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ORIGINAL ARTICLE

# Establishing and evaluating FRAX<sup>®</sup> probability thresholds in Taiwan



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## KEYWORDS

alendronate;  
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cost effectiveness;  
FRAX<sup>®</sup>

**Background/purpose:** The Taiwanese FRAX<sup>®</sup> calculator was launched in 2010. However, cost-effectiveness thresholds for the prescription of antiosteoporosis medications were not established. This study aims to establish and evaluate FRAX<sup>®</sup>-based probability thresholds in Taiwan. **Methods:** Using previous data from Taiwan and literature, we determined cost-effectiveness thresholds for prevention of osteoporotic fractures by alendronate with a Markov model, as well as using two other translational approaches. Sensitivity analysis was applied using different alendronate prices. A clinical sample was used to test these Taiwan-specific thresholds by determining the percentages of high-risk patients who would be qualified for current National Health Insurance reimbursement.

**Results:** With the Markov model, the intervention threshold for hip fracture was 7% for women and 6% for men; for major osteoporotic fracture, it was 15% for women and 12.5% for men. Both translational approach models were cost effective only for certain age groups. However, if branded alendronate was reimbursed at 60% of the current price, they became cost effective in almost all age groups. This clinical screening study showed that the National Health Insurance Administration model identified the highest proportion (44%) of patients qualified for National Health Insurance reimbursements, followed by the Markov model (30%), and the United States model (22%).

Conflicts of interest: The authors have no conflicts of interest relevant to this article.

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**Conclusion:** Three FRAX<sup>®</sup>-based models of alendronate use were established in Taiwan to help optimize treatment strategies. The government is encouraged to incorporate FRAX<sup>®</sup>-based approaches into the reimbursement policy for antiosteoporosis medicines.

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## Introduction

The National Nutrition and Health Survey in Taiwan reported that 41.2% of women and 22.6% of men over 50 years of age have osteoporosis, based on the bone mineral density (BMD) data.<sup>1</sup> The hip fracture (HF) incidence in Taiwan was among the highest in the world.<sup>2</sup> However, a study showed that only 25% of female HF sufferers in Taiwan underwent a BMD test, 33% received antiosteoporosis medications (AOMs), and 60% had a diagnosis of osteoporosis.<sup>3</sup>

To reduce the osteoporosis care gap, efforts were made to improve awareness among patients and healthcare providers, including making osteoporosis a national priority,<sup>4</sup> publishing the Taiwan Osteoporosis Practice guideline<sup>5</sup> with nationwide educational courses for six types of healthcare professionals,<sup>4</sup> training courses for osteoporosis nursing specialists,<sup>6</sup> a nationwide osteoporosis education and screening program covering approximately 5000 adults,<sup>7</sup> press conferences on osteoporosis issues, etc.

In Taiwan, a gap exists between comprehensive osteoporosis care and the current payment standards from National Health Insurance Administration (NHIA) on BMD tests and AOMs. To be reimbursed for dual-energy X-ray absorptiometry, patients must have a fragility fracture or be a woman receiving AOMs. NHI does not reimburse strontium ranelate, and teriparatide is considered a second-line agent. For all other AOMs, reimbursement is granted if the patient experiences a fragility fracture of the hip or spine area and has a BMD T-score of  $\leq -2.5$ , or experiences at least two fragility fractures of the hip or spine area and has a BMD T-score of  $< -1$ .<sup>8</sup> The rules are stricter than those suggested by domestic or international professional societies,<sup>5,9,10</sup> which emphasize treating patients with fragility fractures independent of BMD and considering the incorporation of algorithms based on the World Health Organization FRAX<sup>®</sup> fracture risk assessment tool.

The current NHI payment standards for AOMs were not based on cost-effectiveness analysis. Even though the Taiwanese FRAX<sup>®</sup> calculator was launched in 2010,<sup>5,11</sup> cost-effectiveness probability thresholds, against which AOM treatment has to be assessed, have not been established. The Taiwan Osteoporosis Practice guideline suggested adopting United States of America thresholds [3% for HF, and 20% for major osteoporotic fracture (MOF)], drawing on expert advice.<sup>5</sup> Empirical data showed that the 3% HF cutoff point may be very low in Taiwan, because nearly 90% of older adults ( $\geq 65$  years) were screened as being at high risk in one cohort, compared with 33% using the 20% MOF cutoff point.<sup>12</sup>

The objective of this study is therefore two-fold:

- (1) To establish practical Taiwanese FRAX<sup>®</sup>-based intervention thresholds in Taiwan using the Markov model and translational approach

- (2) To test Taiwan-specific FRAX<sup>®</sup> cutoff points in clinical samples and determine the optimal one, which can identify more high-risk patients for medication reimbursement

## Materials and methods

The Markov model used epidemiological, cost, and quality of life data to estimate the fracture probability at which alendronate treatment became cost effective compared with no treatment. Two translational approach models were developed based on prior guidelines.<sup>5,9,10</sup> The “fracture model” adopted the assumption that individuals with a fracture probability equal to or greater than that of patients with a prior fragility fracture should be considered for treatment. From the Taiwanese NHI AOM payment standards, we developed the “NHIA model” assuming that patients with a fracture probability equal to or greater than that of patients with a prior fragility fracture and BMD T-score =  $-2.5$  should be treated.<sup>8</sup>

### Markov model approach

We constructed a Markov model to estimate the cost-effective MOF and HF intervention thresholds.<sup>13</sup> There are four health states in the model: well, fracture, post-fracture, and death. The cycle was set at 1 year and every patient was followed through the model until death.<sup>14</sup> When the parameters in the model were not available from Taiwan data, we applied estimates from other countries, indexing the data source, a method applied in a previous European osteoporosis burden report.<sup>15</sup>

#### HF Markov model

We used a mathematical formula to derive the 1-year probability of HF from the 10-year probabilities estimated from the Taiwanese FRAX<sup>®</sup> calculator. This number would vary in many simulations until cost-effectiveness cut points were found. All other parameters in Table 1 were obtained from Taiwan data,<sup>5,16</sup> except that transition probability from postfracture to death was derived from a Korean study.<sup>17</sup>

#### MOF Markov model

Fracture incidences were obtained from the Malmo study,<sup>18</sup> and the 2010 Taiwan population figures were used to estimate the proportion of each component of MOF (vertebra, hip, humerus, and forearm) in Taiwan. Taiwanese NHI data were used for calculating the probability of refracture.<sup>19</sup> However, the probability of transition from “fracture” to “death” was estimated from a US study.<sup>20</sup> As there were no

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