated in the manuscript, VFA had a risk of misdiagnosis caused by false negative rates of about 20%, then why the VF prevalence in X-ray following VFA group and VFA only group had the similar result?

Response

In the X-ray following VFA strategy, X-ray can exclude the patients who are false positives in the VFA test, but it cannot diagnose the VF patients who are false negative by VFA. Therefore, the X-ray that follows VFA cannot provide any more protection against new VF than the VFA only strategy. Thus the protection against new VF is the same in the two strategies. However, there are cost differences between them.

2. How did the specificity of VFA cost calculated?

Response

Figure 2 is the results of the univariate sensitivity analysis compared with the base case analysis. We calculated the differences of effect and cost for each strategy when the input parameters were changed (Table 1). When the specificity of VFA was decreased from 0.93 to 0.89, the cost of X-ray following VFA strategy was increased by 3 euros and the cost of VFA was increased by 194 euros.

Page 9, last paragraph, sensitivity analysis

The input parameters of the sensitivity analysis are given in Table 1.

Page 10, 1st paragraph, sensitivity analysis
In addition, when the sensitivity and specificity of VFA were reduced, the costs of the strategies that include VFA changed. However, their relative rankings of the strategies were maintained.

3. Not only patients with VF need anti-osteoporosis treatment, how do authors deal with patients without VFs (such as osteoporosis with back pain) start anti-osteoporosis drug treatment?

Response

We appreciate this important comment. Our study compares the effectiveness of imaging modalities as tools for detecting vertebral fractures because the latter are the most important risk factor for future fractures. Treatment decisions based on bone mineral density (BMD) are another important treatment standard, but they have not been reflected because they are adapted to the same probability for all patients. In other words, the frequency of fracture and BMD as a gold standard were not used because they are equally applicable to the patient population. However, the risk of fracture due to the treatment used was reflected. A model that included information on BMD values in the subject population would be very complex, and it might be better to identify the usefulness of VFA reflecting BMD values by observational studies using real world data. We have added this to the discussion in the form of a limitation and future work.

Page 5, last paragraph, model overview, methods

All patients who tested positive for VF, were assumed to receive anti-osteoporotic therapy for one year, and patients who tested negative for VF were assumed not to receive anti-osteoporotic therapy.

Page 12, last paragraph, Discussion

In addition, the use of anti-osteoporotic agents based on BMD values was not considered, since it would be equally applicable to all the patients. Modeling that included information on BMD values in the subject population would be very complex, but it would be possible to perform such additional modeling if real world data from observational studies were included.