



# Epidemiology of hip fractures in Bulgaria: development of a country-specific FRAX model

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## Abstract

### Summary

A retrospective population-based survey was undertaken in a region of Bulgaria to determine the incidence of hip fracture. The estimated number of hip fractures nationwide for 2015 was 9322 and is predicted to increase to 11,398 in 2050. The hip fracture rates were used to create a FRAX model.

### Objective

To describe the epidemiology of hip fractures in Bulgaria, which was then used to develop the country-specific fracture prediction FRAX® tool.

### Methods

We carried out a retrospective population-based survey in Stara Zagora, Bulgaria, representing approximately 4.6% of the country's population. We identified hip fractures occurring in 2015, 2016 and 2017 from hospital registers and primary care sources held by the regional health insurance agency. Age- and sex-specific incidence of hip fracture and national mortality rates were incorporated into a FRAX model for Bulgaria. Fracture probabilities were compared with those from neighbouring countries having FRAX models.

### Results

The incidence of hip fracture applied nationally suggested that the estimated number of hip fractures nationwide in persons over the age of 50 years for 2015 was 9322 and is predicted to increase to 11,398 in 2050. FRAX-based probabilities were higher in Bulgaria than those in Serbia or Romania, lower than those in Turkey and similar to those in Greece.

### Conclusion

The FRAX model should enhance accuracy of determining fracture probability among the Bulgarian population and help guide decisions about treatment.

**Keywords** Bulgaria · FRAX · Fracture probability · Epidemiology · Hip fracture

## Introduction

Osteoporosis and osteoporotic fractures are becoming more common with advancing age. In Europe, the annual cost of

fractures associated with osteoporosis exceeded € 37 billion in 2010 [1], and disability due to osteoporosis was greater than that caused by any single cancer, with the exception of lung cancer and was comparable or greater than that lost to a variety

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of chronic non-communicable diseases, such as rheumatoid arthritis, asthma and high blood pressure-related heart disease [2]. Fortunately, a wide variety of treatments is available that favourably affect bone mass and thereby decrease the risk of fractures associated with osteoporosis [3]. The use of such interventions by healthcare practitioners is assisted by instruments that assess patients' fracture risk to optimise clinical decisions about prevention and treatment. The most widely used web-based tool FRAX® (<https://www.sheffield.ac.uk/FRAX/>) meets these requirements and computes the 10-year probability of fragility fractures based on several common clinical risk factors and optionally, a DXA scan result [4, 5]. FRAX models are available for 66 countries covering more than 80% of the world population at risk [6] and have been incorporated into more than 100 guidelines worldwide [7].

The availability of FRAX has stimulated studies for the generation of new FRAX models. Specific examples include Brazil, Mexico, Turkey [8–10] and several countries in Eastern Europe [11–14]. The present report describes the epidemiology of fractures at the hip in Bulgaria and the generation of a country-specific FRAX model.

## Methods

Bulgaria is a country in Southeastern Europe with a total area of 110,994 km<sup>2</sup>. It borders the Black Sea to the east, Greece and Turkey to the south, Serbia and Macedonia to the west and Romania to the north [15]. According to the national statistical institute, the Bulgarian population comprises four ethnic groups as follows: Bulgarian (84.8%), Turkish (8.8%), Roma (4.9%) and others (1.5%) [16].

Stara Zagora, in Southern Bulgaria, is the sixth-largest city in Bulgaria. Based on regional health inspection's data, the region's population aged 40 years or above in 2017 amounted to 183,294 people (84,557 men and 98,737 women) and represented 4.6% of the whole Bulgarian population aged 40 years and above (183,294/3,982,770). The ethnic admixture of Stara Zagora is similar to the country as a whole.

We analysed the cases of hip fractures (ICD codes: S72.0, S72.1 and S72.2) in the Stara Zagora region, Bulgaria, for the years 2015, 2016 and 2017. Data were provided by the Regional Health Insurance Fund (RHIF) Stara Zagora using an electronic database of hospitals, general practitioners and specialists in this region. The insurance company covers 81.2% of the total population but coverage varies according to age and sex. The relevant data on coverage was available and the age- and sex-specific insured population comprised the denominator for the calculation of incidence. To minimise double counting, further admissions for the same hip fracture site within 3 months were excluded. Permanent residence in the region was not a criterion for inclusion, so a small number

of patients living temporarily in the catchment area were also included in the database.

Incidence of hip fractures was calculated from the age of 40 years in 5-year age intervals in men and in women. The age of 40 was chosen since FRAX permits the calculation of fracture probability from this age.

The age- and sex-specific incidence for 2015–2017 was applied to the Bulgarian population for 2015 to estimate the number of hip fractures nationwide. Additionally, future projections were estimated up to 2050, assuming that the age- and sex-specific incidence remained stable. Population demography was taken from the United Nations using the medium variant for fertility [17].

The data on hip fracture were used to construct a FRAX model for Bulgaria. For other major osteoporotic fractures (clinical spine, forearm and humeral fractures), it was assumed that the age- and sex-specific ratios of these fractures to hip fracture risk in Bulgaria were comparable with those found in Sweden [4]. This assumption has been used for many of the FRAX models with incomplete epidemiological information on non-hip fractures. Available information suggests that the age- and sex-stratified pattern of fracture is very similar in the Western world and Australia [14, 18–20].

The development and validation of FRAX have been extensively described [4, 5]. The risk factors used were based on a systematic set of meta-analyses of population-based cohorts worldwide and validated in independent cohorts with over 1 million patient-years of follow-up. The construct of the FRAX model for Bulgaria retained the beta coefficients of the risk factors in the original FRAX model with the incidence rates of hip fracture and mortality rates for Bulgaria. National mortality rates used data from the United Nations in 2014 [21]. Ten-year fracture probabilities were compared with those of neighbouring countries with FRAX models (Greece, Serbia, Turkey and Romania).

In order to compare Bulgarian hip fracture probabilities with those of other regions of the world, the remaining lifetime probability of hip fracture from the age of 50 years was calculated for men and women as described by Kanis et al. [22]. In the present analysis, values for Bulgaria were compared with those of China (with and without inclusion of Hong Kong), Canada, Denmark, Finland, France, Greece, Hungary, Portugal, Spain, Sweden, UK and the USA [22], with more recent additions from Mexico [23], Romania [24], Poland [25], Moldova [14], Russia [12], Turkey [10], Ukraine [26] and Serbia [27].

## Results

A total of 367 hip fractures were identified in men and 1017 in women (female/male ratio 2.8). Below the age of 65 years, hip fractures were more prevalent in men than in women (female/

male ratio 0.7), but thereafter were more frequent in women (female/male ratio 3.2). The incidence of hip fracture increased with age in men and women, though more markedly in women (Table 1).

## Hip fracture projections

Assuming that the fracture rates in Stara Zagora were representative for the whole country and based on the UN estimates of the Bulgarian population for 2015, we estimated that the annual number of hip fractures in men and women aged 50 years and older in Bulgaria in 2015 was 9322, comprising 2521 in men and 6801 fractures in women. The number of hip fractures is expected to increase progressively by calendar year with an increase of 22% by 2050 (Table 2). The increase in hip fracture numbers was higher in women (24% in women

**Table 1** Population of the catchment area, number of hip fractures and annual incidence of hip fractures (rate/100,000) in men and women in Stara Zagora, Bulgaria, by age for years 2015, 2016 and 2017 combined

Age (years)	Population <sup>a</sup>	Fractures <sup>b</sup>	Incidence/ 100,000	95% CI
<b>Men</b>				
40–44	28,257	9	32	15–60
45–49	27,267	14	51	28–86
50–54	26,372	18	68	40–108
55–59	27,646	26	94	61–138
60–64	27,889	35	125	87–175
65–69	27,903	37	133	93–183
70–74	20,886	44	211	153–283
75–79	15,632	54	345	259–451
80–84	11,131	54	485	364–633
85–89	4832	53	1097	822–1435
90+	1292	23	1780	1128–2672
40+	219,106	367	167	151–186
<b>Women</b>				
40–44	28,069	3	11	2–31
45–49	26,998	7	26	10–53
50–54	27,768	12	43	22–76
55–59	30,383	24	79	51–118
0–64	34,907	36	103	72–143
65–69	38,011	60	158	120–203
70–74	30,842	95	308	249–377
75–79	24,652	189	767	661–884
80–84	19,278	261	1354	1195–1529
85–89	9247	247	2671	2348–3026
90+	2862	83	2900	2310–3595
40+	273,018	1017	373	350–396

<sup>a</sup> Population corrected for insurance cover

<sup>b</sup> Fractures per year over 3 years

**Table 2** Estimated total number of hip fractures (ICD-10 codes S72.0, S72.1, S72.2) in men and in women aged 50 years and older in 2015 projected up to 2050 in Bulgaria

	2015	2020	2030	2040	2050
Men	2521	2567	2739	2903	2973
Women	6801	7136	7923	8397	8425
Total	9322	9703	10,662	11,300	11,398
Increase (%)	-	4	14	21	22

and 18% in men) due to the high age dependency of hip fracture incidence.

## Fracture probability

The 10-year probability of major osteoporotic fracture and hip fracture in Bulgaria and neighbouring countries is shown in Table 3 in women with a prior fracture by age. Ten-year probabilities were consistently higher than those in the neighbouring countries of Serbia and Romania, lower than those in Turkey and similar to those in Greece.

For the remaining lifetime probability of a hip fracture in Bulgarian women from the age of 50 years was 11.2% which lay midway between Romania and Serbia (7.1 and 7.7%,

**Table 3** Ten-year probability of a major osteoporotic fracture (MOF) and hip fracture in women with a prior fracture by age from Bulgaria, Greece, Turkey, Serbia and Romania. Body mass index set to 25 kg/m<sup>2</sup>

	Bulgaria	Greece	Turkey	Serbia	Romania
<b>MOF</b>					
50	7.7	5.2	8.2	4.5	5.2
55	8.5	7.0	8.2	6.1	6.5
60	9.5	9.8	8.6	8.4	7.9
65	11	13	10	11	9.5
70	15	17	13	13	11
75	19	22	18	14	13
80	22	25	24	15	13
85	23	25	33	15	13
90	20	20	37	14	11
<b>Hip</b>					
50	1.2	0.8	1.3	0.7	0.8
55	1.6	1.3	1.5	1.2	1.2
60	2.1	2.2	1.8	1.9	1.8
65	2.9	3.4	2.3	2.9	2.6
70	4.5	5.4	4.1	4.2	3.5
75	7.0	8.3	7.5	5.3	4.6
80	9.6	11	11	5.8	5.4
85	11	12	16	6.7	5.8
90	9.4	9.3	17	7.3	4.5

respectively) and those of Greece and Turkey (15.4 and 15.9%, respectively) (Table 4).

## Discussion

The present study characterised the regional incidence of hip fracture in a well-defined catchment area. The hip fracture incidence increased with age in both sexes, but below the age of 65 years was higher in men than in women. Thereafter, incidence was higher in women. Similar results have been reported in many studies including other countries in Eastern Europe, namely Russia [12], Armenia [11], Moldova [14] and Belarus, [13]. From these results, Bulgaria belongs to the moderate risk countries for osteoporotic hip fracture for men and women [28].

Based on the regional incidence, the number of hip fractures in 2015 was estimated at 9322 for the whole country and is expected to increase by 22% to 11,398 in 2050. These estimates are relatively robust, in that all individuals who will

be aged 60 years or more in 2050 are currently adults. However, these estimates may be conservative since they assume that the age- and sex-specific risk of hip fracture remains unchanged over this period. Decreases in age-specific rates have occurred in those countries with the higher hip fracture risks [29], whereas increases in incidence with time are commonly found in those countries with the lower risks. It is estimated that modest increases in secular trends (e.g. 1% per year) as seen for example in Mexico [9] together with demographic changes would double the number of hip fractures over 20 years [30]. Such projections are important for healthcare planning.

The incidence of hip fracture and of death was used to create a country-specific FRAX model for Bulgaria. Ten-year probabilities of fracture were consistently higher than those in the neighbouring countries of Serbia and Romania, lower than those in Turkey and similar to those in Greece. These differences in fracture probability cannot be accounted for by differences in mortality but rather reflect differences in the risk of hip fracture. Reasons for the heterogeneity in hip fracture risk are speculative [9]. The factor which best predicts the heterogeneity in hip fracture risk is socioeconomic prosperity that in turn may be related to low levels of physical activity [31]. The fact that there are differences in adjacent countries emphasizes the importance of the use of country-specific FRAX models rather than surrogate models [32].

A minority of countries that have a FRAX model also have robust information on the risk of other major osteoporotic fractures. In the absence of such information, FRAX models are based on the assumption that the age- and sex-specific pattern of these fractures is similar to that observed in Malmo, Sweden [33]. The acquisition of data on the incidence of forearm and humerus fractures in a manner identical to that for hip fracture permitted the adequacy of this assumption to be tested, at least for forearm and humeral fractures. Our findings suggest that the incidence of forearm and humerus fractures can be reasonably predicted from the incidence of hip fracture. Very similar findings have been reported from Canada [20], Iceland [19], USA [34], UK [35], Australia [36] and several additional countries of the Western world and Australia, despite differences in incidence [28]. This commonality of pattern is supported by register studies, which indicate that in those regions where hip fracture rates are high, so too is the risk of forearm fracture and spine fractures (requiring hospital admission) [37, 38].

In most countries, a case finding approach is used for the management of osteoporosis, where certain clinical risk factors (CRFs) for fracture suggest the possible diagnosis of osteoporosis and trigger a more detailed assessment of the need for intervention. Many assessment guidelines recommend that women with a prior fracture are eligible for treatment. By the same token, individuals with a fracture probability that is

**Table 4** Lifetime probability of hip fracture in the Bulgarian population from the age of 50 years compared with selected countries

Country	Lifetime risk at 50 years (%) <sup>a</sup>	
	Women	Men
Sweden	25.6	11.0
Denmark	23.0	11.3
France	19.3	5.9
China (Hong Kong)	17.7	7.6
USA (Caucasian)	16.1	7.5
Turkey	15.9	3.6
Canada	15.5	5.8
Greece	15.4	6.8
UK	14.4	5.0
Portugal	13.7	4.8
Finland	12.9	6.0
Spain	12.6	4.2
Bulgaria <sup>b</sup>	11.2	4.4
Hungary	10.8	4.2
Mexico	10.6	5.0
Poland	10.1	4.2
Moldova	9.3	5.7
Russia	7.7	3.8
Serbia	7.7	3.7
Romania	7.1	3.8
China	5.9	3.3
Ukraine	5.6	2.9

<sup>a</sup> Probabilities derived from fracture as given in FRAX v4.1 and updated death risks

<sup>b</sup> Present study

equivalent to or greater than that of women with a prior fracture should also be eligible. Age-specific intervention thresholds have been widely used in Europe and South America [7]. If the same strategy were used in Bulgaria, the intervention would be recommended in individuals with a 10-year probability of a major osteoporotic fracture that ranged from 7.7 to 23%, depending on age (see Table 3).

There are a number of limitations to this study. The accuracy of the register is not known. With regard to fracture incidence, we examined somewhat less than 5% of the Bulgarian population. Therefore, the extrapolation of these regional estimations to the entire country is an assumption that we were unable to test. This would require a national survey and its validity tested in prospective study of a population-based cohort. Moreover, a minority of the population was not included in the regional health insurance fund and an imbalance in health status may have skewed our estimates. In addition to large variations in fracture rates around the world, fracture rates may vary within countries. In addition to ethnic-specific differences [39], up to twofold differences in hip fracture incidence have been reported using common methodology with the higher rates in urban communities including Croatia [40], Switzerland [41], Norway [42], Argentina [43] and Turkey [44].

Despite the well-defined catchment population, it is possible that not all hip fractures were captured. Indeed, many patients in Eastern Europe are not hospitalized because facilities for surgical management are limited, so that hospital admission is not always feasible. In Belarus, for example, 29% cases of hip fracture did not come to hospital attention [13]. High rates of non-admittance have been reported in Armenia (44%) [11] Pervouralsk in Russia (27%) [12], Georgia (75%) and Kyrgyzstan (50%) [45].

It is relevant, however, that accuracy errors have little impact on the rank order with which the FRAX tool categorises risk in a given population [11, 46], but they do change the absolute number generated and thus have implications where treatment guidelines are based on cost-effectiveness or the economic burden of disease. In order to address these limitations, population representatives of the general population at risk would need to be studied prospectively, preferably over a 10-year time horizon.

In summary, a FRAX model has been created for Bulgaria based on a regional population-based estimate of the incidence of low energy hip fractures. The model should enhance accuracy of determining fracture probability among the Bulgarian population and help to guide decisions about treatment.

## Compliance with ethical standards

**Conflict of interest** E Kirilova, H Johansson, N Kirilov, S Vladeva, T Petranova, E Liu, L Vanderput and Z Kolarov declare that they have no competing interests. M Lorentzon has received lecture or consulting fees

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