

## SUPPLEMENTARY INFORMATION (ONLINE RESOURCE)

Table S1: Country-specific 10-Year Probability Thresholds

Country Name	Threshold (%)	
	10-year probability of hip fracture without BMD	10-year probability of major osteoporotic fracture without BMD
Belgium	5	18
France	4.3	13
Germany	5.3	16
Ireland	6.5	20
Netherlands	4	13
Poland	3.3	10
Slovakia	6.7	19
Sweden	9	25
Switzerland	6.1	25
UK	5	20

### Notes:

The country-specific thresholds for treating high-risk patients were calculated using the FRAX tool and were based on a similar approach as that taken by NOGG (National Osteoporosis Guidance Group) UK. The individual risk factors considered in the derivation of the thresholds when using the FRAX tool are: women of 70 years of age, average BMI of 24.7 (e.g. weight 69 kg and height 167 cm), prior fracture and no other risk factors.

For the overall category, the number of subjects considered to be at high risk of fragility fracture in each country were determined by the country-specific thresholds; and pooled to represent the overall subjects.

Table S2: Proportion patients at increased risk of fragility fracture

Parameter	Definition		
	2 <sup>a</sup>	3 <sup>b</sup>	4 <sup>c</sup>
Number of patients with increased risk of fragility fracture	1985	2192	1362
Meeting 1 of the 3 criteria			
Prior fracture only - n (%)	199 (10.0)	149 (6.8)	986 (72.4)
FRAX threshold only - n (%)	641 (32.3)	848 (38.7)	18 (1.3)
T-score only - n (%)	90 (4.5)	74 (3.4)	108 (7.9)
Meeting 2 of the 3 criteria			
Prior fracture and FRAX threshold - n (%)	827 (41.7)	877 (40.0)	40 (2.9)
Prior fracture and T-score - n (%)	17 (0.9)	9 (0.4)	78 (5.7)
FRAX threshold and T-score - n (%)	54 (2.7)	70 (3.2)	36 (2.6)

Parameter	Definition		
	2 <sup>a</sup>	3 <sup>b</sup>	4 <sup>c</sup>
Meeting all 3 criteria	157 (7.9)	165 (7.5)	96 (7.0)

BMD = bone mineral density; FRAX = Fracture Risk Assessment Tool.

A patient was considered to be at increased risk of fragility fracture if  $\geq 1$  of the 3 following criteria were met:

(1) had a history of fracture; (2):

<sup>a</sup> 10-year probability of hip fracture without BMD > country-specific threshold + 2% and 10-year probability of major osteoporotic fracture without BMD > country-specific threshold + 5%

<sup>b</sup> 10-year probability of hip fracture without BMD > country-specific threshold - 2% and 10-year probability of major osteoporotic fracture without BMD > country-specific threshold - 5%

<sup>c</sup> 10-year probability of hip fracture with BMD > country-specific threshold and 10-year probability of major osteoporotic fracture with BMD > country-specific threshold

(3) BMD T-score  $\leq -2.5$  for any of lumbar spine/total hip/femoral neck.

Mutually exclusive groups met 1, 2 and a combination of all 3 criteria.

Percentages based on number of patients enrolled who are at increased risk of fragility fracture based on definition 2, 3 or 4.

Table S3: Primary Outcome: Proportion of Patients not Receiving any OP Medication Amongst Those With Increased Risk of Fragility Fracture (Sensitivity Analyses)

	Number with increased risk of fracture	Number not receiving OP medication	Proportion of Patients not Receiving any OP Medication % (95% CI)
Definition 2 <sup>a</sup> – increased country-specific threshold	1985	1468	74.0 (72.0, 75.9)
Definition 3 <sup>b</sup> – decreased country-specific threshold	2192	1659	75.7 (73.8, 77.5)
Definition 4 <sup>c</sup> – with BMD	1362	907	66.6 (64.0, 69.1)

BMD = bone mineral density; BPs = bisphosphonates; CI = confidence interval; OP = osteoporosis;

PTH = parathyroid hormone; RANKL = receptor activator of nuclear factor kappa-B ligand;

SERMs = selective estrogen receptor modulators.

A patient will be considered to be at increased risk of fragility fracture if  $\geq 1$  of the 3 following criteria are met: (1) had a history of fracture; (2)

<sup>a</sup> 10-year probability of hip fracture without BMD > country-specific threshold + 2% and 10-year probability of major osteoporotic fracture without BMD > country-specific threshold + 5%;

<sup>b</sup> 10-year probability of hip fracture without BMD > country-specific threshold - 2% and 10-year probability of major osteoporotic fracture without BMD > country-specific threshold - 5%;

<sup>c</sup> 10-year probability of hip fracture with BMD > country-specific threshold and 10-year probability of major osteoporotic fracture with BMD > country-specific threshold.

(3) BMD T-score  $\leq -2.5$  for any of lumbar spine/total hip/femoral neck.

Percentages based on number of patients enrolled who are at increased risk of fragility fracture.

OP medication use is derived considering SERMs, oral BPs, parenteral BPs, strontium, PTH, and denosumab medications.

Table S4: Baseline characteristics of the first 50% vs second 50% of patients enrolled

N = 1886	First 50% Enrolled <sup>a</sup> N = 1912	Second 50% Enrolled <sup>a</sup> N = 1886
Country		
Belgium	135	370
France	70	473

<b>N = 1886</b>	<b>First 50% Enrolled<sup>a</sup> N = 1912</b>	<b>Second 50% Enrolled<sup>a</sup> N = 1886</b>
Germany	197	309
Ireland	245	255
Poland	459	46
Slovakia	288	246
Switzerland	106	99
UK	412	88
Age - median (Q1, Q3), years	77.0 (73.0, 82.0)	77.0 (73.0, 82.0)
Age group – n (%)		
70 – 74 years	647 (33.8)	641 (34.0)
75 – 79 years	591 (30.9)	549 (29.1)
≥ 80 years	674 (35.3)	696 (36.9)
Reason for consultation – n (%)		
Follow up to known disease	1038 (54.3)	940 (49.8)
Medication refill	320 (16.7)	462 (24.5)
New symptoms/complaints	456 (23.8)	368 (19.5)
Other	98 (5.1)	116 (6.2)
Any known OP diagnosis – n (%)		
Yes	382 (20.0)	422 (22.4)
No	1496 (78.2)	1437 (76.2)
Unknown	34 (1.8)	27 (1.4)

OP = osteoporosis; Q = quartile.

<sup>a</sup> Since there were differences in speed of recruitment of patients across centers, we compared the baseline characteristics of the first 50% of patients enrolled to the next 50% within each center to see if biases had gradually influenced the type of patients recruited.

Table S5: Comorbidities in the first 50% vs second 50% of patients enrolled

<b>n (%)</b>	<b>First 50% Enrolled N = 1912</b>	<b>Second 50% Enrolled N = 1886</b>
At least one comorbidity	1722 (90.1)	1639 (86.9)
RA	77 (4.0)	74 (3.9)
Diabetes	531 (27.8)	422 (22.4)
Hypertension	1453 (76.0)	1387 (73.5)
Osteoarthritis	877 (45.9)	825 (43.7)
COPD	159 (8.3)	168 (8.9)

COPD = chronic obstructive pulmonary disease; RA = rheumatoid arthritis.

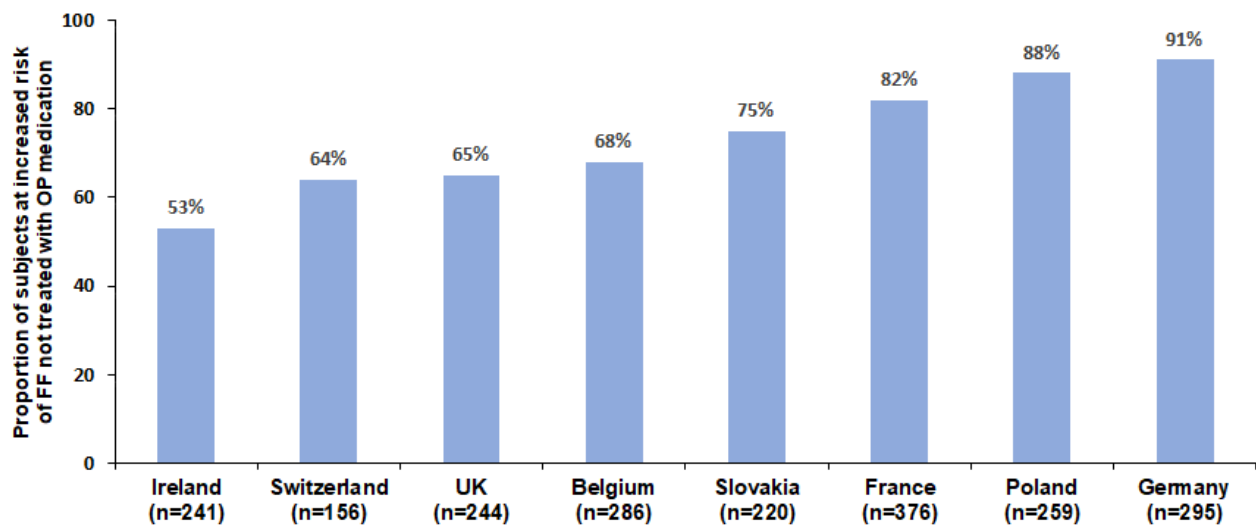
Percentages based on total number of patients in the respective category of enrolled patients.

Table S6: Fracture history of the first 50% vs second 50% of patients enrolled

	First 50% Enrolled N = 1912	Second 50% Enrolled N = 1886
Any fracture after age of 50		
Yes	600 (31.4)	600 (31.8)
No	1303 (68.1)	1285 (68.1)
Unknown	9 (0.5)	1 (<0.1)
Location		
Hip	57 (3.0)	88 (4.7)
Spine	86 (4.5)	92 (4.9)
Wrist	225 (11.8)	210 (11.1)
Other (except skull, finger and toe fractures)	331 (17.3)	303 (16.1)
Time since last fracture (years)		
<1	76 (4.0)	66 (3.5)
≥1 - ≤5	215 (11.2)	214 (11.3)
>5	307 (16.1)	319 (16.9)
Unknown	2 (0.1)	1 (<0.1)

Percentages based on number of patients enrolled in the respective category of enrolled patients. Distribution of first 50% and second 50% enrolled among patients is classified based on median using enrollment date of patients.

Figure S1: OP treatment gap by country



FF=fragility fracture; OP=osteoporosis; UK=United Kingdom

'n' represents the number of patients at increased risk of fragility fracture using the base definition.

Adapted from [27].