

Epidemiology of fragility fractures in Italy

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Summary

Objectives. We aimed to calculate the incidence of major fragility fractures in Italy, including those which do not result systematically in hospital admissions, on the basis of hospitalization rates provided in our previous researches.

Methods. We analyzed Italian national hospital discharge data from year 2004 to 2006 in order to determine age- and sex-specific incidence rates of hip, vertebral, humeral, and forearm fractures occurred in people aged 40 to 100 years of age. Re-hospitalizations of the same patients have been excluded from the analysis. Hospital discharge data have been adjusted taking into account recently published information concerning fracture-specific hospitalization rates. **Results.** We estimated a total of 88,647 hip fractures in year 2006 among people aged 40 to 100 years old, with a +5.9% increase across the three examined years. Women aged >75 years old (n=53,259) accounted for 60% of total fractures observed both in males and females from 40 to 100 years of age. Concerning males, the highest incidence was observed between 80 and 84 years old (about 5,000 hip fractures). Overall incidence rate per 100,000 inhabitants computed for hip fractures was 284.28, with marked age- and sex-specific differences. Clinical vertebral fractures were estimated to be almost 61,000 in 2006, with a +3.1% increase across the three examined years. Overall incidence rate per 100,000 inhabitants computed for clinical vertebral fractures was 195.23, but this value doubled between 75 and 95

years of age. In the same year 2006, a total of 56,129 humeral and 97038 forearm/wrist fractures, with a +5.5% and +3.9% increase across three years, respectively. Overall humeral fractures incidence per 100,000 was 180, with highest rates (up to 600 and over) observed in women between 75 and 95 years of age, while incidence per 100,000 computed for wrist fractures was 311, with top values observed in women between aged 55-85 years old – thus including early postmenopausal age group – and a peak in those between 75 and 79 years of age. **Conclusions.** The burden of major osteoporotic fractures in Italy is very high. Preventive strategies aimed to reduce fractures incidence should be carried out at regional level.

KEY WORDS: incidence; fractures; hip; vertebra; wrist; humerus.

Introduction

Italy has one of the highest life expectancies in the world: according to the Italian National Institute for Statistics (ISTAT), life expectancy at birth increased by a rate of 4 months per year from 1950 to 2005, reaching 78.4 years for men and 87.4 years for women, respectively (1,2). Twenty percent of the Italian population (namely 12,085,058 people) is actually over 65 years of age (1), but 5.6% of these people is already ≥80 years of age (1). The national ageing index has been recently computed in 143.1, with southern Italian regions remaining younger than northern areas of the country (1). Increased life expectancy is associated with a greater frailty of elderly people and a higher prevalence of chronic and degenerative diseases, including osteoporosis. The World Health Organization (WHO) considers osteoporosis to be second only to cardiovascular diseases as a critical health problem (3), and previous analyses have shown that incidence and costs of hip fractures in Italy are already comparable to those of acute myocardial infarction (4). The main Epidemiological Study on the Prevalence of Osteoporosis in Italy (ESOPO) reported a high prevalence of osteoporosis: 23% among all women, with age-specific rates ranging from 9% (40 to 49 year olds) up to 45% (70 to 79 or older), and almost 15% in men aged ≥60 years (5, 6). According to these data, about 4 million of Italian women and 800 thousand men are thought to be affected by osteoporosis (2), although the ESOPO study was conducted by using QUS (Quantitative Ultra-Sounds) measurements and not DEXA (Dual Energy X-rays Absorbiometry), the gold standard tool in the diagnosis of osteoporosis (6-8). It is known that osteoporosis is a condition that enhances the risk of fractures (9), and osteoporotic fractures represent a challenge for health professionals and decision makers in the 21st century. Some data are already available about the incidence of fragility fractures in the Italian population (10-12), and we have recently published a specific study addressing also the issue of fractures occurred in skeletal sites other than hip (13). Vertebral fractures or deformities are the most common osteoporotic fractures (14) and the European Vertebral Osteoporosis Study (EVOS) found that about 12% of both men and women aged 50–80 years old there are vertebral deformities radiologically detectable (15). These deformities are associated with negative

outcomes (including back pain and physical impairment) even when they are asymptomatic (16, 17). Furthermore, vertebral deformities are associated to a higher risk of subsequent osteoporotic fractures (18-20) and an increased risk of mortality (19, 21). It is estimated that two-thirds of vertebral fractures never come to clinical attention (22), so that it is very difficult to assess their incidence among general population. Wrist or forearm fractures represent the most common fractures in women just before and immediately after menopause (typically between 40 and 50 years old), probably as a consequence of a hormone-related fast bone loss (23). Wrist fractures are also frequent in men aged <70, with female-to-male ratio being four to one (23). Wrist fractures increase almost two folds the risk of subsequent hip or vertebral fractures, but also the risk of new forearm and other skeletal fractures is increased by 3.3 times and 2.4 respectively (24). Humeral fractures represent the third most common fracture in people aged >65 years old and have been associated to a five times increase in the risk of subsequent hip fractures (25), thus confirming that all osteoporotic fractures should be considered as the first signal of an evolving diseases. This work was aimed to calculate the incidence of major fragility fractures in Italy, including those which do not result systematically in hospital admissions, on the basis of hospitalization rates provided in our recent research (13).

Materials and methods

The national hospitalization database (SDO), maintained at the Italian Ministry of Health, contains information concerning all hospitalizations occurring in all Italian public hospitals. These information are anonymous and include patient's age, diagnosis, procedures performed, and length of the hospitalization. Based on those databases, we have recently published a paper addressing the issue of the incidence of major osteoporotic fractures in Italy (hip, humeral, forearm, and vertebral fractures), resulting both from hospitalization database analyses and from a 3-years multicentric survey carried out at 10 major Italian Emergency departments, where a specific assessment of the fragility origin of the fracture events was performed by orthopedic surgeons (13). Actually, it is known that most of hip fractures systematically result in hospitalization, thus allowing researchers to perform epidemiological analyses by using hospital discharge records. On the other hand, only a small part of osteoporotic fractures occurred at other different skeletal sites are hospitalized, so that hospital discharge records cannot be simply used to investigate the burden of most osteoporotic fractures. In our previous study (13), we have estimated hospitalization rates for humeral, forearm, hip and vertebral fractures in a sample of about 30,000 patients, so that it has been possible to evaluate the number of fractured patients discharged all over the country from Emergency departments without being hospitalized (13). Overall hospitalization rates were the following: 93.0% for hip fractures, 36.3% for humeral fractures, 22.6% for forearm/wrist fractures, and 27.6% for clinical vertebral fractures (13). On the contrary, Emergency departments directly discharged 7.0% of hip fractured patients, 63.7% of humeral fractures, 77.4% of forearm/wrist fractures, and 72.4% of vertebral fractures were immediately discharged from Emergency department and did not require hospital admission (13). However, in our analyses we have applied age-specific hospitalization rates, as resulted from the study (13). Additional corrective factors have been used for vertebral fractures when performing comparative analyses between the hospitalization rates and data coming from the National Hospitalization Database (SDO), as the majority of vertebral deformities (from 78% to 67%) are asymptomatic and do not require admission at Emergency departments (23-24). For the purpose of this study, only clinical

vertebral fractures (defined as those fractures which come to medical attention) were considered and analyzed. The analysis of hospital discharge records (SDO) was limited to the period 2004-2006, corresponding to the same years of our previous survey on fractures hospitalization rates (13), and were performed by searching for ICD-9CM diagnosis codes (major diagnosis) of hip, humeral, forearm and vertebral fractures. Hip fractures were defined by the following ICD-9CM diagnosis codes (major diagnosis): 820.0-820.1 (femoral neck fractures), 820.2-820.3 (per-trochanteric femoral fractures) and 820.8, 820.9 and 821.1 (other femoral fractures). Other fractures were defined by the following ICD-9CM diagnosis codes (major diagnosis): 812 (humeral fractures), 813 (forearm/wrist fractures) and 805 (vertebral fractures). Re-hospitalizations of the same patients (mostly due to admissions at rehabilitative divisions) were excluded thanks to a specific analysis carried out at central level directly by the Italian Ministry of Health. After the correction for hospitalization rates, data were stratified by gender into 5-years age groups (40-44; 45-49; 50-54; 55-59; 60-64; 65-69; 70-74; 75-79; 80-84; 85-89; 90-94; 95-100 years old) and stratified per 100,000 inhabitants. Population data concerning each year were obtained from the National Institute for Statistics (ISTAT) (1).

Results

The total number of estimated hip fragility fractures occurred in Italy in year 2006 among people aged 40 to 100 years of age was 88 647 (22,032 men and 66,615 women), as resulted by the analysis of hospitalization records (excluding re-admissions of the same patients), with a +5.9% increase across the three examined years (data presented according to gender and five years intervals in Table 1). Women aged >75 years old (n=53,259) accounted for 60% of total fractures observed both in males and females from 40 to 100 years of age. Concerning males, the highest incidence was observed between 80 and 84 years old (about 5,000 hip fractures). Overall incidence rate per 100,000 inhabitants computed for hip fractures was 284.28, with marked age- and sex-specific differences (Table 2). The total number of estimated clinical vertebral fragility fractures occurred in Italy in year 2006 among people aged 40 to 100 years of age was 60 880 (26,579 men and 34,229 women), with a +3.1% increase across the three examined years (data presented according to gender and five years intervals in Table 3). Overall incidence rate per 100,000 inhabitants computed for clinical vertebral fractures was 195.23, but this value doubled between 75 and 95 years of age (Table 4). The total number of estimated humeral fragility fractures occurred in Italy in year 2006 among people aged 40 to 100 years of age was 56 129 (13,775 men and 42,355 women), with a +5.5% increase across the three examined years (data presented according to gender and five years intervals in Table 5). Overall incidence rate per 100,000 inhabitants computed for humeral fractures was 180, with highest values (up to 600 and over) observed in women between 75 and 95 years of age (Table 6). The total number of estimated forearm/wrist fragility fractures occurred in Italy in year 2006 among people aged 40 to 100 years of age was 97,038 (29,727 men and 67,259 women), with a +3.9 increase across the three examined years (data presented according to gender and five years intervals in Table 7). Overall incidence rate per 100,000 inhabitants computed for wrist fractures was 311, with highest values observed in women between aged 55-85 years old (thus including early post-menopausal age group), and a peak in those between 75 and 99 years of age (Table 8).

Discussion

While confirming the extremely high burden of hip fractures in the

Table 1 - Estimated overall number of hip fractures (Italy, 2004-2005-2006).

Age-group		40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85-89	90-94	95-100	Total
2004	Men	586	588	653	787	951	1,462	2,351	3,266	4,439	2,670	2,128	455	83,415
	Women	250	325	617	1,089	1,779	3,155	6,275	11,202	16,368	10,878	8,978	2,163	
2005	Men	575	609	609	812	931	1,423	2,237	3,580	4,696	2,856	2,302	503	86,395
	Women	227	328	590	1,060	1,654	3,087	6,265	11,375	17,029	11,634	9,528	2,485	
2006	Men	672	566	633	842	961	1,487	2,278	3,657	4,929	3,243	2,158	606	88,647
	Women	230	340	664	1,163	1,637	3,214	6,108	11,444	17,278	12,576	9,278	2,683	

Table 2 - Estimated overall number of hip fractures per 100,000 (Italy, 2004-2005-2006).

Age-group		40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85-89	90-94	95-100	Total
2004	Men	26.72	30.35	35.80	44.43	58.99	98.80	186.94	344.22	768.13	1,248.78	2,093.73	2,678.52	276.90
	Women	11.38	16.50	32.80	58.78	101.25	186.11	395.28	803.77	1,574.76	2,305.62	3,225.79	3,278.51	
2005	Men	25.10	30.63	33.31	44.27	59.20	93.73	175.62	370.39	751.15	1,376.35	2,156.64	2,623.34	281.34
	Women	9.93	16.27	31.26	55.27	96.86	178.69	392.94	812.17	1,524.36	2,546.42	3,259.64	3,389.95	
2006	Men	28.45	27.78	34.45	44.29	63.29	95.90	178.57	366.94	773.39	1,395.23	1,996.58	2,843.47	284.28
	Women	9.79	16.49	35.05	58.54	99.74	183.11	386.59	802.61	1,533.57	2,486.74	3,122.65	3,358.70	

Table 3 - Estimated overall number of clinical vertebral fractures (Italy, 2004-2005-2006).

Age-group		40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85-89	90-94	95-100	Total
2004	Men	2,380	2,407	2,523	2,603	2,730	3,150	3,046	2,969	2,112	754	450	38	58,987
	Women	1,093	1,250	1,857	2,633	3,187	4,125	5,018	5,838	5,231	2,292	1,119	181	
2005	Men	2,523	2,347	2,317	2,693	2,637	3,304	3,200	2,969	2,215	850	423	69	59,116
	Women	950	1,150	1,803	2,770	2,990	4,096	5,036	5,835	5,242	2,346	1,142	208	
2006	Men	2,710	2,293	2,363	2,763	2,650	3,579	3,175	3,196	2,388	954	458	50	60,880
	Women	1,023	1,280	1,920	2,660	3,030	4,379	4,846	5,642	5,635	2,654	1,042	188	

Table 4 - Estimated number of clinical vertebral fractures per 100,000 (Italy, 2004-2005-2006).

Age-group		40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85-89	90-94	95-100	Total
2004	Men	108.51	124.20	138.34	146.98	169.33	212.87	242.23	312.94	365.38	352.58	442.75	226.42	195.81
	Women	49.77	63.46	98.69	142.14	181.36	243.33	316.09	418.92	503.25	485.86	402.14	274.00	
2005	Men	110.15	118.02	126.73	146.82	167.67	217.59	251.22	307.20	354.36	409.63	396.36	361.07	192.51
	Women	41.55	57.05	95.54	144.44	175.09	237.12	315.84	416.59	469.27	513.52	390.80	283.33	
2006	Men	114.73	112.54	128.62	145.35	174.51	230.80	248.89	320.70	374.76	410.37	423.46	234.61	195.23
	Women	43.55	62.08	101.34	133.90	184.61	249.46	306.74	395.72	500.12	524.76	350.80	235.92	

Table 5 - Estimated number of humeral fractures (Italy, 2004-2005-2006).

Age-group		40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85-89	90-94	95-100	Total
2004	Men	1,275	1,222	1,283	1,176	1,154	1,302	1,364	1,785	1,345	614	305	54	53,036
	Women	647	815	1,450	2,396	2,999	4,834	6,204	7,933	7,649	3,094	1,791	344	
2005	Men	1,234	1,191	1,297	1,241	1,132	1,403	1,453	1,758	1,542	614	320	69	54,182
	Women	655	839	1,465	2,553	3,201	4,759	6,261	8,248	7,370	3,396	1,881	299	
2006	Men	1,401	1,275	1,324	1,368	1,181	1,453	1,505	1,659	1,557	686	294	72	56,129
	Women	698	834	1,433	2,633	3,235	4,974	6,230	8,365	7,871	3,854	1,839	389	

Table 6 - Estimated number of humeral fractures per 100,000 (Italy, 2004-2005-2006).

Age-group		40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85-89	90-94	95-100	Total
2004	Men	58	63	70	66	72	88	108	188	233	287	301	317	176
	Women	29	41	77	129	171	285	391	569	736	656	643	522	
2005	Men	54	60	71	68	72	92	114	182	247	296	300	359	116
	Women	29	42	78	133	187	275	393	589	660	743	643	409	
2006	Men	59	63	72	72	78	94	118	166	244	295	272	337	180
	Women	30	40	76	133	197	283	394	587	699	762	619	487	

Table 7 - Estimated number of forearm/wrist fractures (Italy, 2004-2005-2006).

Age-group		40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85-89	90-94	95-100	Total
2004	Men	5,658	4,507	4,167	3,903	3,045	2,048	1,847	1,600	1,182	399	211	19	93,260
	Women	2,455	3,217	5,063	7,811	8,334	7,711	8,281	9,761	7,545	2,744	1,509	240	
2005	Men	5,505	4,953	3,922	3,874	2,963	2,218	1,795	1,605	1,235	471	163	48	94,586
	Women	2,652	3,299	5,131	7,998	8,156	7,771	8,402	9,881	7,670	2,999	1,634	240	
2006	Men	5,907	5,241	4,397	4,167	2,685	2,199	1,628	1,677	1,163	437	183	43	97,038
	Women	2,608	3,275	5,471	8,286	8,756	7,749	8,092	10,366	7,617	3,503	1,360	226	

Italian population, at the same time this paper represents a full attempt to evaluate the incidence of "minor" fragility fractures among different age groups in the Italian population. Actually, fragility fractures occurring at skeletal sites other than hip are an underestimated issue which is difficult to analyze because they do not systematically result in hospital admissions and as a consequence of the lack of specific diagnostic codes for fragility fractures. In this paper we have continued the analyses on the national hospitalization database by using hospitalization rates coming from our previously published survey (13), which had involved orthopaedic surgeons and personnel from Emergency Department at 10 major Italian hospitals: Milan (Othopedic Institute "Gaetano Pini"), Turin (Maria Vittoria Hospital), Brescia (Riuniti Hospital), Rome (Tor Vergata University Hospital, St. Camillo Hospi-

tal and St. Giovanni Addolorata Hospital), Cagliari (University Hospital), Palermo (University Hospital), Bari (University Hospital), and Catania (University hospital). Some discrepancies in the number of estimated fractures compared to data presented in the previous paper (13) are exclusively due to the following methodological choices adopted in the present research: we have presented also data concerning people aged 40-44 years old and those regarding men aged 45-64 years of age, which were not included in the final analysis of our previous paper. Furthermore, patients in the age group 95-100 years old were poorly represented in the previously published work (13). Fractures occurred in people aged >65 years old and particularly over 75 years of age should be considered as fragility fractures, given the high prevalence of osteoporosis in these age groups. This assumption is confirmed

Table 8 - Estimated number of forearm/wrist fractures per 100,000 (Italy, 2004-2005-2006).

Age-group		40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85-89	90-94	95-100	Total
2004	Men	258	233	228	220	189	138	147	169	205	187	208	113	310
	Women	112	163	269	422	474	455	522	700	726	582	542	364	
2005	Men	240	249	215	211	188	146	141	166	198	227	153	251	203
	Women	116	164	272	417	478	450	527	705	687	656	559	328	
2006	Men	250	257	239	219	177	142	128	168	182	188	169	203	311
	Women	111	159	289	417	533	441	512	727	676	693	458	283	

by the finding that most of fractures are suffered by elderly women. Actually, women aged >75 accounted for 60% of total hip fractures observed in people between 40 and 100 years old both males and females. Having observed that wrist fractures show high rates also in women aged 55-64 years old is consistent with available incidence data concerning this kind of fracture even in early post-menopausal women (23). Furthermore, our analyses assumed as starting point the specific assessment concerning the fragility origin of the fracture events performed by orthopedic surgeons involved in the previous study (13). Our data show that the absence of ICD9-CM codes for fragility fractures results in a lack of perception of hip and "minor fractures" burden, thus leading to problems in the full evaluation of osteoporosis impact in elderly people. Underdiagnosis of osteoporosis in patients at higher risk (particularly postmenopausal women) may be a possible cause of the underestimation of fragility fractures and consequently results in undertreatment of this pathology. This ultimately leads to an additional increase of osteoporotic fractures among people affected by osteoporosis and not treated. Finally, the low compliance that usually characterize antifracture therapies in Italy could make ineffective also treatments correctly prescribed to high risk patients. The issue of identifying subjects at higher risk of future fractures has been already addressed by the IOF FRAX algorithm (which has been developed in order to estimate patients' individual risk of fragility fractures based on data obtained from Sweden), although an updated version of the Italian FRAX tool is still not available (26). The availability of updating incidence rates in the Italian version of the FRAX could possibly provide physicians with a reliable instrument for determining which patients are really at higher risk of future osteoporotic fractures. Our data call for specific preventive strategies based on actions (such as optimization of access to anti-fracture therapies and compliance to the treatments, proper dietary calcium intake during the whole life, vitamin D supplementations, physical activity programs) to be carried out at regional level all over the country, as stated in the conclusions of the official inquiry promoted by the Italian Senate in 2002, specifically addressing the burden of osteoporosis in Italy. Some experiences have just started, such as the TARGET project carried out by Tuscany region in order to reduce the incidence of hip re-fractures in the elderly on the whole regional population. However, the problem needs to be addressed all over Italy.

Conclusion

These results confirm that the burden of major osteoporotic fractures in Italy is very high. Specific preventive strategies aimed to reduce the incidence of osteoporotic fractures should be carried out at regional level.

References

1. Italian Statistics 2005. National Institute for Statistics, Rome.
2. WHO statistical information system (WHOSIS), available at http://apps.who.int/whosis/database/life_tables/life_tables_process.cfm?path=whosis,life_tables&language=english.
3. Kanis JA et al. European guidance for the diagnosis and management of osteoporosis in postmenopausal women, *Osteoporos Int.* 2008;19(4):399-428.
4. Piscitelli P, Guida G, Iolascon G et al. Incidence and costs of hip fractures vs. acute myocardial infarction in the Italian population: a 4 years survey, *Osteoporos. Int.* 2007;18: 211-219.
5. Adami S, Giannini S, Giorgino R et al. The effect of age, weight, and lifestyle factors on calcaneal quantitative ultrasound: the ESOP study. *Osteoporos. Int.* 2003;14:198-207.
6. Siris ES, Brenneman SK, Barrett-Connor E, Miller PD, Sajjan S, Berger ML, Chen YT. The effect of age and bone mineral density on the absolute, excess, and relative risk of fracture in postmenopausal women aged 50-99: results from the National Osteoporosis Risk Assessment (NORA), *Osteoporos Int.* 2006;17(4):565-74.
7. Krieg MA, Cornuz J, Ruffieux C et al., Prediction of hip fracture risk by quantitative ultrasound in more than 7000 Swiss women > or =70 years of age: comparison of three technologically different bone ultrasound devices in the SEMOF study, *J Bone Miner Res.* 2006 Sep;21(9):1457-63.
8. Maggi S et al. Quantitative heel ultrasound in a population-based study in Italy and its relationship with fracture history: the ESOP study. *Osteoporosis Int.* 2006;17:237-244.
9. Riggs BL, Melton LJ 3rd. The worldwide problem of osteoporosis: insights afforded by epidemiology. *Bone* 1995;17(5 Suppl):505S-511S17.
10. Iolascon G, Guida G et al. Hip fractures in Italy, analysis of DRG data, *Aging clinical and experimental research.* 2007;19(Suppl 3): 2-4.
11. Piscitelli P, Iolascon G et al. Incidence and costs of hip fractures vs. acute myocardial infarction in the Italian population: a 4 years survey, *Osteoporosis International.* 2007;18: 211-219.
12. Piscitelli P, Iolascon G, Brandi ML et al. Hip Fractures in Italy: 2000-2005 extension study, *Osteoporosis International* (2009), published online 7 October 2009.
13. Tarantino U, Piscitelli P, Brandi ML et al. The Incidence of Hip, Forearm, Humeral, Ankle and Vertebral Fragility Fractures in Italy: Results from a 3-Years Multicentric Study, *Arthritis Research & Therapy* published online 29/12/2010.
14. Cummings SR, Melton LJ. Epidemiology and outcomes of osteoporotic fractures, *Lancet.* 2002 May 18;359(9319):1761-7.
15. O'Neill TW, Felsenberg D, Varlow J, et al. The prevalence of vertebral deformity in European men and women: the European Vertebral Osteoporosis Study. *J Bone Miner Res.* 1996;11:1010-1018.
16. Ettinger B, Black DM, Nevitt MC, et al. Contribution of vertebral deformities to chronic back pain and disability. The Study of Osteoporotic Fractures Research Group. *J Bone Min Res.* 1992;7:449-456.
17. Nevitt MC, Ettinger B, Black DM, et al. The association of radio-

- graphically detected vertebral fractures with back pain and function: a prospective study. *Ann Intern Med.* 1998;128:793-800.
18. Hasserijs R, Karlsson MK, Nilsson BE, et al. Prevalent vertebral deformities predict increased mortality and increased fracture rate in both men and women: a 10-year population-based study of 598 individuals from the Swedish cohort in the European Vertebral Osteoporosis Study. *Osteoporos Int.* 2003;14:61-68.
 19. Lindsay R, Silverman SL, Cooper C, et al. Risk of new vertebral fracture in the year following a fracture. *JAMA.* 2001;285:320-323.
 20. Pongchaiyakul C, Nguyen ND, Jones G, et al. Asymptomatic vertebral deformity as a major risk factor for subsequent fractures and mortality: a long-term prospective study. *J Bone Min Res.* 2005;20:1349-1355.
 21. Ismail AA, O'Neill TW, Cooper C, et al. Mortality associated with vertebral deformity in men and women: results from the European Prospective Osteoporosis Study (EPOS). *Osteoporos Int.* 1998;8:291-297.
 22. Fechtenbaum J et al., Reporting of vertebral fractures on spine X-rays, *Osteoporosis Int* Volume 16, Number 12/December, 2005).
 23. Steven R Cummings, L Joseph Melton, Epidemiology and outcomes of osteoporotic fractures, *The Lancet* Vol. 359, May 18, 2002.
 24. Klotzbuecher CM, Ross PD, Landsman PB, Abbott TA 3rd, Berger M. Patients with prior fractures have an increased risk of future fractures: a summary of the literature and statistical synthesis. *J Bone Miner Res.* 2000 Apr;15(4):721-39.
 25. Jeremiah Clinton, Proximal Humeral Fracture as a Risk Factor for Subsequent Hip Fractures, *The Journal of Bone and Joint Surgery (American)*. 2009;91:503-511.
 26. Kanis JA, Johnell O, Oden A, Johansson H, McCloskey E. FRAX™ and the assessment of fracture probability in men and women from the UK. *Osteoporos Int.* 2008;19: 385-397.



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