ORIGINAL ARTICLE

Fracture Risk and Risk Factors for Osteoporosis

Results From Two Representative Population-Based Studies in North East Germany (Study of Health in Pomerania: SHIP-2 and SHIP-Trend)

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SUMMARY

Background: As the population ages, diseases of the elderly are becoming more common, including osteoporosis. Ways to assess the risk of fracture and the distribution and effects of known risk factors for osteoporosis will be important in planning for future healthcare needs, as well as in the development of preventive strategies.

Methods: The study population included 6029 men and women aged 20–90 who underwent examination in the second follow-up wave of the Study of Health in Pomerania (SHIP-2) or in the basal SHIP-Trend Study. The risk of fracture was estimated on the basis of quantitative ultrasonography of the calcaneus. Prior fractures and risk factors for osteoporosis were ascertained in standardized interviews.

Results: 4.6% of the male subjects and 10.6% of the female subjects were judged to have an elevated risk of fracture. The corresponding percentages among subjects over age 65 were 8.8% for men and 28.2% for women. Even among subjects under age 55, risk factors for osteoporosis were associated with lower bone stiffness: the mean stiffness index was 103/98 (men/women) without risk factors, 99/96 with one risk factor, and 93/95 with more than one risk factor. Logistic regression analysis yielded an odds ratio of 1.89 (95% confidence interval: 1.44–2.50; $p<0.01$) for prevalent fractures among subjects aged 75 and older compared to subjects under age 55.

Conclusion: The data indicate a high prevalence of osteoporosis from age 65 onward. These findings are consistent with those of other studies from Germany and across Europe. Younger men and women should already begin taking steps to counteract modifiable risk factors.

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According to current predictions, the proportion of the population older than 65 in the OECD countries will rise to 21% by 2030. In Germany, this proportion is predicted to be as high as 29% (1). Age-related diseases, such as osteoporosis, will therefore gain in importance (2). Because of the enormous relevance of osteoporosis for the individual and the substantial costs to the healthcare system (2), epidemiological osteoporosis research is of essential importance (2–5). To date, however, only few studies have reported data on the prevalence and risk factors for osteoporosis in Germany (3–5). At the same time, such investigations (3–5) are often limited in terms of the selection of study subjects. For example, studies to date have included only information on women from the 45th year of life (5), men and women from the 50th year of life (4), or members of an insurance scheme from the 50th year of life (3). In addition to the prevalence of osteoporosis, risk factors for osteoporotic bone changes are also of interest as knowledge and awareness of these helps to deploy preventive measures in a targeted fashion (6, 7).

In the present study, we analyzed primarily—on the basis of quantitative ultrasound (QUS) measurements—how common a high risk of osteoporotic fractures is in men and women of different ages in the North East of Germany. Secondarily, we investigated how often osteoporotic fractures and risk factors for osteoporosis occur and whether their occurrence is associated with reduced bone stiffness.

Methods

Study population

The study population is based on data from two independent epidemiological cohorts: the Study of Health in Pomerania (SHIP) and SHIP-Trend (8, 9). Both are based on representative samples of the population aged 20–79 in the region of Western Pomerania (8, 9). In SHIP, two-stage cluster sampling was used, whereas SHIP-Trend used a random sample stratified by age and sex. The baseline investigation in SHIP (SHIP-0) took place between 1997 and 2001, the 11-year follow-up investigation (SHIP-2) at the same time as SHIP-Trend in 2008 to 2012. For the analysis we used data

TABLE 1

Charakteristics of study population

Charakteristic*	Men (N = 2 968)	Women (N = 3 061)
Age (years)	49.0 (36.0–62.0)	53.0 (39.0–68.0)
BMI (kg/m²)	27.6 (25.0–30.6)	26.5 (23.1–30.4)
Waist circumference (cm)	94.6 (86.7–103.8)	83.0 (74.0–93.0)
Diabetes mellitus (%)	358 (12.1)	342 (11.2)
Tobacco smoking (%)	900 (30.5)	742 (24.3)
Physically inactive (%)	1482 (50.1)	1578 (51.7)
High-risk alcohol consumption (%)	403 (13.8)	82 (2.7)
Liver disease (%)	222 (7.6)	191 (6.3)
eGFR (mL/min/1.73m²)	90.5 (78.2–104.5)	85.3 (72.7–99.7)
Inflammatory joint disorder (%)	106 (3.6)	182 (6.0)
Hyperthyroidism (%)	55 (1.8)	83 (2.7)
Postmenopausal (%)	–	1780 (58.2)
Subject takes		
Bisphosphonates (%)	6 (0.2)	33 (1.1)
SERM (%)	0 (0.0)	4 (0.1)
Vitamin D (%)	11 (0.4)	38 (1.2)
PTH (%)	0 (0.0)	1 (0.1)
Calcium (%)	14 (0.5)	98 (3.2)
Steroids (%)	28 (1.0)	45 (1.5)
Opiates (%)	34 (1.1)	57 (1.9)
Antidepressants (%)	88 (3.0)	207 (6.7)
Antiepileptic drugs (%)	43 (1.5)	78 (2.5)
Sedatives (%)	23 (0.8)	73 (2.4)
Oral contraceptives (%)	–	462 (15.1)
Hormone replacement therapy (%)	–	115 (3.8)
Osteoporosis (self reported) (%)	57 (2.0)	276 (9.2)
BUA (dB/MHz)	116.9 (108.2–127.3)	107.1 (97.6–118.4)
SOS (m/s)	1 562.9 (1 540.5–1 587.9)	1 557.4 (1 535.5–1 581.9)
Bone stiffness index	95.8 (84.5–109.5)	87.9 (76.3–101.3)
High risk for osteoporotic fractures (%)	138 (4.6)	323 (10.6)

Reported as numbers (proportions) or medians (1^{st}–3^{rd} quartile).
The age and sex structure were standardized to the population of the state of Mecklenburg–Western Pomerania at the end of 2010.
BMI, body-mass-Index; BUA, broadband ultrasound attenuation; eGFR, estimated glomerular filtration rate; PTH, parathyroid hormone; SERM, selective estrogen receptor modulators; SOS, speed of sound
* Lacking values occurred in the following variables in men/women and were excluded when calculating proportions: Diabetes mellitus n = 7/10. Tobacco smoking n= 10/9. Physically inactive n = 12/9. High-risk alcohol consumption n = 41/26. Liver disease n = 37/26. Inflammatory joint disorder n = 28/46. Hyperthyroidism n = 1/0. Postmenopausal n = 0/3. Self reported osteoporosis n = 55/66

from SHIP-2 (30–90 years) and SHIP-Trend (20–79 years) because these studies included quantitative ultrasound (QUS) measurements. 6067 subjects (90%) with valid QUS measurements were eligible for the study; 11 pregnant women and 27 participants with renal failure were excluded. The study population included 6029 participants.

Risk factors for osteoporosis

We selected risk factors for osteoporosis on the basis of the guidelines of the Umbrella Organization for Osteology ("Dachverband Osteologie") (10) and the World Health Organization's fracture risk assessment tool (FRAX) (11). We used standardized interviews to inquire about these risk factors and categorized them as modifiable and non-modifiable risk factors.

Modifiable factors included:

- Underweight (body mass index [BMI] <20 kg/m²)
- Nicotine use
- High-risk alcohol use (men ≥30 g/day, women ≥20 g/day)

Non-modifiable risk factors included:

- Liver disease
- Inflammatory joint disorders
- Diabetes mellitus
- Hyperthyroidism
- Previous fractures in subjects from age 55
- Medication with steroids, aromatase inhibitors, androgen antagonists, antiepileptic drugs, sedatives, opiates, neuroleptic drugs, antidepressants, or glitazone in women.

In all our analyses of risk factors and earlier fractures, we excluded participants for whom the relevant data on modifiable or non-modifiable risk factors were lacking.

Quantitative ultrasound measurements

We used the Achilles InSight (GE Medical Systems Ultrasound, GE Healthcare, Chalfont St Giles, UK) system to perform the QUS measurements. The system measures the speed of sound (SOS) and the frequency dependent attenuation (FDA; broadband ultrasound attenuation [BUA]) of a sound wave by penetrating the heel bone and calculates the bone stiffness index on this basis: (0.67×BUA) + (0.28×SOS) −420. The bone stiffness index indicates the risk of an osteoporotic fracture (12). It can also be expressed as a *t* value—that is, as the individual deviation from the mean for young adults—in standard deviations (SD). A high risk for osteoporotic fractures exists in *t* values <−2.5 SD, a medium risk between −1 and −2.5 SD, and a low risk > −1 SD. A high risk indicates osteoporosis (12).

Statistical analysis

Categorical variables were reported as numbers and proportions, and continuous variables as medians (1^{st}–3^{rd} quartile). The results were visualized as box plots or bar charts. Significance tests were used as follows: group differences in the bone stiffness index, which was distributed approximately normally, were

tested by using the *t* test, group differences in the categorical variables by using the chi-square test. A p-value <0.05 was defined as significant. Logistic regression analysis was used to determine whether fractures were associated with subjects' sex, age, and study cohort. We reported odds ratios (OR) and 95% confidence intervals (CI). We standardized all data to the age/sex structure of the population of the federal state of Mecklenburg–Western Pomerania as at year-end 2010. Furthermore we used a sensitivity analysis for weighting the drop-out between SHIP-0 and SHIP-2 and for non-responses in SHIP-Trend—based on age, sex, and health-relevant data. We used SAS to conduct all our analyses.

The *eBox* lists further methodological details.

Results

Table 1 shows data on lifestyle, medication use, and risk factors for osteoporosis.

Bone stiffness and osteoporotic fracture risk

For both sexes the QUS measurements fell in all age groups. The highest values were seen in the youngest age group (20–34 years) and the lowest in the oldest age group (≥ 75 years). The median of the bone stiffness index at age 20–34 years versus ≥ 75 years in men was 101 versus 91.3 and in women, 96.8 versus 71.4. In male subjects the measurements fell evenly over the age groups under study, whereas in female subjects, the decrease was minimal between the ages of 20 years and 54 years but deteriorated in the older age groups. The difference by sex of the bone stiffness index therefore widens greatly from age 55 onward, with the values in women dramatically dropping compared with those of men (*Figure 1*). Altogether 4.6% of men and 10.6% of women were at high risk of fracture. The sensitivity analysis provided comparable results: a high risk of fracture in 5.1% of men and 10.6% of women. In the individual age groups, the following proportions of men and women were found to be at high risk of fracture:

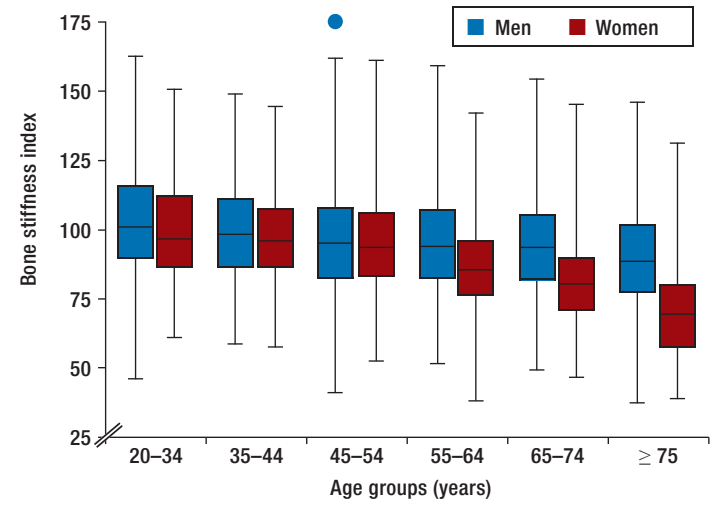
- 20–34 years: 1.5% and 0.9%
- ≥ 50 years: 7.2% and 17.9%
- ≥ 65 years: 8.8% and 28.2%
- ≥ 75 years: 12.5% and 46.0%.

Previous fractures

225 (11%) of SHIP-2 subjects and 236 (6%) of SHIP-Trend subjects reported previous fractures *(Table 2)*. The proportions of study participants with previous fractures for all age groups under study were higher in SHIP-2 than in SHIP-Trend, as SHIP-2 recorded all fractures, whereas SHIP-Trend recorded only proximal humeral, hip, femoral, and vertebral fractures.

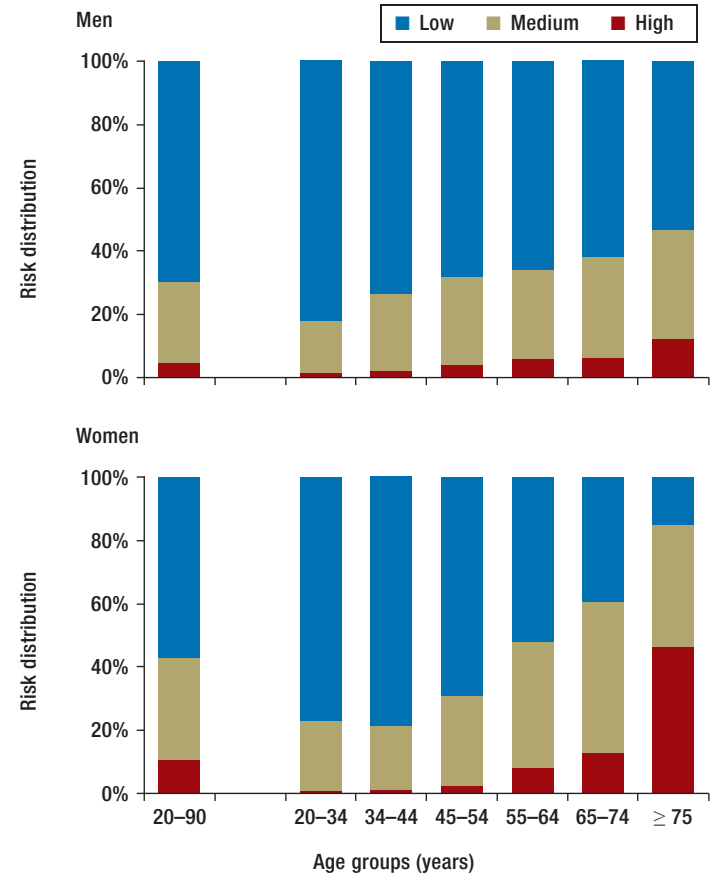
Men and women ≥ 55 years of age who reported previous fractures had a significantly lower bone stiffness index than subjects without fractures. The median of the bone stiffness index in study participants without fracture was 93.2 (men) and 79.9 (women) and with fracture, 89.8 (men) and 75.3 (women), with the *t* test result p = 0.02 (men) and p<0.01 (women). Accordingly,

FIGURE 1



Bone stiffness index by age group and sex in 6029 SHIP-2 and SHIP-Trend subjects. An extreme value (blue circle) is shown schematically at the top end of the y axis

FIGURE 2



Fracture risk based on the bone stiffness index by age group and sex in 6029 SHIP-2 and SHIP-Trend subjects. The high, medium, and low fracture risks are defined as an individual bone stiffness index < –2.5-fold, –1 to –2.5-fold, and > –1-fold standard deviation from healthy young adults

TABLE 2

Previous fractures in 6009 SHIP-2 and SHIP-Trend subjects by age group and sex

Study	Age group	Men		Women	
		n	Fractures	n	Fractures
SHIP-Trend: Any proximal humerus, hip, femoral, and vertebral fracture after an accident, as well as all fractures without prior trauma	<55	1389	78 (5.6%)	1219	53 (4.3%)
	55–64	299	23 (7.6%)	297	13 (4.5%)
	65–74	243	14 (5.8%)	264	27 (10.1%)
	≥ 75	104	7 (6.8%)	143	21 (14.7%)
	Total	**2035**	**122 (6.0%)**	**1923**	**114 (5.9%)**
SHIP-2: Any fracture after an accident since SHIP-0 and any fracture without prior trauma	<55	431	45 (10.5%)	433	35 (8.2%)
	55–64	193	17 (8.8%)	193	23 (12.1%)
	65–74	165	14 (8.6%)	217	31 (14.1%)
	≥ 75	134	10 (7.6%)	285	50 (17.6%)
	Total	**923**	**86 (9.3%)**	**1128**	**139 (12.3%)**

Subjects in whom data on fractures were lacking were excluded from this analysis. The age and sex structure were standardized to the population of the state of Mecklenburg–Western Pomerania at end-2010

people older than 55 with previous fractures were significantly more often at high risk for osteoporotic fractures than people without previous fractures: with fractures, 15 men (17.2%) and 54 women (32.9%); without fracture 71 men (6.8%) and 242 women (19.6%); the chi-square test result for both sexes was $p<0.01$.

In the logistic regression analysis, age was found to be a significant predictor for previous fractures. Older subjects had a greater risk than younger subjects of displaying fractures. Compared with those younger than 55, the OR in those aged 55–64 was 1.19 (95% CI 0.91 to 1.57), in 65–74 year olds 1.47 (95% CI 1.13 to 1.92), and in those aged 75 and older, 1.89 (95% CI 1.44 to 2.50). Sex was not a significant predictor of fractures across all age groups (OR 1.09, 95% CI 0.90 to 1.33). When looking only at subjects aged 55 and older, however, women were at higher risk of fractures than men (OR 1.55, 95% CI 1.17 to 2.05) *(Table 3, Table 4)*.

Risk factors for osteoporosis

Almost half (45.3%) of study subjects did not have any risk factors, but one third (36.1%) had one, and one in six (18.4%) had two or more. In subjects younger than 55, the modifiable risk factors—underweight, nicotine consumption, and high-risk alcohol consumption—had an obvious role *(eTable)*. More than 40% of men and 36% of women in this age range reported at least one of the three modifiable risk factors. From age 55 years onward, the non-modifiable risk factors became crucial for both sexes. The bone stiffness index of subjects younger than 55 without risk factors was significantly higher than in those with one or two risk factors. The median of the bone stiffness index in men and women without risk factors was 101.3 and 96.7; in those with one risk factor, 96.5 and 94.6; and in those with at least two risk factors, 91.4 and 94.0. The result for all *t* tests was $p<0.02$. The same was the case for study subjects aged 55 and older, but the differences in women did not reach significance: the medians of the bone stiffness index were 94.5 and 79.8; with one risk factor, 91.5 and 78.3; and with at least two risk factors, 90.4 and 78.9. The *t* test results were $p<0.01$ for men and $p>0.05$ for women.

Discussion

Bone stiffness and risk of osteoporotic fractures

In the European Union (EU 27), an estimated 5.5 million men and 22 million women have osteoporosis (13). About 6.6% of men and 22.1% of women aged 50 years and older are affected (13). Three large studies have reported on the prevalence rates of osteoporosis in Germany: BEST (3), BoneEVA (4), and GSTe103 (5) *(Table 5)*. The BEST study (3) provides the most recent estimates. The men in this study and in northern Germany have comparable rates of osteoporosis diagnoses and fracture risk (BEST study: 6%; SHIP: 7.2%). By contrast, women differ, especially in the younger age groups. The proportions of subjects with a high fracture risk in North East Germany (50–64 years: 6.2%; 65–74 years: 12.4%) are notably lower than the osteoporosis prevalence rates in the BEST study (3) (50–64 years: 17%; 65–74 years: 32%). In people aged 75 years and older the values are comparable (BEST: 48% [3]; SHIP: 46%). It is conceivable that women in North East Germany develop osteoporosis to a lesser extent than the national average, for example as a result of the higher BMI (15), which has protective effects (14). On the other hand, it has to be assumed that the present study underestimates the prevalence of osteoporosis. The reasons include the exclusion criteria of the QUS measurements—for example, injuries in the

12 months before the examination. The study population is therefore on average healthier than the average population. Furthermore, the present results are not equal to a diagnosis of osteoporosis. Dual x-ray absorptiometry (DXA) scans are the gold standard in the diagnostic evaluation of osteoporosis. Such an investigation was not possible in SHIP-2 and SHIP-Trend. QUS, however, allows a risk prediction of comparable quality to DXA (10, 16, 17). Several studies have shown that the QUS measurements on the calcaneus predictively indicated the risk of hip fracture (16, 17), and that, like DXA scanning, they predicted prevalent (18) and incident (19) vertebral fractures.

Overall, these initial data on bone stiffness in North East Germany underline the vast importance of osteoporosis, since 8.8% of men and 28.2% of women aged 65 and older are at high risk of osteoporotic fractures.

TABLE 3

Previous fractures in the entire study population

Exposition	OR (95% CI)	p value
Women vs men	1.09 (0.90 to 1.33)	0.37
55–64 years vs <55 years	1.19 (0.91 to 1.57)	0.20
65–75 years vs <55 years	1.47 (1.13 to 1.92)	<0.01
≥ 75 years vs <55 years	1.89 (1.44 to 2.50)	<0.01
SHIP-2 vs SHIP-Trend	1.71 (1.40 to 2.09)	<0.01

OR, odds ratio; 95% CI, 95% confidence interval
Odds ratio with 95% confidence intervals for reporting of previous fractures in the entire study population
SHIP, Study of Health in Pomerania

TABLE 4

Previous fractures in subjects ≥ 55 years

Exposition	OR (95% CI)	p value
Women vs men	1.55 (1.17 to 2.05)	<0.01
65–74 years vs 55–64 years	1.22 (0.88 to 1.68)	0.24
≥ 75 years vs 55–64 years	1.55 (1.11 to 2.16)	<0.01
SHIP-2 vs SHIP-Trend	1.52 (1.16 to 1.99)	<0.01

OR, odds ratio; 95% CI, 95% confidence interval
Odds ratio with 95% confidence intervals for reporting of previous fractures in subjects ≥ 55 years
SHIP, Study of Health in Pomerania

Previous fractures

Any osteoporotic fracture is associated with an increased risk for further bone fractures (10, 20–22). Prospective studies (20, 23, 24) have reported an association between the occurrence of radius fractures and subsequent hip fracture or neck of femur fractures (20, 23, 24). Accordingly, SHIP-2 and SHIP-Trend participants with previous bone fractures had a lower bone stiffness index and often had a higher risk of fractures than study participants without previous fractures. The risk of osteoporotic fracture is furthermore largely determined by age (10, 25, 26). The increased risk in older subjects compared with younger ones is consistent with the results of a study from the city of Rostock, which is based on emergency surgical reports (27).

Risk factors for osteoporosis

If risk factors for osteoporosis were present the bone stiffness index was reduced. In the age group younger than 55, even only one of the factors under consideration—underweight, nicotine consumption, or high-risk alcohol consumption—contributed to a lower bone stiffness index. The negative effect of these factors on bone density has often been shown (28–30), and the underlying mechanisms are at least partly known (28–30). Malnutrition, nicotine consumption, and alcohol misuse change the trabecular and cortical microarchitecture, lower bone mineral density, and thus increase fracture risk (28–30). In persons with chronic alcoholism, for example, fractures are four times as common as in healthy controls (28). In smokers, the relative risk for bone fractures compared with non-smokers is 1.25 (31). Since the extent of loss of bone mineral density in osteoporosis is crucially dependent on total bone mass (32), which is acquired up to about the 30th year of life, it is of vital importance to avoid risk factors at this age. In subjects aged 55 or older with or without risk factors, differences in the bone stiffness index are significant only in men. In women, the effect of the studied risk factors on bone mineral density may possibly be overlaid by hormonal changes during the menopause.

Altogether, our study showed that osteoporosis goes hand in hand with the lifestyle factors and comorbidities under study. Especially in younger men and women, the potential exists to affect bone stiffness in a positive way and thereby counteract osteoporosis, by adopting health promoting behaviors and avoid modifiable risk factors or use targeted interventions (33, 34). It is well known that in persons with chronic alcoholism, bone mineral density remains constant after six months' abstinence, whereas it notably falls if alcohol consumption is continued (35). Furthermore, bone mineral density is lower in smokers than in non-smokers, but it does not differ between non-smokers and former smokers (36). Similarly, the increased hip fracture risk in smokers compared with non-smokers notably decreases after 10 years' abstinence from tobacco (37).

Strenthgs and limitations of the study

The main strengths of the present study are the number of participants and the population-based study design. Another strength is the standardized and detailed data collection, which allows for exact characterization of subjects. On the other hand, it cannot be ruled out that non-response and dropout introduced selection bias in the study population as people refused to participate, for example, or moved away from the study region. It is

TABLE 5

Comparison of the prevalence of osteoporosis in the BEST, BoneEVA, and GSTe103 studies with the results of SHIP-2 and SHIP-Trend

	BEST (3)	BoneEVA (4)	GSTe103 (5)	SHIP-2/SHIP-Trend
Study population	1.7 million members of the Techniker Krankenkasse sickness fund	1.5 million members of the Gmünder Ersatzkasse sickness fund and billing data from the Scientific Institute of the National Association of Statutory Health Insurance Physicians (Zentralinstitut für die Kassenärztliche Versorgung) of 0.6 million patients	2330 participants in the National Health Telephone Survey 2003	6029 participants in the SHIP-2 and SHIP-Trend studies
Age range	50 years or older	50 years or older	45 years or older	20–90 years
Osteoporosis prevalence*[1]				
All age ranges under study	6% men/24% women	9.7% men/39.0% women	14.2% women	4.6% men/10.6% women
50–64 years	4% men/17% women	7.1% men/23.3% women	10.0% women*[2]	5.9% men/6.2% women
65–74 years	8% men/32% women	11.4% men/46.7% women	17.1% women	6.7% men/12.4% women
75 years or older	15% men/48% women	16.1% men/59.2% women	23.7% women	12.5% men/46.0% women

BEST, Bone Evaluation Study; GSTe103, German National Health Telephone Survey 2003; SHIP-Trend, baseline investigation of the Study of Health in Pomerania; SHIP-2, second follow-up study of the Study of Health in Pomerania

*[1] SHIP-2 and SHIP-Trend: prevalence of a high risk for osteoporotic fractures

*[2] 55–64 years

possible that subjects with osteoporotic fractures refused to participate in particularly substantial numbers because of resultant impairments to their mobility or because they required care. The sensitivity analysis showed, however, that non-response in SHIP-Trend and dropout between SHIP-0 and SHIP-2 affected the risk of osteoporotic fracture only minimally. Not all subjects were examined by using QUS; reasons included implants or malpositioning. It is therefore probable that especially study participants with low bone stiffness were not considered in the analysis and that bone stiffness in general is therefore overestimated. Additionally, it was not possible to study all potentially relevant risk factors for osteoporotic fractures—for example, no data were collected on participants' coordination skills or on falls. Information about previous fractures came exclusively from subjects' own recollections. For this reason, we should assume that the prevalence of fractures was underestimated—for example, because of undetected vertebral fractures.

Conclusion

The present study analyzed for the first time comprehensive data on bone health in North East Germany. The results indicate a high prevalence of osteoporosis in those aged 65 and above, which is consistent with the results from other studies in Germany and the EU. Furthermore, we found that modifiable risk factors for osteoporosis are common, particularly in young men and women, and that previous fractures are associated with an increased risk for future osteoporotic fractures. Altogether the study results underline the importance of the diagnostic evaluation, prevention, and therapy of osteoporosis.

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Conflict of interest statement

Dr. Wallaschofski has received honoraria for lectures on the subject "Biomarkers of bone metabolism" from Amgen and Lilly.

The remaining authors declare that no conflict of interest exists.

KEY MESSAGES

- In North East Germany, 4.6% of men and 10.6% of women aged between 20 and 90 have a high risk for a future osteoporotic fracture.
- In Western Pomerania's persons older than 65, 8.8% of men and 28.2% of women have a high fracture risk; the same is true for 12.5% of men and 46.0% of women in those older than 75. This means that osteoporosis has a crucial role in these age groups.
- Bone stiffness, as measured by using quantitative ultrasound of the calcaneus, is lower in the over 55 year olds in both sexes who have had previous fractures than in those without previous fractures.
- The main risk factors for osteoporosis in men and women younger than 55 are modifiable risk factors—that is, underweight, nicotine use, or high-risk alcohol consumption. Modifiable risk factors are associated with reduced bone stiffness.

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eTABLE

Proportions of subjects with modifiable and non-modifiable risk factors*

Risk factors	Men		Women	
	<55 years (n = 1 769)	≥ 55 years (n = 1 105)	<55 years (n = 1 606)	≥ 55 years (n = 1 359)
No risk factors (%)	816 (46.1%)	447 (40.5%)	774 (48.2%)	608 (44.8%)
Only modifiable risk factors (%)	712 (40.3%)	157 (14.2%)	574 (35.7%)	66 (4.9%)
At least one non-modifiable risk factor (%)	241 (13.7%)	501 (45.4%)	258 (16.1%)	685 (50.3%)

* By age group and sex in 5816 SHIP-2 and SHIP-Trend subjects
Modifiable risk factors: underweight, tobacco smoking, high-risk alcohol consumption
Non-modifiable risk factors: inflammatory joint disorder, liver disease, diabetes mellitus, hyperthyroidism, subject takes steroids, glitazone (in women), aromatase inhibitors, antiandrogens, antiepileptic drugs, sedatives, opiates, neuroleptics, antiepileptic drugs, or antidepressants, any fracture after accident since SHIP-0 in SHIP-2 subjects aged 55 years and older, any proximal humeral, hip, femoral, or vertebral fractures in SHIP-Trend subjects after an accident from age 55 and any spontaneous fracture without preceding trauma in SHIP-2 and SHIP-Trend subjects aged 55 and older.
Subjects, in whom data on risk factors were lacking, were excluded from this analysis. The age and sex structure were standardized to the population of the federal state of Mecklenburg–Western Pomerania at end-2010.

eBOX

Risk factors for osteoporosis

The following risk factors are based on data collected from study subjects in standardized interviews: tobacco smoking, high-risk alcohol consumption (men ≥ 30 g/day, women ≥ 20 g/day), liver disease, inflammatory joint disorders and previous fractures. In SHIP-2, study participants were asked whether since SHIP-0 they had had fractures of the upper arm near the shoulder, hip fractures, femoral neck fractures, wrist fractures, or ankle fractures, or other bone fractures after an accident, or whether they had ever had a fracture without a prior accident. In SHIP-Trend, subjects were asked to provide information on whether they had ever had fractures of the upper arm near the shoulder, hip fractures, femoral neck fractures, or vertebral fractures after an accident and whether they had ever had a fracture without a prior accident. Body height, weight, and waist circumference were measured in a standardized manner. The body mass index (BMI) was calculated from body height and weight. Underweight was defined as a BMI <20 kg/m^2. Participants were asked to bring along all medications they had taken in the previous seven days. The name of the effective substance was assigned to the preparations by using the official German version of the Anatomical Therapeutic Chemical classification (ATC) (29). The use of steroids, aromatase inhibitors, antiandrogens, antiepileptic drugs, sedatives, opiates, neuroleptics, antidepressants, or glitazone in women was regarded as a risk factor for osteoporosis. Blood was taken from reclining subjects' cubital veins between 7.30 and 13.00. Serum concentrations of creatinine, glucose, HbA_{1C}, and thyroid-stimulating hormone (TSH) were measured in all subjects. Hyperthyroidism was present if the TSH value was <0.25 mU/L. Diabetes mellitus was diagnosed in cases of the relevant doctor's diagnosis, use of antidiabetic medication, HbA_{1C} ≥ 6.5%, or a spontaneous blood glucose measurement ≥ 11.1 mmol/L.

Quantitative ultrasound measurements

Quantitative ultrasound (QUS) measurements of the calcaneus were conducted by using one of two Achilles InSight systems (GE Medical Systems Ultrasound, GE Healthcare, Chalfont St Giles, UK). The QUS was done on sitting-down subjects, on one foot after the other. Alcohol was used as the coupling agent. No systematic measuring differences were seen in the two devices used. The QUS was conducted by certified investigators. Variation coefficients for intraobserver variability (frequency dependent attenuation [broadband ultrasound attenuation] (BUA): 2.98%; speed of sound [SOS]: 0.39%; bone stiffness index: 2.74%) and for interobserver variability (BUA: 3.47%, SOS: 0.36%; bone stiffness index: 3.29%) were calculated. QUS was not conducted in subjects who had implants, prostheses, or amputations within or below the knee. Similarly, no measurements were conducted in subjects with open wounds or infections below the knee. QUS data of subjects using a wheelchair, subjects whose feet could not be placed correctly in the device, and subjects who in the 12 months preceding the SHIP study had had an injury or operation distally to the knee were not used for the statistical analyses. Where QUS measurements for both feet were available, the data from the foot that had the lower bone stiffness index were used in the analyses.