Cost-Effectiveness Analysis of CT2S screening for osteoporosis in Dutch postmenopausal women

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1. Introduction

In the last decade, specialized fracture and osteoporosis clinics, the so-called fracture liaison services (FLS) run by nurse practitioners, supervised by physicians, have been started in several countries also in the Netherland. Typically, if patients are referred to an FLS, osteoporosis screening will be performed to measure the bone density and a treatment advice will be given by a practitioner if necessary. The actual gold standard for osteoporosis diagnosis and follow-up is areal bone mineral density measurement via dual-energy X-ray absorptiometry (aBMD-DXA). This radiological exam directly gives a simple measure of the bone mineral content, that is compared with epidemiological data to evaluate its deviation from the healthy population average value. Although direct and rapid, aBMD-DXA showed poor performance in fracture risk prediction [1].

In recent years, various authors proposed an alternative method where the patient is examined with a low-dose Computed Tomography scan, and the resulting data are used in a patient-specific computer biophysics model that predicts the force required to fracture the patient's femur; the alternative biomarker is known as Biomechanical Computed Tomography (BCT). CT2S is a concrete implementation of the BCT method, developed in collaboration by University of Sheffield (UOS) and University of Bologna (UNIBO). This kind of models shows a higher stratification accuracy on discriminating between fractured and non-fractured women populations in a pair-matched cohort, with an area under the ROC curve of 0.85, vs 0.75 of the aBMD-DXA predictor [2].

Within the activities of CompBioMed phase I, Sheffield has developed the CT2S hospital workflow to enable access to HPC workflows directly from clinical settings without concerning the underlying complexity of the HPC resources and software. The workflow is implemented on ShARC (USFD) HPC cluster. Besides, the codes are currently running also on the other two HPC clusters, namely, Cartesius (Tier-1, hosted by SURF, The Netherlands), and Galileo (Tier-1, hosted by CINECA, Italy) to test the scalability of the solution in silico clinical trial. In this study, we conducted the effectiveness analysis for a new osteoporosis screening tool (CT2S) comparing it with a traditional one (DXA) and no screening scenario for Dutch postmenopausal women using the state-transition microsimulation model.

2. Methods

In the cost-effectiveness analysis, we used the decision tree and finite state Markov microsimulation model to simulate individual level state transition and calculate the accumulated cost and health utility throughout the patient journey with 1-year cycle length. In the Markov model (figure1), we defined nine health status: No Osteoporosis, Osteoporosis, three main types of fractures (Hip, Vertebral and Forearm), the corresponding post fracture status and Death. In the simulation process, no osteoporosis patient may develop osteoporosis within one cycle and both no osteoporosis patient and osteoporosis patient may have a fracture. Patients who had fractures were entered into corresponding post fracture status. They might stay in the same post fracture status, have another fracture or die. The corresponding transition probabilities of the status are defined.

The clinical and epidemiological data are collected from Dutch and European studies and one-way sensitivity analysis was conducted to evaluate the impact of each input parameter on the outcome of the model. The corresponding distributions are created for the top 10 parameters which have the most impact on the model outcome in order to cover the uncertainty of the parameters when performing the probabilistic sensitive analysis (PSA) using Monte Carlo simulation [3]. The values are randomly sampled from the distribution created 10000 times and each time the variables was given a new value. The variable set was used in the microsimulation to run 1000 trials and the mean of the cost, effectiveness and Incremental Cost-Effectiveness Ratio (ICER) are recorded. Then the second variable set was used to run microsimulation again and this leads to another cost, effectiveness and ICER value. The ICER values were presented in the ICER scatter plot for further analysis and the mean of the incremental cost, incremental effectiveness and ICER of cohort simulation are recorded for comparison. Both cost and quality-adjusted life year (QALY) were discounted with an annual rate of 3% [4]. We ran the simulation for three age groups (60s, 70s and 80s) over a life time. Besides, we also generated the cost-effectiveness acceptability curve to show the probability of accepting different screening strategies across different ICER threshold by comparing the net monetary benefit (NMB) for each strategy.

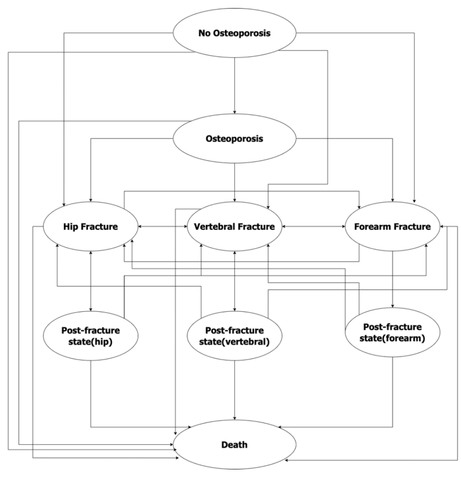

Figure 1 *Structure of the Markov model*

3. Result

We conducted the cost-effectiveness analysis of No screening vs DXA vs CT2S in three age groups (60s, 70s and 80s) in the condition of screening interval equal to 5 years and the cost of CT2S is around 384 euro. The ICERs of DXA vs CT2S in the age group 60s, 70s and 80s are €15,079, €9,892, and €5,792. considering the ICER threshold in the Netherlands which is varied from €20,000 to €80,000[5]. The CT2S screening is cost effective in all three age groups compared with DXA. The result also shows CT2S tends to be more cost effective in elder age groups.

The cost of CT2S (around €384) is much higher than DXA cost (around €97). Personnel costs (around €200) dominate the total cost of CT2S due to the required pre-processing of CT scan (femur bone segmentation) for the simulation and this is done manually. However, if we automate the pre-processing those costs can be avoided in the future. Therefore, we reran the analysis in the condition of reduced CT2S cost (around €184). We can see that the ICERs of DXA vs CT2S in age group 60s, 70s and 80s decreased significantly which makes the CT2S screening much more cost effective. One important finding is that the simulation result of age group 80s, compared with DXA, CT2S screening can contribute to a high health utility value and at the same time even reduce the cost. It means CT2S dominated DXA and no screening in the age group 80s.

The cost-effectiveness acceptability curve of No screening vs DXA vs CT2S in two age groups (60s, 80s) in the condition of screening interval equal to 5 years and the cost of CT2S is equal to €384 are shown in the subfigures a and b of figure 2. As we can see, the starting ICER threshold of CT2S screening becoming the most cost effective is decreasing when the screening age group is getting older. The probability of CT2S becoming more cost effective compared with DXA and no screening is also increasing when the screening age group is getting older. Subfigures c and d of figure 2. show the cost-effectiveness acceptability curve of No screening vs DXA vs CT2S in two age groups (60s, 80s) in the condition of screening interval equal to 5 years and the cost of CT2S is equal to €184. The starting ICER threshold of CT2S screening becoming the most cost effective is decreasing further when the cost of CT2S is reduced . The probability of CT2S to be more cost effective compared with DXA and no screening is also increasing compared with full cost scenario. And for age group 80s, CT2S becomes the most cost-effectiveness screening option immediately.

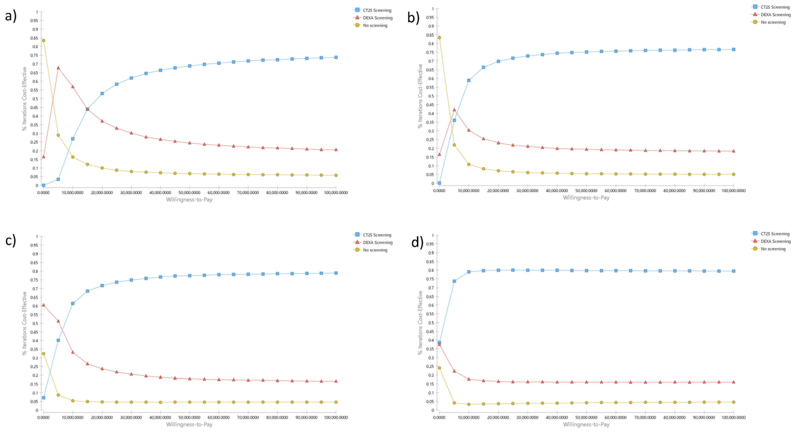

Figure 2

a) Cost-effectiveness acceptability curve (60 Age group, CT2S cost = 384.16 euro) b) Cost-effectiveness acceptability curve (80 Age group, CT2S cost = 384.16 euro). c) Cost-effectiveness acceptability curve (60 Age group, CT2S cost = 185.16 euro). d) Cost-effectiveness acceptability curve (80 Age group, CT2S cost = 185.16 euro)

4. Conclusion

Compared to no screening scenario, both DXA and CT2S are cost effective among all age groups tested in our study (60s, 70s, 80s) when considering the ICER threshold of the Netherlands. Besides, compared with DXA, direct access to CT2S is also cost effective. Particularly for age group 80s CT2S screening is highly recommended when the cost of CT2S is around €184 for the reason that it can bring high health utility and at the same time even reduce the cost which dominated DXA.

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Reference

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