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LETTER TO THE EDITOR

# Correspondence in response to OSIN-D-18-00831 quantifying imminent risk

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## Quantifying imminent risk

We thank Drs. Geusens and van den Bergh for their interest in our paper. We agree that quantifying imminent risk is an important next step. However, there are several factors that need to be considered that impact on such a development, including the following:

The recency of a sentinel fracture. As we report [1], the magnitude of "imminent" risk reduces with time, and thus the timing of the index fracture prior to assessment, be it one day, one week or one year, is critical.
The age at fracture. A prior fracture history is a significant risk factor for fracture at all ages, but the relative risk is highest at younger ages and decreases progressively with age [2].
Age dependency of imminent risk. A recent population-based study showed that the phenomenon of immediate risk was also age-dependent, the transient effect being more evident at older ages [3].
The site of sentinel fracture [1].
Sex. The difference in risk is greater for men than for women for all ages [1]
The non-linear mortality following a hip or vertebral fracture [4, 5].

All these factors need to be taken into account to quantify risks for individuals. Thus, the request of Geusens and van den Bergh cannot be instantly accommodated.

Drs. Geusens and van den Bergh have also suggested that we provide absolute one- and two-year subsequent fracture incidence in women and men according to each sentinel fracture. Average hazard ratios following each sentinel fracture as a function of time are provided in our paper (Fig. 1) but, as detailed above, will not suffice for assessing risk in individuals. Moreover, incidence at one or two years will depend critically on the epidemiology of fracture that varies widely worldwide [6]. Thus, incidence at one or two years for Iceland will have little relevance for other countries. It may be more fruitful to apply hazard ratios derived from Iceland to incidence of fractures in the country of interest.

The question arises how to quantify the additional risk associated with recent fractures in a manner that can be of value for the development of practice guidelines or health technology assessment. The most commonly used risk assessment tool is FRAX®, which integrates the information derived from clinical risk factors and BMD [7]. It is incorporated into more than 100 clinical guidelines worldwide [8] and provides a metric used in health technology assessment [9–11] and regulatory guidance [12]. FRAX has a ten-year time horizon for several reasons discussed elsewhere [7]. Of some importance is that the time frame provides numbers that physicians and patients can understand. A ten-year probability of a major osteoporotic fracture of, say, 25% has the same import

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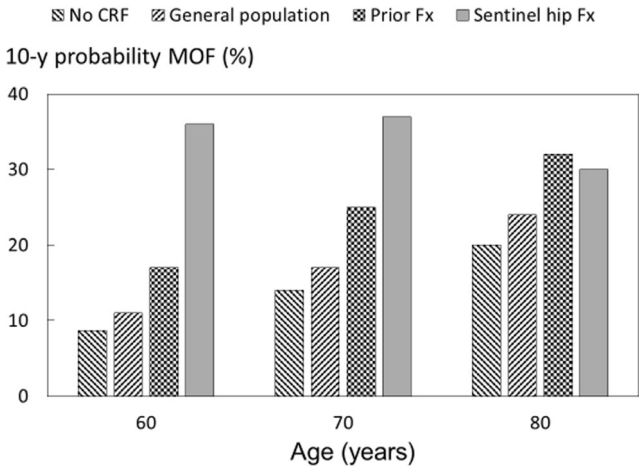


**Fig. 1** Age-specific ten-year probabilities of a major osteoporotic fracture (MOF) in women from Iceland with no clinical risk factors (calculated from FRAX), in the general population (from the cohort), with a prior fragility fracture (from FRAX) and immediately following a sentinel hip fracture

but a greater impact on patients and physicians than a one-year probability of 2.5%. For this reason, we are reluctant to recommend probabilities over a shorter period.

Although imminent risk appears to apply over a relatively short time frame, the magnitude of the effect is such that it will impact on 10-year probabilities. An example is shown in the figure. The very high immediate risk has a marked impact on 10-year probability and is substantially higher than that which FRAX would predict in the presence of a prior fracture. Note that the impact is inversely related to age. For these reasons, we predict that the consideration of imminent risk may well form an important component of future iterations of FRAX.

## Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

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