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Estimated number of women likely to benefit from bone mineral density measurement in France

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Abstract

Objectives. – To determine the number of women in France at least 50 years of age with risk factors for osteoporosis likely to lead to bone mineral density measurement, an investigation reimbursed by the French national health insurance system in patients at risk for osteoporosis. The study was commissioned by the French health authorities.

Materials and methods. – Risk factors for osteoporosis were defined as recommended by the French Agency for Accreditation and Evaluation in Health (ANAES) in 2001. The study data were from nine cohort studies done in France and from the National Health Insurance Agency for the Rhône-Alpes region of France. Risk factor prevalences in France were standardized by extrapolation according to the age distribution in France.

Results. – Overall, data were collected in 123 986 women aged 50 years or older. From these data, risk factor estimates were as follows: menopause before 40 years of age, 1.5 million women; body mass index (BMI) lower than 19 kg/m^2, nearly 700 000; history of fracture, more than 2 million; history of femoral neck fracture in the mother, more than 1 million; history of health problems potentially responsible for osteoporosis, 400 000; and history of long-term glucocorticoid therapy, 612 000. In all, 3186 318 (30%) women were estimated to have at least one risk factor and 785 512 (7.5%) at least two risk factors.

Conclusions. – Although our study sample was not representative of the population residing in France, the large sample size and diversity of data sources support the validity of our estimate of the prevalence of risk factors for osteoporosis in postmenopausal women living in France.

Author Keywords: Osteoporosis; Prevalence; Risk factors; Absorptiometry; Bone mineral density; Menopause

Introduction

The prevalence of osteoporosis is rising, most notably in postmenopausal women. Fractures caused by trivial trauma are the main clinical manifestations. The vertebras and distal forearm are the most commonly affected sites, whereas fractures of the proximal femur are the most severe[1,2,3 and 4]. In 1994, the World Health Organization defined osteoporosis as an unacceptable risk of fracture detected on the basis of a bone mineral density (BMD) *T*-score value by absorptiometry lower than –2.5 standard deviation (S.D.). The *T*-score reflects the difference, in S.D., between the BMD in the patient and the mean BMD in a reference population of young healthy women examined when their bone mass was at its peak. Several

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recommendations about selecting patients for BMD measurement have been issued, in particular by the Osteoporosis Research and Information Group (Groupe de Recherche et d'Information sur les Ostéoporoses, GRIO) and the European Foundation against Osteoporosis (EFO)[5,6,7,8,9,10,11,12 and 13]. Compliance with these recommendations has not yet been evaluated. In 2001, at the request of the Ministry of Health and national health insurance system, the French Agency for Accreditation and Evaluation in Health (ANAES) developed a tentative definition of women at high risk for osteoporosis[14]. Absorptiometry was not reimbursed by the national health insurance system at the time. Yet, this investigation may be extremely helpful in women at high risk for osteoporosis, and many risk factors for osteoporosis have been identified.

To obtain recognition of absorptiometry as a medical procedure warranting reimbursement by the universal health insurance system, the French Agency for Health asked us to estimate the number of women in France who were at risk for osteoporosis according to the ANAES guidelines. These women constitute the population likely to benefit from absorptiometry, that is, the population for which absorptiometry should be reimbursed by the national health insurance system.

The objective of this study was to estimate the prevalence in France of women with risk factors for osteoporosis listed in the ANAES guidelines. To achieve this objective, we used available databases.

Materials and methods

Materials

We looked for computerized databases of cohort studies in women older than 50 years living in France[15,16,17,18,19,2021,22 and 23] at the following institutions: National Institute for Health Statistics and Research (Institut National de la Santé et de la Recherche Médicale, INSERM, web site <inserm.fr>), National Institute for Statistics and Economic Evaluations (Institut National des Statistiques et des Études Économiques, INSEE, 1990 census), National Health Insurance Agency for the Rhônes-Alpes region, and the national utility company (Électricité de France, EDF). The cohort studies identified by our search are listed in appendix A. We excluded four studies for one or more of the following reasons: major selection bias likely to affect the validity of our estimate, population younger than 50 years, or data not relevant to the risk factors studied in our work. For instance, in the study "second cancer after breast cancer", the population with a history of breast cancer was not representative of the general population in terms of the risk factors investigated in our study. Possible sources of bias included differences in menopausal status and in bone tissue status. The GAPIC study investigated coronary heart disease and other cardiovascular disorders. As a result, males predominated. In addition, the restrictive selection criteria produced a population that differed markedly from the general population. The study "health effects of exposure to water side products" was conducted in selected groups such as underground miners and swimmers. Most of the study participants were males, which was not relevant to our objective. Finally, in the study "benign breast disease and breast cancer risk", the mean age of the women was too young to be relevant to our study.

The risk factors investigated in our study were those listed in the 2001 ANAES guidelines on patient selection for absorptiometry[1]. These guidelines deal primarily with the tools used to diagnose osteoporosis in postmenopausal women and in male and female adults on glucocorticoid therapy. One of their objectives is to indicate when investigations to evaluate the risk of osteoporotic fractures are appropriate. In brief, absorptiometry is recommended in postmenopausal women with any of the following: one or more vertebral fractures discovered on radiographs in the absence of a tumor or major trauma; history of peripheral fracture in the absence of major trauma (not counting fractures of the skull, toes, fingers, and cervical spine); and documented history of conditions potentially responsible for osteoporosis (e.g. prolonged hypogonadism, active untreated hyperthyroidism, hypercorticism, and primary hyperparathyroidism)[1]. In addition, absorptiometry can be recommended to postmenopausal women with one or more of the following risk factors: history of vertebral or femoral neck fracture in the absence of major trauma in a first-degree relative, body mass index (BMI) lower than 19 kg/m^2, menopause before 40 years of age regardless of the cause or iatrogenic menopause, and history of glucocorticoid therapy for longer than 3 months in a dose of at least 7.5 mg prednisone-equivalent per day[1]. Absorptiometry is not recommended in postmenopausal women taking hormone replacement therapy in a dosage effective in preventing osteoporosis and under appropriate medical supervision[1].

We also collected information on several additional factors (such as history of fracture after 50 years of age or after the menopause) relevant to recommendations issued by other evaluation agencies or likely to have a major influence on our estimate of at risk women.

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Risk factors used for our estimate

A review of the ANAES recommendations and of the cohort study data indicated that the main risk factors for osteoporosis in women older than 50 years were menopause before 40 years of age, history of fracture after 50 years of age, history of fracture in the mother, BMI lower than 19 kg/m^2, history of conditions potentially responsible for osteoporosis, and history of glucocorticoid therapy for at least 3 months in a daily dosage of at least 7.5 mg. To evaluate the heterogeneity of the data used for our estimate, we asked the main investigators of the cohort studies to supply us with the exact wording of the items in their study questionnaires. In the database maintained by the Rhônes-Alpes Insurance Agency, we selected data on women who were older than 50 years, resided in the Rhône-Alpes area, were covered by the National Health Insurance Agency for salaried workers, and had obtained reimbursement for at least two prescriptions of glucocorticoids written on different dates in the course of 2000.

The EPIDOS cohort study collected data on five risk factors: menopause before 40 years of age, BMI lower than 19 kg/m^2, history of fracture, fracture in the mother, and history of glucocorticoid therapy. The PAQUID and EVA cohort studies recorded only menopause before 40 years of age and BMI lower than 19 kg/m^2. Risk factors recorded in the OFELY study were menopause before 40 years of age or iatrogenic menopause, BMI lower than <19 kg/m^2, history of fracture after 50 years of age (not due to a tumor or major trauma), hip fracture in the mother, and history of glucocorticoid therapy or hyperthyroidism. In the ESTEV 95 study, four risk factors were investigated: menopause before 40 years of age, BMI lower than 19 kg/m^2, history of fracture after 50 years of age, and history of conditions potentially responsible for osteoporosis. The E3N study recorded menopause before 40 years of age, BMI lower than 19 kg/m^2, history of fracture after 50 years of age, and history of hip fracture in the mother. Three factors were recorded in the GAZEL study: menopause before 40 years of age, BMI lower than 19 kg/m^2, and fracture after 50 years of age. Finally, the MONICA study investigated only two risk factors, menopause before 40 years of age and BMI lower than 19 kg/m^2.

We sent a questionnaire to the investigators of each of the nine cohort studies. Our first analysis of the responses was done study-by-study. Then, we analyzed the pooled data from the nine studies, by age group and risk factor. Finally, we standardized the results to obtain estimates of risk factor prevalences. Because the age distribution of our study sample differed from that of the overall population of women older than 50 years living in France, we selected the direct standardization method to correct our results. Furthermore, the data on glucocorticoid therapy in the nine cohort studies were also standardized on the age distribution in the population living in the Rhône-Alpes area (1999 INSEE census) to allow a comparison between the prevalence in the cohort studies and in the Rhône-Alpes Insurance Agency database.

Results

Eleven cohort studies met our eligibility criteria, and the main investigators for nine of these studies completed our study questionnaire. Table 1 describes the objectives of each study, the population, and the follow-up dates. In all, the nine cohorts included 123 986 women older than 50 years.

For each of the four most often studied risk factors (menopause before 40 years of age, history of fracture, history of fracture in the mother, and BMI lower than 19 kg/m^2), Table 2, Table 3 and Table 4 report the prevalences per age group and the number of women for whom data were available.

Menopause before 40 years of age

The prevalence of menopause before 40 years of age is shown in Table 2. This risk factor was investigated in six of the nine cohort studies. For each study, the table shows the age groups and sample size (first column for each study). Wide variations in prevalence were seen across studies, from 5.5% in the PAQUID cohort to 23.4% in the EPIDOS cohort. The figures in the last column of the table are strongly influenced not only by age but also by the number of studies providing data for each age group and by their relative contribution to the total number of women in each age group.

The mean overall prevalence of menopause before 40 years of age was 15%. The E3N cohort had the largest influence on the prevalence in the 50–65-year age group and the EPIDOS cohort on the prevalence in the 75 years or older age group. In the 65–74-year age group, the sample size was far smaller (500–600 women) and the data came only from two studies, the OFELY cohort and, above all, the PAQUID cohort (90% of data for the 65–69-year group and 82% for the 70–74-year group). Within each age group, marked differences were noted across cohorts. In the 55–59-year group, for instance, the prevalence of menopause before 40 years ranged from 12% in OFELY and 13% in E3N to 24% in ESTEV95. In the 80–

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84-year group, the lowest prevalence was 5.4% in PAQUID and the highest was 22% in EPIDOS. Thus major prevalence differences occurred across the nine studies both overall and within age groups. In the PAQUID cohort, the prevalence of menopause before 40 years of age was substantially lower than in the other cohorts, in all age groups. In contrast, in each age group, the prevalence of a BMI lower than 19 kg/m^2 in PAQUID was greater than in the other cohorts (Table 3).

Table 1. **Main characteristics of the nine cohort studies used to estimate the prevalence of risk factors for osteoporosis in women older than 50 years living in France**

Study	Primary focus of the study	Sample size	Sample source	Recruitment and data collection dates
EPIDOS	Osteoporosis	7517	Voter rosters (Montpellier, Toulouse, Lyon, Paris, Amiens)	1/92–1/94
ESTEV95	Health, work, and aging	7425	Employees followed by 380 occupational physicians (seven regions)	1990/1995
EVA	Hormone replacement therapy	469	Volunteers from voter rosters	6/1991–6/1993
E3N	Risk factors for cancer and chronic disease	98 998	Female members of the MGEN	1990
GAZEL	Understanding of "indications" for hormone replacement therapy and poor compliance with this treatment	3157	French public utility company	1989
MONICA	Cardiovascular disease (morbidity, mortality, risk factors)	1730	Three registries (Strasbourg, Toulouse, and Lille)	1985
OFELY	Osteoporosis	1039	Volunteers among members of the MGEN	1992
PAQUID	Brain aging and loss of self-sufficiency in individuals >65 years living at home	2200	75 counties in Gironde and Dordogne (two districts in south-western France)	1988–1990
POLA	Cataract and age-related macular degeneration (risk factors)	1451	Sète (city in southern France)	6/1995–7/1997

MGEN, Mutuelle Générale de l'Education Nationale.

Table 2. **Menopause before 40 years of age: prevalence among women older than 50 years of age included in six cohort studies**

Age group (years)	Name of the study												Pooled data (% total)
	EPIDOS		ESTEV95		E3N		MONICA		OFELY		PAQUID		
	Total sample size	%	Total sample size	%	Total sample size	%	Total sample size	%	Total sample size	%	Total sample size	%	
50–54	–	–	1995	16.1	15 758	12.75	279	11.8	127	10.2	–	–	13.1
55–59	–	–	1668	23.6	11 820	12.97	298	17.1	202	11.9	–	–	14.3
60–64	–	–	–	–	7273	14.71	326	21.2	100	12.0	–	–	14.9
65–69	–	–	–	–	–	–	–	–	61	11.5	601	5.2	5.2
70–74	–	–	–	–	–	–	–	–	89	16.9	436	6.9	6.9
75–79	3880	23.5	–	–	–	–	–	–	46	19.6	549	6.0	21.3
80–84	2611	22.1	–	–	–	–	–	–	33	12.1	333	5.4	20.2
85–89	834	25.9	–	–	–	–	–	–			205	3.9	21.6
≥90	133	29.3	–	–	–	–	–	–			76	2.6	30.8
Total	7458	23.4	3663	19.5	34 851	13.2	903	16.9	669	12.6	2200	5.5	15.0

Table 3. **BMI lower than 19 kg/m^2: prevalence among women older than 50 years of age included in seven cohort studies**

Age group (years)	Name of the study														Pooled data (% total)
	EPIDOS		ESTEV95		E3N		MONICA		OFELY		PAQUID		POLA		
	Total sample size	%	Total sample size	%	Total sample size	%	Total sample size	%	Total sample size	%	Total sample size	%	Total sample size	%	
50–54	–	–	1995	2.3	15 758	9.1	279	3.2	127	4.7	–	–	–	–	8.2
55–59	–	–	1668	2.2	11 820	9.1	298	1.0	202	4.0	–	–	–	–	8.0
60–64	–	–	–	–	7273	9.5	326	1.5	100	4.0	–	–	333	3.3	8.9
65–69	–	–	–	–	–	–	–	–	61	6.6	601	3.7	370	1.9	3.2
70–74	–	–	–	–	–	–	–	–	89	1.1	436	7.6	357	2	4.7
75–79	3880	3.8	–	–	–	–	–	–	46	2.2	549	7.7	220	4.1	4.3
80–84	2611	4.2	–	–	–	–	–	–	33	3.0	333	9.6	112	2.7	4.7
85–89	834	5.5	–	–	–	–	–	–			205	11.7	47	0	6.4
≥90	133	13.5	–	–	–	–	–	–			76	21.1	7	0	15.8
Total	7458	4.3	3663	2.2	34 851	9.2	903	1.9	669	3.7	2200	7.7	1446	2.6	7.5 **

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Table 4. **History of fracture: prevalence among women older than 50 years of age included in four cohort studies**

Age group (years)	Name of the study								Pooled data (% total)
	E3N [a]		EPIDOS [a]		ESTEV95 [b]		OFELY [c]		
	Total sample size	%	Total sample size	%	Total sample size	%	Total sample size	%	
50–54	15 758	10.6	–	–	1995	2.1	127	2.4	9.7
55–59	11 820	16.0	–	–	1668	4.4	202	1.0	14.5
60–64	7273	22.2	–	–	–	–	100	5.0	22.2
65–69	–	–	–	–	–	–	61	4.9	4.9
70–74	–	–	–	–	–	–	89	11.2	11.2
75–79	–	–	3880	36.4	–	–	46	19.6	36.7
80–84	–	–	2611	37.8	–	–	33	30.3	38.2
85–89	–	–	834	39.1	–	–			39.1
≥90	–	–	133	31.6	–	–			31.6
Total	34 851	14.8	7458	37.1	3663	3.1	669	6.3	17.6

The prevalence of women with a history of menopause before 40 years increased significantly with age in four of the six cohorts, the two exceptions being EPIDOS and PAQUID. In the PAQUID cohort, the prevalence seemed to decrease with age. Thus, we noted both an age effect and a cohort effect, which in some cases could not be separated from each other given the marked age distribution differences between the two studies, with some pairs of studies having no shared age groups.

Prevalence of a body mass index lower than 19 kg/m^2

As shown in Table 3, the prevalence of a BMI smaller than 19 kg/m^2 ranged from 1.9% in the MONICA cohort to 9.2% in the E3N cohort. The overall prevalence was higher in the PAQUID cohort (7.7%) than in the EPIDOS cohort (4.3%). Similar differences were found in each age group. For instance, in the 75–79-year group, 7.7% of women in the PAQUID cohort and 3.8% in the EPIDOS cohort had a BMI lower than 19 kg/m^2. These are the only two studies in which age had a significant influence. No such effect was seen in the POLA cohort, which collected data in the same age groups.

History of fracture after 50 years of age

Again, prevalence values varied widely, from 3.1% (ESTEV95) to 37.1% (Table 4). Prevalence increased with age in all the studies. Given the heterogeneity of the cohorts related to differences in patient selection criteria and in definitions of a history of fracture, results varied markedly even within age groups. Thus, among women aged 50–54 years, the prevalence was 2.1% in ESTEV95 (n = 1995), 2.4% in OFELY (n = 127), and 10.63% in E3N (n = 15 758) (Table 4). Similar differences were found in the other age groups. Higher prevalences were seen in the studies that used broader definitions for a history of fracture. The increase with age within a given study was statistically significant in all the cohorts except EPIDOS.

History of proximal femoral fracture in the mother

The prevalence of a history of proximal femoral fracture in the mother (Table 5) ranged from 8.7% (E3N) to 11.1% (OFELY). Thus, variability across studies was less marked than for other risk factors. Age did not seem to affect the prevalence of this risk factor. An age effect was seen only in the E3N cohort, which contributed 80% of the total sample for this risk factor. The overall prevalences in the E3N, EPIDOS, and OFELY cohorts were about 8.7%, 9.1%, and 11.1%, respectively. In the GAZEL study, the overall prevalence was 8.8% and age group data were not available. The overall prevalence in our sample was 8.8%. After standardization for the age distribution in the population of women older than 50 years living in France, the overall prevalence was 10.3% (9.7–10.9%) (Table 8).

History of disorders potentially responsible for osteoporosis

Five cohort studies collected the history of disorders listed by the ANAES as potentially responsible for osteoporosis (prolonged hypogonadism, active untreated hyperthyroidism, hypercorticism, and primary hyperparathyroidism). However, the definitions used for this risk factor showed substantial heterogeneity. The prevalences ranged from 3% to 7%. Their validity is limited, however, by the very small sample sizes, particularly in women older than 60 years. For instance, a history of “untreated hyperthyroidism” was nearly impossible to evaluate because the four studies that investigated this factor used different definitions; prevalences were 1% (20/2200) in PAQUID, 1.9% (54/2917) in ESTEV95, 4.3% (29/669) in OFELY, and 4.98% (3322/66 710) in E3N. The prevalence in the Rhône-Alpes Health Insurance Agency database was 4.7% (3425/72 496), which is similar to the values in the E3N and OFELY cohorts. In the GAZEL cohort,

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17.9% of participants reported a history of prolonged amenorrhea (more than 3 months before the menopause).

Table 5. **History of fracture of the proximal femur in the mother: prevalence among women older than 50 years of age included in three cohort studies**

Age group (years)	Name of the study						Pooled data (%)
	E3N		OFELY		EPIDOS		
	Total sample size	%	Total sample size	%	Total sample size	%	
50–54	15 758	7.5	127	6.3	–	–	7.5
55–59	11 820	8.9	202	15.3	–	–	8.9
60–64	7273	10.7	100	8.0	–	–	10.7
65–69	–	–	61	13.1	–	–	13.1
70–74	–	–	89	14.6	–	–	14.6
75–80	–	–	46	6.5	3880	9.1	9.1
80–84	–	–	33	9.1	2611	8.8	8.8
85–89	–	–			834	9.8	9.8
≥90	–	–			133	8.3	8.3
Total	34 851	8.7	669	11.1	7458	9.1	8.8

Table 8. **Estimated numbers of women with each risk factor for osteoporosis**

Risk factor	Crude prevalence (%)	$T(s)$ (%) [a]	95% CI of $T(s)$ (%)	Estimated number of women [b]	95% CI of the estimated number
Menopause before 40 years	15	14.11	13.92–14.29	1490 593	1470 521–1509 609
BMI < 19 kg/m^2	7.5	6.6	6.48– 6.71	697 230	684 553–708 851
History of fracture [c]	17.6	19.0	18.47–19.41	2007 177	1951 188–2050 490
History of fracture in the mother [d]	8.8	10.3	9.67–10.9	1088 101	1021 548–1151 486
History of diseases associated with osteoporosis	4.3	3.8	3.31–4.37	401 435	349 671–461 651
History of glucocorticoid therapy	6.6	5.79	5–6.58	611 661	528 205–695 117

95% CI, 95% confidence interval.

History of glucocorticoid therapy

This factor was investigated in three cohort studies (EPIDOS, OFELY, and PAQUID), in which the overall mean prevalence was 6.6%. The prevalence in the Rhône-Alpes health insurance database was 5.7%. Standardization of the cohort data for the age distribution among women older than 50 years living in the Rhône-Alpes area yielded a mean prevalence of 5.7%. Thus, we found close agreement between the cohort data and the health insurance data. The prevalence standardized for the age distribution of the population living in France was 5.8% (5–6.6%). The method used to collect data on glucocorticoid therapy differed across cohorts. No age effect was noted.

Prevalence of one or more risk factors

Table 6 and Table 7 report the prevalence of women with at least one or at least two risk factors in each cohort and age group. The overall prevalence of women with at least one risk factor was derived from eight studies that collected data in various age groups (Table 6). The number of risk factors studied ranged from two to six. The overall prevalence of women with at least one risk factor ranged from 12.7% in the PAQUID study to 51.7% in the EPIDOS study. Even in the same age groups, marked variations occurred across cohorts. Prevalences were highest in EPIDOS and OFELY, two studies designed to identify risk factors for osteoporosis; the lowest prevalence was in the PAQUID study, which investigated aging and loss of self-sufficiency. In the 65–69 and 70–74-year groups, the numbers of patients were small. For these reasons, the results are more difficult to interpret in these two age groups.

Table 6. **Overall prevalence of women with at least one risk factor for osteoporosis among women older than 50 years of age included in eight cohort studies**

Age groups (years)	At least one risk factor																		Pooled data (% total)
	EPIDOS		ESTEV95		GAZEL		MONICA		EVA		E3N		OFELY		PAQUID				
Number of factors	5		4		3		2		2		4		5		2				
	Total sample size	%	Total sample size	%	Total sample size	%	Total sample size	%	Total sample size	%	Total sample size	%	Total sample size	%	Total sample size	%			
50–54	–	–	1083	28.0	703	28.0	279	14.5	–	–	15 758	21.8	127	38.6	–	–	22.45		
55–59	–	–	1565	26.0	380	24.2	298	17.8	–	–	11 820	26.7	202	46.5	–	–	26.6		
60–64	–	–	–	–	–	–	326	22.4	–	–	7273	33.5	100	45	–	–	33.2		
65–69	–	–	–	–	–	–	–	–	110	30.9	–	–	61	54.1	601	8.8	13.5		
70–74	–	–	–	–	–	–	–	–	290	30.8	–	–	89	55.9	436	13.1	23.5		
75–79	3880	51.1	–	–	–	–	–	–	109	31.2	–	–	46	58.7	549	13.5	46.2		
80–84	2611	51.5	–	–	–	–	–	–	–	–	–	–	33	60.6	333	14.4	47.4		
85–89	834	54.6	–	–	–	–	–	–	–	–	–	–	–	–	205	15.1	46.8		
≥90	133	52.6	–	–	–	–	–	–	–	–	–	–	–	–	76	23.7	42.1		
Total	7458	51.7	2648	15.4	1083	26.7	903	18.4	469	30.9	34 851	25.9	666	48.1	2200	12.7	29.4		

Table 7. **Overall prevalence of women with at least two risk factors for osteoporosis among women older than 50 years of age included in eight cohort studies**

Age groups (years)	At least two risk factors																		Pooled data (% total)
	PAQUID		GAZEL		MONICA		EVA		E3N		OFELY		EPIDOS		ESTEV95				
Number of factors	2		3		2		2		4		5		5		4				
	Total sample size	%	Total sample size	%	Total sample size	%	Total sample size	%	Total sample size	%	Total sample size	%	Total sample size	%	Total sample size	%			
50–54	–	–	703	5.4	279	0.7	–	–	15 758	4.8	127	9.8	–	–	1083	1.5	4.5		
55–59	–	–	380	1.6	298	0.3	–	–	11 820	6.6	202	5.0	–	–	1565	1.3	5.3		
60–64	–	–	–	–	326	0.5	–	–	7273	9.2	100	10.0	–	–	–	–	8.8		
65–69	601	0.0	–	–	–	–	110	1.8	–	–	61	11.5	–	–	–	–	1.0		
70–74	436	1.4	–	–	–	–	290	2	–	–	89	6.7	–	–	–	–	2.2		
75–79	549	0.4	–	–	–	–	109	1.8	–	–	46	21.7	3880	17.1	–	–	14.8		
80–84	333	0.6	–	–	–	–	–	–	–	–	33	39.2	2611	16.6	–	–	14.8		
85–89	205	0.5	–	–	–	–	–	–	–	–	–	–	834	20.4	–	–	16.5		
≥90	76	0.0	–	–	–	–	–	–	–	–	–	–	133	25.3	–	–	14.8		
Total	2200	0.5	1083	2.8	903	0.4	469	1.9	34 851	6.3	699	8.8	7458	17.4	2648	1.4	7.3		

The variations across studies can be ascribed in part to differences in selection bias, which are difficult to characterize, and in part to the number of risk factors on which the estimates are based, which varies across cohorts but is easy to determine (Table 6 and Table 7). In each cohort, the prevalence of women with at least one risk factor increased with age, although the magnitude of this increase varied across cohorts, being greatest and statistically significant in E3N, MONICA, PAQUID, and OFELY. In EPIDOS, the increase was not statistically significant. A difference was found between the 90-year or older group and the other age groups within this study.

The prevalence of women older than 50 years of age who had at least two risk factors, as determined from eight studies (Table 7) ranged from 0.4% in MONICA to 17.4% in EPIDOS. In most studies, the prevalence of women with at least two risk factors was far smaller than the prevalence with at least one risk factor. In the EPIDOS study, which investigated five risk factors (menopause before 40 years of age, BMI lower than 19 kg/m^2, history of fracture, history of hip fracture in the mother, and history of glucocorticoid therapy), 51.1% of the women aged 75–79 years had at least two risk factors, as compared to only 13.3% in the PAQUID study, which collected only two risk factors (menopause before 40 years of age and BMI <19 kg/m^2). However, there was clearly a cohort effect, as the prevalences in matching age groups were very different in the EVA study, which also collected only the same two risk factors.

Number of women at risk for osteoporosis in France

We estimated the number of women at risk for osteoporosis based on the prevalences of women with at least one or two risk factors and on the 1999 French census data (INSEE). The crude and standardized results are reported for each risk factor (Table 8) and according to the number of risk factors (Table 9).

Table 9. **Estimated number of women with at least one or at least two risk factors for osteoporosis**

Number of risk factors	Crude rate $T(x)$ (%)	Standardized rate $T(S)$ (%) [a]	95% CI for $T(S)$ (%)	Estimated number of women [b]	95% CI for the estimated number
≥1 RF	29,44	30,16	30,1617–30,1618	3186 318	3186 316–3186 321
≥2 RF	7,28	7,44	7,43567–7,43568	785 512	785 511–785 512

95% CI, 95% confidence interval; RF, risk factor.

About 1.5 million postmenopausal women in France had their menopause before 40 years of age and may, therefore, be at risk for osteoporosis (Table 8). Nearly 700 000 women older than 50 years may have a BMI smaller than 19 kg/m^2, over 2 million a history of fracture, over 1 million a history of proximal femoral fracture in their mother, and slightly less than 612 000 a history of glucocorticoid therapy. Our estimate of about 400 000 women older than 50 years with a history of disorders potentially responsible for osteoporosis should be viewed with caution. Overall, we estimate that 3186 318 (30%) women older than 50 years living in France may have at least one risk factor for osteoporosis (Table 9). The prevalence of women with at least two risk factors may be far lower, from 0.4% in the MONICA cohort to 8.8% in the OFELY cohort (Table 7). Overall, we estimate that, in France, about 785 512 (7.4%) women older than 50 years have at least two risk factors for osteoporosis (Table 9).

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Discussion

The sample sizes used for our prevalence computations ranged from only 4321 for disorders potentially responsible for osteoporosis to 51 179 for a BMI lower than 19 kg/m^2. Mean prevalences calculated from our samples were 15% for early menopause, 7.5% for BMI; 17.6% for a history of fracture, 8.8% for a history of proximal femoral fracture in the mother, 4.3% for a history of disorders potentially responsible for osteoporosis, and 6.6% for a history of long-term glucocorticoid therapy.

We based our choice of risk factors on the ANAES recommendations, which are fairly general, similar to other recommendations. For instance, they do not consider age, although the impact of risk factors varies with age. Thus, from a clinical viewpoint, menopause before 40 years of age has a far greater impact in younger women than in older women. Conversely, a history of proximal femoral fracture in the mother seems to have a greater impact at 70 than at 50 years of age.

The sample of women older than 50 years used for our study was obtained from a heterogeneous source and was not representative of the population living in France. We obtained information from nine cohorts totaling 123 986 women. The cohort studies differed in terms of their objectives, recruitment method, sampling method, selection criteria, and geographic location. In addition, there were differences in the methods used to collect data on risk factors. Not all the studies obtained information on all the risk factors used in our study. In addition, differences in risk factor definitions occurred across studies.

Although the ANAES recommendations apply to postmenopausal women, we studied women older than 50 years of age. This change was necessary to derive reasonable estimates from demographic data, which include age but not hormonal status. It may have introduced a small degree of overestimation, as a small proportion of women older than 50 years of age are premenopausal.

When each risk factor is analyzed separately using the pooled data from all the cohorts, the results suggest an age effect (last column in Table 2). The prevalence of early menopause seems to increase from 13% in the 50–54-year group to 31% in the 90-year or older group. However, the 65–69, 70–74, and 90-year or older groups comprised small numbers of women (662, 525, and 133, respectively). These small sample sizes exacerbate the effect of sampling variations. The results in these three groups differ noticeably from those in the other age groups: prevalences were lower in the 65–69 and 70–74-year groups than in the younger groups and substantially higher in the 90-year and older group than in the younger groups. This complicates the interpretation of the results. A cohort effect occurred, as shown clearly in Table 2. In the PAQUID study, for instance, the prevalence of early menopause was considerably lower than in the other five cohorts, including the two that investigated similar age groups. For the 65–69 and 70–74-year groups, the data came from only two studies; in addition, one of these studies (PAQUID) supplied 80–91% of the sample. Thus, Table 2 shows greater variability across cohorts than across age groups within each cohort. Nevertheless, because we had no objective data indicating which cohort was the most representative, we computed the final estimations on the total sample obtained by pooling the nine cohort studies.

Regarding low BMI, the E3N cohort provided more than half the sample (34 851/51 179 women) used to calculate the mean prevalence (7.5%) for the seven cohorts. The prevalence standardized for the population in France was estimated at 6.6% (6.5–6.7%). No major age-related variations occurred within each cohort (Table 3).

The prevalence of a history of fracture was highest in the EPIDOS cohort (37.1%). This cohort was composed only of women older than 75 years of age, and identification of risk factors for osteoporosis was the main objective of the study, suggesting that the prevalence may have been higher than in the general population. In the ESTEV95 study, only peripheral fractures were taken into account, whereas the other studies also recorded vertebral fractures. This may have contributed to the low prevalence in the ESTEV95 study. After standardization, the mean prevalence was 19% (18.5–19.4%) (Table 8). As with early menopause, the prevalences in the 65–69 and 70–74-year groups were based on small numbers of women (61 and 89, respectively) and were considerably lower than in the other studies (Table 2).

Finally, for all the risk factors except a history of fracture, differences across cohorts were greater than differences across age groups. In addition, because age often varied widely across cohorts (e.g. older than 75 years in EPIDOS and younger than 65 years in E3N), the age effect cannot be separated from the cohort effect. Moreover, sample sizes were small for the 65–69 and 70–74-year groups.

The data on the disorders potentially responsible for osteoporosis listed in the ANAES recommendations did not allow a reliable evaluation of this factor.

After analyzing the prevalence of each risk factor, it was important to evaluate the subset of women with more than one risk factor. Therefore, we estimated the overall prevalence of women at risk for

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osteoporosis according to the number and type of risk factors. The prevalence of women with at least one risk factor varied from 12.7% in the PAQUIS study to 30.9% in the EVA study (Table 5). In most cohorts, the prevalence of women with at least one risk factor increased from one age group to the next (Table 6). Considerable variation was noted across studies for identical age groups. In women older than 80 years, similar discrepancies were found between the two cohorts of older women (PAQUID and EPIDOS). In the cohort composed of women living in Dordogne and Gironde, the prevalence of women with at least one risk factor was substantially lower than in the other cohorts. However, this finding cannot be construed as evidence of geographic differences, since the population in each cohort may not have been representative of the female population in the region.

Whereas 30.16% of women older than 50 years had at least one risk factor, only 7.44% had at least two risk factors. This prevalence was markedly influenced by the 65–69 and 70–74-year age groups, which had small numbers of women. Data on these two age groups came from the PAQUID and EVA studies, which investigated only two risk factors, and from the OFELY study, which recorded five risk factors but had a very small sample size. For instance, the 65–69-year group in the OFELY study contributed only 8% of the total number of women in this age group. The cohort effect should be considering when interpreting the results. However, there was no age effect.

Thus, our results provide a reasonable estimate of the prevalence of the risk factors for osteoporosis identified by the ANAES and therefore of the number of women at risk for osteoporosis in France, based on a nonrepresentative sample of over 50 000 women older than 50 years. The significant differences across cohorts evidenced in our study are a reminder that estimates are influenced by recruitment bias and sampling fluctuations. However, even a study in a representative sample would provide only a rough estimate of the number of women likely to undergo absorptiometry, since this number depends not only on the presence of risk factors but also on the behavior of women regarding their health and on the prevalence of hormone replacement therapy among postmenopausal women.

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Appendix A

The cohorts identified for this study are listed below.

(1) E3N, Etude Epidémiologique de femmes de la MGEN, Unité INSERM XR 521, Institut Gustave Roussy, 94805 Villejuif cedex, France; study coordinator Françoise Clavel-Chapelon.

(2) Effets sur la santé de l'exposition aux sous-produits de l'eau,* INSERM U 420, School of Medicine, 54505 Vandoeuvre Les Nancy, France; Department head Jean-Marie Mur, study coordinator Rachel Nadif.

(3) EPIDOS, INSERM U 403, Edouard Herriot Teaching Hospital, Pavillion F, 69003 Lyon, France. Study coordinators Gérard Breart and Pierre Meunier.

(4) ESPRIT,* INSERM U 9930, Crlc Val d'Aurelle, 34298 Montpellier cedex, France; research unit director, Karen Ritchie.

(5) ESTEV, évolution des déficiences en fonction de l'âge et des caractéristiques physiques et organisationnelles de cours au la vie active, INSERM U 170, 94807 Villejuif cedex, France; research unit director Denis Hemon, study coordinator Francis Deffiennic.

(6) EVA, étude des three cites, INSERM U 360, GH Pitie-Salepetriere, 75651 Paris cedex 13, research unit director Annick Alperovitch, study coordinator Claudine Berr.

(7) GAPIC*, INSERM U 525 (Génétique épidémiologique et moléculaire des pathologies cardiovasculaires) Pitié-Salpêtrière School of Medicine, 75634 Paris cedex 13, research unit director François Cambien, study coordinator S. Blankenberg.

(8) Cohorte Gazel, INSERM U 88, St. Maurice National Hospital, 94415 St. Maurice cedex, France; research unit head Marcel Goldberg.

(9) "Les femmes dans la ville": épidémiologie en santé périnatale & santé des femmes, INSERM U149, Tenon Teaching Hospital, 75970 Paris cedex 20, France; research unit director Gérard Breart.

(10) Mastopathies bénignes et risque de cancer du sein[*°], INSERM U 521, Institut Gustave Roussy, 94805 Villejuif cedex, France; research unit director Catherine Bonaiti, study coordinator Monique LE.

(11) MONICA, INSERM U 258, Paul Brousse Teaching Hospital, 94807 Villejuif cedex, France; research unit director Pierre Ducimetiere.

[°] This study was not included.

(12) OFELY, INSERM U 403, Edouard Herriot Teaching Hospital, Pavillion F, 69003 Lyon, France; research unit director Pierre Dominique Delmas.
(13) PAQUID, INSERM U 330, Victor Segalen University, 33076 Bordeaux cedex, France; research unit director Roger Salamon, study coordinator Jean-François Dartigues.
(14) POLA, INSERM U 500, 34093 Montpellier cedex 05, France; research unit director Laure Papoz, study coordinator Cécile Delcourt.
(15) Etude SU VI MAX (SUpplémentation en VItamines et Minéraux AntioXydants), Institut Scientifique et Technique de la Nutrition et de l'Alimentation, 75003 Paris, Investigateur principal Serge Hercberg.
(16) Health Insurance Database, regional National Health Insurance Agencye, 69436 Lyon cedex 03, France; Head physician Pierre Vermorel, statistician Valérie Tainturier.

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