FOLIA MEDICA CRACOVIENSIA
Vol. LXII, 4, 2022: 137–153
PL ISSN 0015-5616
DOI: 10.24425/ fmc.2022.144088

# Higher milk consumption is not associated with fracture risk reduction: systematic review and meta-analysis

Grzegorz Goncerz[1,2], Patrycja Kojm[3], Sylwia Skocelas[3], Krzysztof Więckowski[3], Tomasz Gallina[3], Paulina Pietrzyk[3], Sebastian Goncerz[3]

[1]Department of Anatomy, Jagiellonian University Medical College, Kraków, Poland
[2]Polish Institute of Evidence Based Medicine, Kraków, Poland
[3]Jagiellonian University Medical College, Kraków, Poland

**Corresponding author:** Grzegorz Goncerz, M.D., Ph.D.
Department of Anatomy, Jagiellonian University Medical College,
ul. Kopernika 12, 31-034 Kraków, Poland
Phone: +48 12 422 95 11; E-mail: goncerz@mp.pl

**Abstract:** Introduction: Osteoporosis affects over 200 million people worldwide causing nearly 9 million fractures annually, with more than half in America and Europe.
Objectives: This meta-analysis was conducted to investigate whether low milk intake is associated with an increased risk of fractures by summarizing all the available evidence.
Methods: Relevant studies were identified by searching the PubMed and EMBASE databases up to June 2020. The pooled relative risks with 95% confidence intervals were calculated.
Results: In a meta-regression analysis of 20 included studies (11 cohort and 9 case-control studies), a higher milk intake was not associated with a reduction in the total fracture risk in both sexes (OR 0.95, 95% CI: 0.84–1.08), either in cohort (OR 0.91; 95% CI: 0.79–1.05) or case-control studies (OR 1.09; 95% CI: 0.82–1.44), as well as separately in men (OR 0.87; 95% CI: 0.71–1.07) and women (OR 0.95; 95% CI: 0.80–1.13).
Conclusion: Higher milk consumption is not associated with fracture risk reduction and should not be recommended for fracture prevention.

**Keywords:** milk, fracture, meta-analysis.

**Submitted:** 12-Sep-2022; **Accepted in the final form:** 25-Nov-2022; **Published:** 29-Dec-2022.

## Introduction

Osteoporosis, defined as reduced bone mineral density and increased bone fragility, is one of the major public health problems. The disease affects over 200 million people worldwide [1]. In the 27 countries of the European Union, approximately 21% of women and 6.6% of men aged over 50 years have osteoporosis (defined as a T-score of ≤−2.5 SD at the femoral neck), which translates into more than 22 million women and nearly 5.5 million men [2]. In women aged 80 years or older the prevalence of osteoporosis reaches almost 50% [2].

Nearly 9 million fractures occur annually due to osteoporosis, with more than half in America and Europe [3]. The number of fractures in some Middle East and African countries is estimated to quadruple by 2050, mostly because of the aging population [4]. In the European Union, the number of new fractures in 2010 reached 3.5 million (610,000 hip fractures; 520,000 vertebral fractures; 560,000 forearm fractures; and 1,800,000 other fractures) [2]. In 2017 in 4 largest European Union countries, the United Kingdom, and Sweden there were 2.7 million new fragility fractures and a 23% increase (to 3.3 million) is expected in 2030 [5]. In the Swedish study, the remaining lifetime probability of a major osteoporotic fracture (forearm, hip, spine, humerus) at the age of 50 years was 46.4% in women and 22.4% in men [6].

Fractures are associated with high morbidity and mortality (~50% of fracture-related deaths were due to hip fractures), significant disability, increased dependency, reduced quality of life, and increased healthcare costs [3]. In the European Union the economic cost of fractures in 2010 was estimated at €37 billion and is expected to increase by 25% in 2025 [2]. Fractures accounted for 1,180,000 quality-adjusted life years lost in 2010 [2]. In 2017 in 4 largest European Union countries, the United Kingdom, and Sweden new fragility fractures were associated with a loss of 1.0 million quality-adjusted life years and annual cost of €37.5 billion and a 27% increase is expected in 2030 [5]. One-year mortality after proximal humerus fracture was 16%, and after hip fracture 23.5%, with a higher rate in men (32%) [7].

Milk is a valuable source of bioavailable calcium (1.150 mg/L). In Western countries, milk and dairy products provide 50% to 65% of calcium intake, and only 9% to 14% of the total energy consumed [8]. European [9], American [10], and World Health Organization [11] dietary guidelines recommend consumption of 2 to 4 servings of milk and dairy products daily. The average intake of dairy products in most age groups is much below the recommended values [10]. In many individuals, low intake of milk and dairy is associated with lower intake of calcium and other nutrients [12].

The consumption of milk and milk products (especially low-fat) may reduce the risk of arterial hypertension, stroke, metabolic syndrome [13], type 2 diabetes mellitus [14], cardiovascular diseases [8], frailty, sarcopenia, cognitive decline in elderly people [15], and colorectal cancer [14], but on the other hand, elevated dairy consumption may increase the risk of cardiovascular diseases and prostate cancer [14]. High milk consumption was related to higher mortality in a study by Michaëlsson *et al.* [16], but in another study, no association was found between dairy product consumption and the risk of all-cause mortality [17].

Milk and dairy products may reduce the risk of osteoporosis and fractures [14, 18–22], but in individuals drinking higher quantities of milk, the risk of fractures may be elevated [16]. These conflicting results may be due to methodological bias and a large number of confounders [23]. The aim of this study was to investigate the relationship between cow milk consumption and fracture risk, excluding other dairy products.

## Methods

This study was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.

### *Search strategy*

The search was conducted on June 1, 2020 and included articles indexed in the PubMed and EMBASE databases. The search terms were (((milk[Title/Abstract]) OR milk[MeSH Terms]) NOT milk, human[MeSH Terms]) AND (((fractures, bone [MeSH Terms]) OR fracture[Title/Abstract]) OR fractures[Title/Abstract]) in the PubMed and (milk:ti,ab,kw OR 'milk'/exp) AND (fracture$:ti,ab,kw OR 'fracture'/exp) in the EMBASE. The references of selected articles were also reviewed. The titles and abstracts of the identified studies were screened by 2 investigators (PP and KW). Then, the full texts of the remaining articles were evaluated independently for inclusion according to the criteria listed below. A definite list of the included studies was determined by discussion and consensus between authors. Any disagreements were resolved by the third reviewer (GG).

### *Inclusion criteria*

Studies were included if they met the following criteria: (1) had an observational design — cohort, case-control, or cross-sectional; (2) were conducted on adults (≥18 years old); (3) investigated the relationship between milk intake and the risk of fractures; (4) reported odds ratios (ORs), relative risks (RRs), or hazard ratios (HRs) with 95% confidence intervals (CIs) for fractures; and (5) were published in English.

### *Exclusion criteria*

During screening of the initial results, some of the studies were excluded for the following reasons: (1) duplicates; (2) not original studies (reviews, systematic reviews, meta-analyses); (3) non-English publications; (4) pediatric population; (5) investigating dietary patterns; (6) investigating calcium intake; (7) assessment of osteoporosis rather than bone fractures as an outcome; (8) assessment of high-energy stress fractures only in a specific population or pathological fractures (cancer related); (9) milk intake included in dairy product intake and not presented separately; and (10) conference reports, letters, comments.

### *Search*

According to the search strategy described above, 1,165 articles were identified in both databases. Additionally, 8 publications were added from other sources. After removal of duplicates, titles and abstracts of 844 records were screened and a total of 34 studies were selected, based on the above inclusion and exclusion criteria, to be assessed for eligibility. 9 studies were excluded from further analysis due to the inclusion of only high-energy stress fractures in runners [24], an irrelevant comparison of dosage of exposure variable [25–30], an assessment of only childhood milk intake [31], and combined milk and vegetables intake [32]. Additionally, 5 studies were excluded in order to avoid double inclusion of data from the same or updated population [33–36]. Finally, 20 studies were included in the meta-analysis (Fig. 1).

### *Population*

Of the 20 included studies, 11 were cohort studies [16, 20–22, 37–43] and 9 were case-control studies [18, 19, 44–50]. Studies were published between 1994 and 2019. In total, 586,665 participants were studied, including 329,630 women and 179,324 men. 4 studies included 77,711 people without sex distinction [20, 41, 45, 50]. The sample size ranged from 498 [50] to 123,906 people [22]. Seven studies were conducted on women [18, 19, 37, 42, 47–49], 2 on men [44, 46], and 11 on both sexes [16, 20–22, 38–41, 43, 45, 50]. Patients over 18 years old were included in the meta-analysis, but most of them were over 50 years old. The duration of follow-up was between 3.8 [38] and 50 years [20]. 5 studies were conducted in the United States of America [18, 20, 22, 37, 45], 8 in Europe (Norway, Sweden, Portugal, Spain, France, Turkey, Greece, Italy, etc.) [16, 19, 21, 38, 40, 41, 44, 47], 5 in Asia (China [48], Taiwan [49], Japan [39, 43, 50]), and 2 in Australia [42, 46].

### *Assessment of milk intake*

During data extraction from the eligible studies, patient groups were selected based on the original classification according to milk intake applied by the authors as well as the RR values for every group.

The studies varied in terms of the method of obtaining data on milk intake, the measurement of milk intake, and the number of study groups. Although the difference

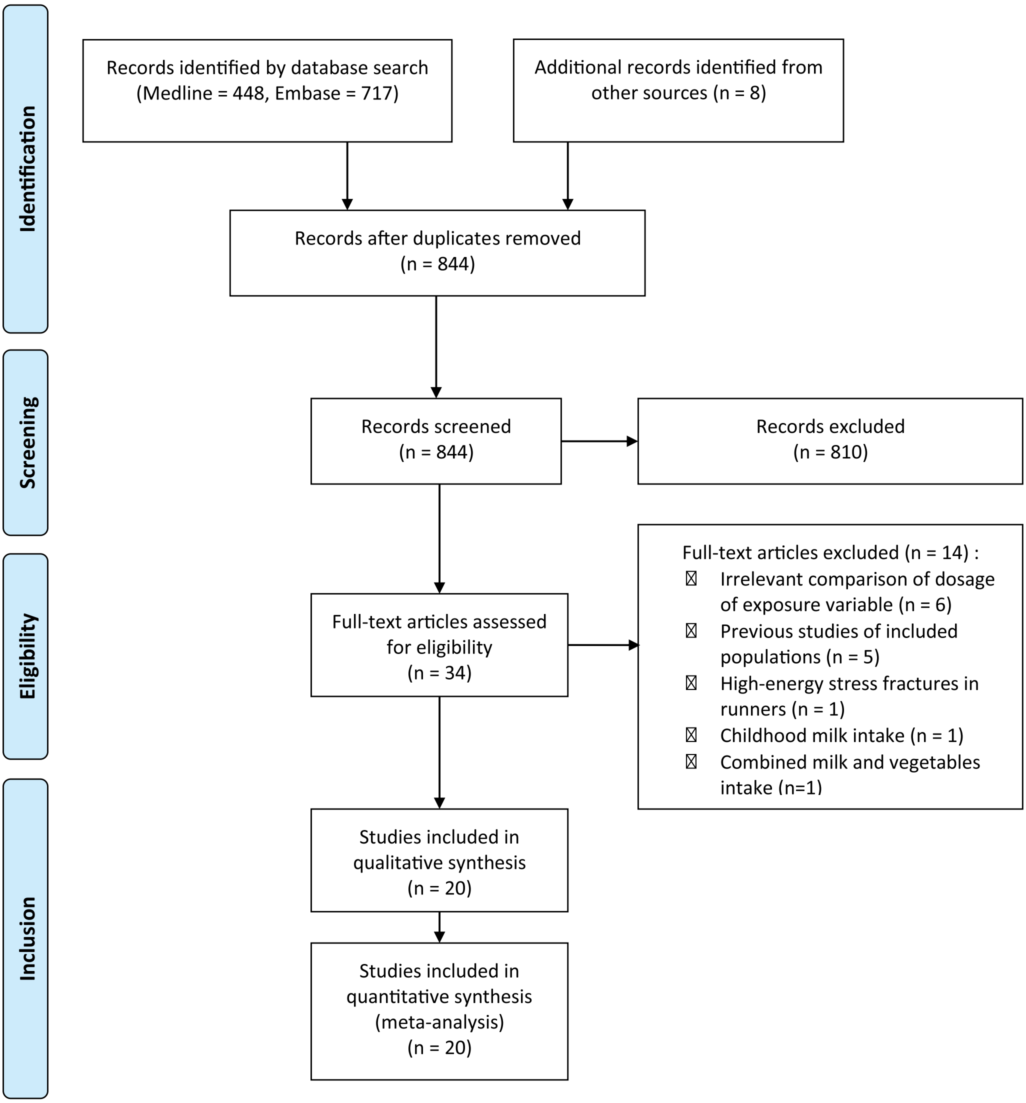


**Fig. 1.** The flow diagram of study selection.

in the method of data collection seemed to be insignificant (food frequency questionnaires (FFQ) vs. other surveys), the disparity in the method of milk intake measurement and the number of study groups was important. Therefore, all the extracted data were put in Table 1, which allowed us to choose the best comparison method: we compared the group with the highest milk intake (study group) with the one with the lowest milk intake (control group) in every study.

**Table 1.** Characteristics of included studies.

| Authors (year) | Setting | Gender | Age | | | Number of patients | Number of fractures | Duration follow-up, y | Exposure assessment | Outcome assessment | Outcome variable (fracture type) | Comparison | Assessment of quality (NOS) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Mean | Standard deviation | Range | | | | | | | | |
| COHORT STUDIES | | | | | | | | | | | | | |
| Aslam (2019) [42] | Geelong Osteoporosis Study (GOS) (Australia) | F | 70 | – | >50 | 833 | 206 | 10 | Questionnaire | Radiography | Hip, forearm, clinical spine | None<br><1 glass/d (refferent)<br>1–2 glass/d<br>>2 glass/d | 8 |
| Bergholdt (2018) [41] | CCHS study, CGPS study and GESUS study (Denmark) | F, M | 57 | 13.28 | ≥20 | 73.715 | 686 | 5.5 | Questionnaire | – | Hip | Any milk vs. no milk | 7 |
| Cumming (1997) [37] | Study of Osteoporotic Fractures, (USA) | F | 71.5 | – | >65 | 9.704 | 1.950 | 6.6 | FFQ | Radiography | Any nonvertebral | Never (refferent)<br><1 glass/d<br>1–2.5 glass/d<br>>3 glass/d | 7 |
| | | | | | | | 389 | | | | Vertebral | | |
| Feskanich (2018) [22] | Nurses' Health Study (NHS) of women, the Health Professionals Follow-up Study (HPFS) of men (USA) | M | 53.6 | – | 34–60 | 43.306 | 694 | 17.5 | FFQ | Self-reported and 30 confirmed by medical records | Hip | <1 glass/w (refferent)<br>1 glass/w<br>2–4 glass/w<br>5–6 glass/w<br>1 glass/d<br>≥2 glass/d | 6 |
| | | F | 57.7 | – | 50–57 | 80.600 | 2.138 | 20.8 | | | | | |

**Table 1.** cont.

| Authors (year) | Setting | Gender | Age | | | Number of patients | Number of fractures | Duration follow-up, y | Exposure assessment | Outcome assessment | Outcome variable (fracture type) | Comparison | Assesment of quality (NOS) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Mean | Standard deviation | Range | | | | | | | | |
| Fujiwara (1997) [39] | Adult Health Study (AHS) (Japan) | M | 58.2 | 13.2 | >32 | 1.586 | 6 | 14 | Questionnaire | Radiography | Hip | ≤1 glass/w (refferent)<br>2–4 glass/w<br>≥5 glass/w | 6 |
| | | F | 58.6 | 11.6 | | 2.987 | 49 | | | | | | |
| Holvik (2018) [40] | Norwegian Counties Study; Five Counties Study (Norway) | M | 50 | 4.8 | >50 | 17.175 | 603 | 19 | FFQ | Database analysis | Hip | <1 glass/d<br>1 glass/d (refferent)<br>2 glass/d<br>3 glass/d<br>≥4 glass/d | 8 |
| | | F | 50 | 4.7 | | 17.939 | 1262 | | | | | | |
| | | M | 66 | 8 | | 10.802 | 473 | 13 | | | | | |
| | | F | 67 | 8 | | 12.457 | 993 | | | | | | |
| Meyer (1997) [21] | Three Norwegian counties of Finnmark, Sogn og Fjordane, Oppland (Norway) | M | 47.1 | 4.5 | 35–49 | 19.752 | 56 | 4 | Questionnaire | Medical report | Hip | ≤1 glass/d (refferent)<br>2 glass/d<br>3 glass/d<br>≥4 glass/d | 7 |
| | | F | 47.1 | 4.6 | | 20.035 | 154 | | | | | | |
| Michaëlsson (2014) [16] | Swedish Mammography Cohort; Cohort of Swedish Men (Sweden) | M | – | – | 45–79 | 45.339 | 5.379 | 11.2 | FFQ | Hospital record | All fractures | <1 glass/d (refferent)<br>1–2 glass/d<br>2–3 glass/d<br>>3 glass/d | 8 |
| | | | | | | | 1.266 | | | | Hip | | |
| | | F | | | 39–74 | 61.433 | 17.252 | 20.1 | | | All fractures | | |
| | | | | | | | 4.259 | | | | Hip | | |

**Table 1.** cont.

| Authors (year) | Setting | Gender | Age | | | Number of patients | Number of fractures | Duration follow-up, y | Exposure assessment | Outcome assessment | Outcome variable (fracture type) | Comparison | Assessment of quality (NOS) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Mean | Standard deviation | Range | | | | | | | | |
| Nakumura (2009) [43] | Japan Public Health Centre-based Prospective Study (Japan) | F | 49.3 | 5.9 | 40–59 | 18.524 | 78 | 10 | FFQ | Self-reported | Vertebral | <1/w<br>1–2 times/w<br>2–4 times/w<br>5 times/w (refferent) | 6 |
| | | M | 49.2 | 6 | | 15.520 | 52 | | | | | | |
| | | F | 53.6 | 8.7 | 40–69 | 22.596 | 145 | | | | | Rarely<br>Occasionally<br>1–2 times/w<br>2–4 times/w<br>5 times/w (refferent) | |
| | | M | 53 | 8.6 | | 19.239 | 82 | | | | | | |
| Roy (2003) [38] | European Vertebral Osteoporosis Study (EPOS) | M | 63.1 | 7.8 | 50–79 | 3.173 | 48 | 3.8 | Questionnaire | Radiography | Vertebral | <1 glass/d (refferent)<br>≥1 glass/d | 7 |
| | | F | 62.2 | 7.6 | | 3.402 | 116 | | | | | | |
| Sahni (2014) [20] | Framingham Osteoporosis Study (USA) | F, M | 77 | 4.9 | 68–96 | 764 | 97 | 50 | FFQ | Hospital report | Hip | <1 glass/w (referent)<br>1–7 glass/w<br>>7 glass/w | 6 |

**Table 1.** cont.

| Authors (year) | Setting | Gender | Age | | | Number of patients | Number of fractures | Duration follow-up, y | Exposure assessment | Outcome assessment | Outcome variable (fracture type) | Comparison | Assesment of quality (NOS) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Mean | Standard deviation | Range | | | | | | | | |
| CASE-CONTROL STUDIES | | | | | | | | | | | | | |
| Holloway (2015) [46] | Geelong Osteoporosis Study Fracture Cohort (Australia) | M | – | – | >20 | 1.570 | 33 | – | Questionnaire | Radiography | All humeral | <1 cup/d (refferent)<br>>1 cup/d | 3 |
| | | | | | | | 23 | | | | Proximal humeral | | |
| Johnell (1995) [19] | The MEDOS Study (Portugal, Spain, France, Italy, Greece and Turkey) | F | 78.1 (case) 77.7 (control) | 9.4 (case) 8.8 (control) | >50 | 5.618 | 2.086 | – | Questionnaire | Medical report | Hip | Never (refferent)<br>Sometimes<br>1–2 glass/d<br>3–4 glass/d<br>>5 glass/d | 9 |
| Kalkwarf (2003) [18] | The third National Health and Nutrition Examination Survey (USA) | F | 35 (20–49) 69 (>50) | 8 (20–49) 11 (>50) | 20–49 >50 | 3.251: 1.371 (20–49), 1.880 (>50) | – | – | Questionnaire | Self-reported | Osteoporotic | <1 serving/w<br>1–6 servings/w<br>1 serving/d<br>>1 serving/d (refferent) | 3 |
| Kanis (1999) [44] | The MEDOS Study (Portugal, Spain, France, Italy, Greece and Turkey) | M | 73.9 (case) 74.1 (control) | 10.6 (case) 10.1 (control) | 50–98 (case) 50–100 (case) | 1.862 | 730 | – | Questionnaire | Medical report | Hip | Never (refferent)<br>Sometimes<br>1–2 glass/d<br>3–4 glass/d<br>>5 glass/d | 9 |

**Table 1.** cont.

| Authors (year) | Setting | Gender | Age | | | Number of patients | Number of fractures | Duration follow-up, y | Exposure assessment | Outcome assessment | Outcome variable (fracture type) | Comparison | Assesment of quality (NOS) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Mean | Standard deviation | Range | | | | | | | | |
| Lan (2010) [49] | Taiwan University Hospital (Taiwan) | F | 80.1 | 7.9 | >60 | 508 | 163 | – | Questionnaire | Medical report | Hip | <1 times/w (refferent)<br>1–5 times/w<br>>5 times/w | 8 |
| Slavens (2006) [45] | The Utah Study of Nutrition and Bone Health (USA) | F, M | 75 | 9.5 | 50–89 | 2.734 | 1.366 | – | FFQ | Hospital report | Hip | 0–1 cup/w (refferent)<br>2–7 cup/w<br>8–14 cup/w<br>>15 cup/w | 6 |
| Suzuki (1997) [50] | Six prefectures from western Japan | F, M | 78.6 (case)<br>78.3 (control) | 6.5 (case)<br>6.3 (control) | 65–89 | 498 | 249 | – | Questionnaire | Medical records | Hip | Never (refferent)<br>Sometimes<br>1 glass/d<br>>2 glass/d | 9 |
| Tavani (1994) [47] | Northern Italy | F | – | – | 45–74 | 960 | 241 | – | Questionnaire | Medical report | Hip | <7 glass/w (refferent)<br>7 glass/w<br>>7glass/w | 6 |
| Zhu (2018) [48] | China National Fracture Survey (CNFS) database (China) | F | – | – | Postmenopausal <70 | 68.783 | 309 | – | Questionnaire | Medical records | Low energy | Never (refferent)<br><1 glass/w<br>1–6 glass/w<br>>1 glass/d | 7 |

Abbreviations: d — day; F — female; FFQ — food frequency questionnaires; M — male; w — week.

Importantly, in some studies, milk was one of the numerous compared variables (such as cheese, yogurt, total dairy products), and only the data regarding milk intake were included in our meta-analysis.

In the original studies, data regarding milk intake were obtained by the FFQ [16, 20, 22, 37, 40, 43, 45] or other questionnaires [18, 19, 21, 38, 39, 41, 42, 44, 46–50]. The most common criterion for milk intake assessment was the number of milk glasses per day [16, 18, 19, 21, 37, 38, 40, 42, 44, 46, 48, 50], followed by the number of milk glasses per week [18, 20, 22, 39, 43, 45, 47–49], and other criteria [41].

### *Assessment of fractures*

The data regarding the number and type of fractures were obtained from the original studies. The method of fractures reporting differed between the studies, the most common being medical documentation [16, 19–21, 40, 44, 45, 47–50], radiological verification [37–39, 42, 46], and patient questionnaire/self-reporting [22, 43]. Depending on the study, data on fractures were validated in different ways (ranging from highly reliable radiological verification, through data obtained from medical history, to the least reliable method of self-reporting by patients with a random verification). Radiological verification was most often used in cohort studies (when the fracture occurred during the study), and the other 2 methods were used mainly in retrospective (case-control) studies, as per methodology. The studies differed also in the classification of fractures (most often general fractures, but some studies differentiated by bone type). Data regarding the fracture verification method as well as the number and location of fractures were put in Table 1, which enabled a precise analysis. In the meta-analysis, we included all osteoporotic fractures without breakdown into bone types but with differentiation between sexes.

## Statistical analysis

Our meta-analysis was performed with Review Manager 5.3 and Jamovi 0.9.5.12. From each study, we extracted RRs or ORs with 95% CIs associated with the highest, as compared with the lowest, dosage of milk. Due to study heterogeneity, for our calculations, we used a random-effects model applying restricted maximum likelihood estimates. Odds ratios and 95% CIs were used.

Statistical heterogeneity was defined as a p value of 0.05 or lower, assessed with the Q, $I^2$, and Tau tests. Statistical significance was defined as a p value of 0.05 or lower. Publication bias was assessed graphically using funnel plots.

## Ethics

The study does not need approval of an institutional review board or an ethics committee, and the patients' written informed consent to participate in the study was not required.

## Results

In a meta-regression analysis of the 20 included studies, higher milk intake was not associated with a reduced risk of total fractures in both sexes (OR 0.95, 95% CI: 0.84–1.08), either in cohort (OR 0.91; 95% CI: 0.79–1.05) or case-control studies (OR 1.09; 95% CI: 0.82–1.44) (Fig. 2), as well as separately in men (OR 0.87; 95% CI: 0.71–1.07) (Fig. 3) and women (OR 0.95; 95% CI: 0.80–1.13) (Fig. 4).

| Cohort Studies | | Gender | OR | 95%CI | Weight |
|---|---|---|---|---|---|
| Aslam (osteoporotic) [42] | 2019 | F | 1.15 | 0.75-1.76 | 4.39% |
| Bergholdt (hip) [41] | 2018 | F+M | 0.93 | 0.80-1.09 | 6.46% |
| Cumming (nonvertebral) [37] | 1997 | F | 1.00 | 0.82-1.22 | 6.14% |
| Cumming (vertebral) [37] | 1997 | F | 1.40 | 0.83-2.37 | 3.65% |
| Feskanich (hip) [22] | 2018 | F | 0.77 | 0.64-0.93 | 6.21% |
| Feskanich (hip) [22] | 2018 | M | 0.77 | 0.57-1.04 | 5.41% |
| Fujiwara (hip) [39] | 1997 | F | 0.58 | 0.28-1.21 | 2.51% |
| Fujiwara (hip) [39] | 1997 | M | 0.54 | 0.26-1.12 | 2.56% |
| Holvik (hip) a [40] | 2019 | F | 1.14 | 0.88-1.47 | 5.73% |
| Holvik (hip) b [40] | 2019 | F | 1.72 | 1.23-2.40 | 5.10% |
| Holvik (hip) a [40] | 2019 | M | 0.71 | 0.49-1.02 | 4.84% |
| Holvik (hip) b [40] | 2019 | M | 0.99 | 0.63-1.55 | 4.21% |
| Meyer (hip) [21] | 1997 | F | 0.83 | 0.44-1.56 | 3.02% |
| Meyer (hip) [21] | 1997 | M | 0.46 | 0.22-0.97 | 2.47% |
| Michaëlsson (hip) [16] | 2014 | F | 1.60 | 1.39-1.84 | 6.54% |
| Michaëlsson (hip) [16] | 2014 | M | 1.01 | 0.85-1.20 | 6.35% |
| Nakamura (vertebral) a [43] | 2009 | F | 0.56 | 0.31-1.01 | 3.29% |
| Nakamura (vertebral) b [43] | 2009 | F | 0.60 | 0.38-0.94 | 4.21% |
| Nakamura (vertebral) a [43] | 2009 | M | 1.51 | 0.69-3.32 | 2.30% |
| Nakamura (vertebral) b [43] | 2009 | M | 0.62 | 0.33-1.16 | 3.07% |
| Roy (vertebral) [38] | 2003 | F | 1.04 | 0.72-1.51 | 4.78% |
| Roy (vertebral) [38] | 2003 | M | 0.74 | 0.44-1.25 | 3.66% |
| Sahni (hip) [28] | 2013 | F+M | 0.58 | 0.31-1.07 | 3.12% |
| Overall for cohort studies | | | 0.91 | 0.79-1.05 | 100.00% |
| **Case-control Studies** | | **Gender** | **OR** | **95%CI** | **Weight** |
| Holloway (humeral) [46] | 2015 | M | 2.84 | 1.38-5.84 | 7.77% |
| Johnell (hip) [19] | 1995 | F | 0.77 | 0.66-0.89 | 15.07% |
| Kalkwarf (osteoporotic) [18] | 2003 | F | 0.77 | 0.45-1.32 | 9.96% |
| Kanis (hip) [44] | 1999 | M | 0.94 | 0.57-1.56 | 10.44% |
| Lan (hip) [49] | 2010 | F | 0.58 | 0.37-0.91 | 11.24% |
| Slavens (hip) [45] | 2006 | F+M | 1.12 | 0.91-1.38 | 14.49% |
| Suzuki (hip) [50] | 1997 | F+M | 1.86 | 0.84-4.13 | 6.97% |
| Tavani (hip) [47] | 1995 | F | 1.00 | 0.61-1.63 | 10.67% |
| Zhu (osteoporotic) [48] | 2018 | F | 1.79 | 1.33-2.41 | 13.39% |
| Overall for case-control studies | | | 1.09 | 0.82-1.44 | 100.00% |
| **Total for cohort and case-control studies** | | | **0.95** | **0.84-1.08** | **100.00%** |

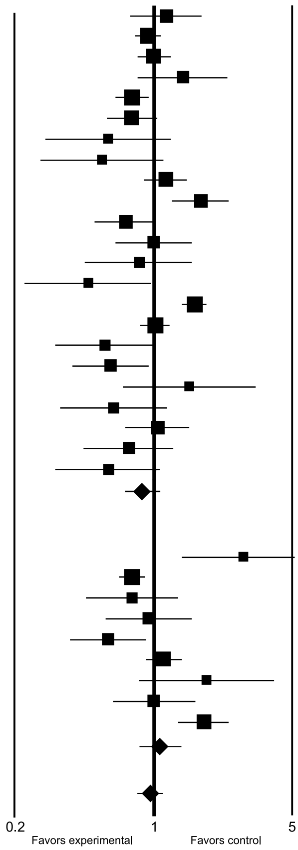


**Fig. 2.** Association between milk consumption and fracture risk in cohort and case-control studies.

| Studies | | OR | 95%CI | Weight |
|---|---|---|---|---|
| Feskanich (hip) [22] | 2018 | 0.77 | 0.57-1.04 | 13.78% |
| Fujiwara (hip) [39] | 1997 | 0.54 | 0.26-1.12 | 5.78% |
| Holloway (humeral) [46] | 2015 | 2.84 | 1.38-5.84 | 5.85% |
| Holvik (hip) a [40] | 2019 | 0.71 | 0.49-1.02 | 12.03% |
| Holvik (hip) b [40] | 2019 | 0.99 | 0.63-1.55 | 10.20% |
| Kanis (hip) [44] | 1999 | 0.94 | 0.57-1.56 | 9.01% |
| Meyer (hip) [21] | 1997 | 0.46 | 0.22-0.97 | 5.56% |
| Michaëlsson (hip) [16] | 2014 | 1.01 | 0.85-1.20 | 16.88% |
| Nakamura (vertebral) a [43] | 2009 | 1.51 | 0.69-3.32 | 5.16% |
| Nakamura (vertebral) b [43] | 2009 | 0.62 | 0.33-1.16 | 7.08% |
| Roy (vertebral) [38] | 2003 | 0.74 | 0.44-1.25 | 8.65% |
| **Overall (random-effects model)** | | **0.87** | **0.71-1.07** | **100.00%** |

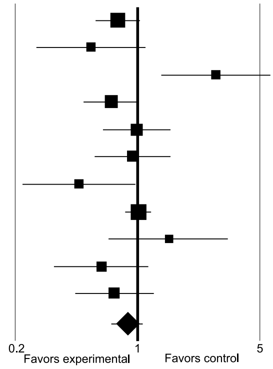


**Fig. 3.** Association between milk consumption and fracture risk in men.

| Studies | | OR | 95%CI | Weight |
|---|---|---|---|---|
| Aslam (osteoporotic) [42] | 2019 | 1.15 | 0.75-1.76 | 5.71% |
| Cumming (nonvertebral) [37] | 1997 | 1.00 | 0.82-1.22 | 7.28% |
| Cumming (vertebral) [37] | 1997 | 1.40 | 0.83-2.37 | 4.94% |
| Feskanich (hip) [22] | 2018 | 0.77 | 0.64-0.93 | 7.34% |
| Fujiwara (hip) [39] | 1997 | 0.58 | 0.28-1.21 | 3.63% |
| Holvik (hip) a [40] | 2019 | 1.14 | 0.88-1.47 | 6.94% |
| Holvik (hip) b [40] | 2019 | 1.72 | 1.23-2.40 | 6.38% |
| Johnell (hip) [19] | 1995 | 0.77 | 0.66-0.89 | 7.57% |
| Kalkwarf (osteoporotic) [18] | 2003 | 0.77 | 0.45-1.32 | 4.84% |
| Lan (hip) [49] | 2010 | 0.58 | 0.37-0.91 | 5.51% |
| Meyer (hip) [21] | 1997 | 0.83 | 0.44-1.56 | 4.24% |
| Michaëlsson (hip) [16] | 2014 | 1.60 | 1.39-1.84 | 7.61% |
| Nakamura (vertebral) a [43] | 2009 | 0.56 | 0.31-1.01 | 4.54% |
| Nakamura (vertebral) b [43] | 2009 | 0.60 | 0.38-0.94 | 5.53% |
| Roy (vertebral) [38] | 2003 | 1.04 | 0.72-1.51 | 6.08% |
| Tavani (hip) [47] | 1994 | 1.00 | 0.61-1.63 | 5.21% |
| Zhu (osteoporotic) [48] | 2018 | 1.79 | 1.33-2.41 | 6.65% |
| **Overall (random-effects model)** | | **0.95** | **0.80-1.13** | **100.00%** |

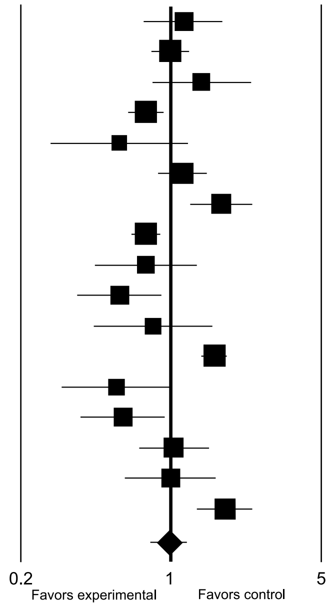


**Fig. 4.** Association between milk consumption and fracture risk in women.

The heterogeneity assessed with the $I^2$ test was extreme for cohort studies ($I^2$ = 77.01%), case-control studies ($I^2$ = 81.88%) and for both types of studies ($I^2$ = 77.98%). For men heterogeneity was large ($I^2$ =56.37%), but it was extreme for women ($I^2$ = 84.81%). To compare the results, we used the following scale: $I^2$ = 0%–25%, no heterogeneity; $I^2$ = 25%–50%, moderate heterogeneity; $I^2$ = 50%–75%, large heterogeneity; and $I^2$ = 75%–100%, extreme heterogeneity.

## Discussion

Epidemiological studies, particularly retrospective ones, can be biased by data collection. In some studies, a relatively high percentage of missing data leads to the exclusion of participants from the final analysis. The risk of recall bias was high in a few studies because of long follow-up, old age of participants, and an increasing risk of mental impairment with data provided by proxies.

In observational studies some residual confounders are not considered or may remain unadjusted due to the lack of information. In most of the included studies age, sex, BMI, smoking, and alcohol consumption were considered, but there was no information on important confounders as glucocorticoids use, diabetes mellitus, history of osteoporosis, vitamin D and hormones levels, frailty and falls.

Imprecise estimation of FFQs data is related to memory and sincerity – unhealthy foods are underreported, but foods perceived as healthy tend to be overreported. Some FFQs included limited food items and were not validated for milk. There was no specification of analyzed milk (raw, pasteurized, skim or whole, lactose free, vitamin D and calcium fortified, etc.). This meta-analysis did not compare the same doses of milk but categories of the highest vs. lowest intake that differed between the included studies. Although a positive effect of milk on fracture risk is mostly observed in calcium-deficient populations, the intake of other dairy products and the amount of calcium in the diet were not assessed in many of the included studies and therefore were not analyzed in this meta-analysis.

The method of fracture reporting differed between the studies, which might have affected the results, particularly regarding the risk of vertebral fractures, as they often are asymptomatic.

Largest included studies were conducted in Scandinavia and the United States of America, countries of relatively high milk consumption and risk of osteoporotic fractures.

## Conclusions

The results of our meta-analysis indicate that there is no association between milk intake and the risk of fractures. Increased milk consumption should not be recommended for fracture prevention.

## Summary

Osteoporosis is the main cause of bone fractures. Milk is a good source of calcium and vitamin D which are commonly believed to be beneficial for bone health, but available data on the relation between milk intake and fracture risk are contradictory. This large

meta-analysis includes over half a million patients and investigates influence of milk consumption on fracture risk in adults. The results show that higher milk intake is not associated with fracture risk reduction. We conclude that higher milk consumption should not be recommended for fracture prevention.

## Contribution statement

G.G. was responsible for the study concept and design, and supervised the study, K.W. and P.P. designed and conducted the literature search, S.G. and T.G. assessed risk of bias and quality of includes studies, S.G. and T.G. were responsible for extraction and acquisition of data, S.S. and P.K. conducted the statistical analysis and designed the graphs, G.G. supervised literature search, data extraction, interpreted the data analysis, and drafted the manuscript, K.W. undertook the critical revision of the manuscript for important intellectual content, all authors provided critical conceptual input and revised the manuscript.

## Conflict of interest

None declared.

## References

1. International Osteoporosis Foundation. Osteoporosis: Epidemiology. Available from: https://www.iofbonehealth.org/epidemiology [19.08.2020].
2. *Hernlund E., Svedbom A., Ivergård M., et al.*: Osteoporosis in the European Union: Medical management, epidemiology and economic burden: A report prepared in collaboration with the International Osteoporosis Foundation (IOF) and the European Federation of Pharmaceutical Industry Associations (EFPIA). Arch Osteoporos. 2013; 8: 136.
3. *Johnell O., Kanis J.A.*: An estimate of the worldwide prevalence and disability associated with osteoporotic fractures. Osteoporos Int. 2006; 17 (12): 1726–1733.
4. International Osteoporosis Foundation. The Middle East & Africa Regional Audit. Epidemiology, costs & burden of osteoporosis in 2011. Available from: https://www.iofbonehealth.org/sites/default/files/PDFs/Audit%20Middle%20East_Africa/Middle_East_Africa_audit.pdf [19.08.2020].
5. *Borgström F., Karlsson L., Ortsäter G., et al.*: Fragility fractures in Europe: burden, management and opportunities. Arch Osteoporos. 2020; 15 (1).
6. *Kanis J.A., Johnell O., Oden A., et al.*: Long-term risk of osteoporotic fracture in Malmo. Osteoporos Int. 2000; 11 (8): 669–674.
7. *Yombi J.C., Putineanu D.C., Cornu O., et al.*: Low haemoglobin at admission is associated with mortality after hip fractures in elderly patients. Bone Joint J. 2019; 101-B (9): 1122–1128.
8. *Yu E., Hu F.B.*: Dairy Products, Dairy Fatty Acids, and the Prevention of Cardiometabolic Disease: a Review of Recent Evidence. Curr Atheroscler Rep. 2018; 20 (5): 24.
9. European Food Safety Authority. Dietary reference values for nutrients. Summary report. Available from: https://efsa.onlinelibrary.wiley.com/doi/pdf/10.2903/sp.efsa.2017.e15121 [19.08.2020].

10. US Department of Health and Human Services and US Department of Agriculture. Dietary guidelines for Americans 2015–2020. Available from: https://health.gov/sites/default/files/2019-09/2015-2020_Dietary_Guidelines.pdf [19.08.2020].
11. World Health Organization. Diet, nutrition and the prevention of chronic diseases: report of a joint WHO/FAO expert consultation. Available from: https://apps.who.int/iris/bitstream/handle/10665/42665/WHO_TRS_916.pdf;jsessionid=7CD4E0398ED9BD7910817EDE575CC10B?sequence=1 [19.08.2020].
12. *Olza J., Aranceta-Bartrina J., González-Gross M., et al.*: Reported dietary intake, disparity between the reported consumption and the level needed for adequacy and food sources of calcium, phosphorus, magnesium and vitamin D in the Spanish population: Findings from the ANIBES study. Nutrients. 2017; 9 (2): 168.
13. *Drouin-Chartier J.-P., Brassard D., Tessier-Grenier M., et al.*: Systematic Review of the Association between Dairy Product Consumption and Risk of Cardiovascular-Related Clinical Outcomes. Adv Nutr An Int Rev J. 2016; 7 (6): 1026–1040.
14. Food and Agriculture Organization of the United Nations. Milk and dairy products in human. Available from: http://www.fao.org/3/i3396e/i3396e.pdf [19.08.2020].
15. *Cuesta-Triana F., Verdejo-Bravo C., Fernández-Pérez C., Martín-Sánchez F.J.*: Effect of Milk and Other Dairy Products on the Risk of Frailty, Sarcopenia, and Cognitive Performance Decline in the Elderly: A Systematic Review. Adv Nutr. 2018; 10 (2): S105–119.
16. *Michaëlsson K., Wolk A., Langenskiöld S., et al.*: Milk intake and risk of mortality and fractures in women and men: cohort studies. BMJ. 2014; 349: g6015.
17. *Cavero-Redondo I., Alvarez-Bueno C., Sotos-Prieto M., et al.*: Milk and Dairy Product Consumption and Risk of Mortality: An Overview of Systematic Reviews and Meta-Analyses. Adv Nutr. 2018; 10 (2): S97–104.
18. *Kalkwarf H.J., Khoury J.C., Lanphear B.P.*: Milk intake during childhood and adolescence, adult bone density, and osteoporotic fractures in US women. Am J Clin Nutr. 2003; 77 (1): 257–265.
19. *Johnell O., Gullberg B., Kanis J.A., et al.*: Risk factors for hip fracture in European women: The MEDOS study. J Bone Miner Res. 1995; 10 (11): 1802–1815.
20. *Sahni S., Mangano K.M., Tucker K.L., et al.*: Protective Association of Milk Intake on the Risk of Hip Fracture Results from the Framingham Original Cohort. J Bone Miner Res. 2017; 29 (8): 1–10.
21. *Meyer H.E., Pedersen J.I., Loken E.B., Tverdal A.*: Dietary Factors and the Incidence of Hip Fracture in Middle-aged Norwegians: A Prospective Study. Am J Epidemiol. 1997; 145 (2): 117–123.
22. *Feskanich D., Meyer H.E., Fung T.T., et al.*: Milk and other dairy foods and risk of hip fracture in men and women. Osteoporos Int. 2018; 29 (2): 385–396.
23. *Fardellone P., Séjourné A., Blain H., et al.*: Osteoporosis: Is milk a kindness or a curse? Jt Bone Spine. 2017; 84 (3): 275–281.
24. *Nieves J.W., Melsop K., Curtis M., et al.*: Nutritional Factors That Influence Change in Bone Density and Stress Fracture Risk Among Young Female Cross-Country Runners. PM R. 2010; 2 (8): 740–750.
25. *Jha R.M., Mithal A., Malhotra N., et al.*: Pilot case-control investigation of risk factors for hip fractures in the urban Indian population. BMC Musculoskelet Disord. 2010; 11: 49.
26. *Bergholdt H.K.M., Larsen M.K., Varbo A., et al.*: Lactase persistence, milk intake, hip fracture and bone mineral density: a study of 97 811 Danish individuals and a meta-analysis. J Intern Med. 2018; 284 (3): 254–269.
27. *Benetou V., Orfanos P., Pettersson-Kymmer U., et al.*: Mediterranean diet and incidence of hip fractures in a European cohort. Osteoporos Int. 2013; 24 (5): 1587–1598.
28. *Sahni S., Tucker K.L., Kiel D.P., et al.*: Milk intake is associated with lower risk of hip fracture in older men & women: The framingham original cohort. FASEB J. 2013; 27.
29. *Wyshak G., Frisch R.E.*: Carbonated beverages, dietary calcium, the dietary calcium/phosphorus ratio, and bone fractures in girls and boys. J Adolesc Heal. 1994; 15 (3): 210–215.
30. *Feart C., Lorrain S., Ginder Coupez V., et al.*: Adherence to a Mediterranean diet and risk of fractures in French older persons. Osteoporos Int. 2013; 24 (12): 3031–3041.

31. *Sanchez-Santos M.T., Davey T., Leyland K.M., et al.*: Development of a prediction model for stress fracture during an intensive physical training program: The royal marines commandos. Orthop J Sport Med. 2017; 5 (7): 1–12.
32. *Michaëlsson K., Wolk A., Lemming E.W., et al.*: Intake of Milk or Fermented Milk Combined With Fruit and Vegetable Consumption in Relation to Hip Fracture Rates: A Cohort Study of Swedish Women. J Bone Miner Res. 2018; 33 (3): 449–457.
33. *Owusu W., Willett W.C., Feskanich D., et al.*: Calcium intake and the incidence of forearm and hip fractures among men. J Nutr. 1997; 127 (9): 1782–1787.
34. *Michaëlsson K., Melhus H., Bellocco R., Wolk A.*: Dietary calcium and vitamin D intake in relation to osteoporotic fracture risk. Bone. 2003; 32 (6): 694–703.
35. *Feskanich D., Willett W.C., Stampfer M.J., Colditz G.A.*: Milk, Dietary Calcium, and Bone Fractures in Women: A 12-Year Prospective Study. Am J Public Health. 1997; 87 (6): 992–997.
36. *Feskanich D., Willett W.C., Colditz G.A.*: Calcium, vitamin D, milk consumption, and hip fractures: A prospective study among postmenopausal women. Am J Clin Nutr. 2003; 77 (2): 504–511.
37. *Cumming R.G., Cummings S.R., Nevitt M.C., et al.*: Calcium Intake and Fracture Risk: Results from the Study of Osteoporotic Fractures. Am J Epidemiol. 1997; 145 (10): 926–934.
38. *Roy D.K.K., O'Neill T.W.T.W., Finn J.D.D., et al.*: Determinants of incident vertebral fracture in men and women: Results from the European Prospective Osteoporosis Study (EPOS). Osteoporos Int. 2003; 14 (1): 19–26.
39. *Fujiwara S., Kasagi F., Yamada M., Kodama K.*: Risk Factors for Hip Fracture in a Japanese Cohort. J Bone Miner Res. 1997; 12 (7): 998–1004.
40. *Holvik K., Meyer H.E., Laake I., et al.*: Milk drinking and risk of hip fracture: The Norwegian Epidemiologic Osteoporosis Studies (NOREPOS). Br J Nutr. 2019; 121 (6): 709–718.
41. *Bergholdt H.K.M., Larsen M.K., Varbo A., et al.*: Lactase persistence, milk intake, hip fracture and bone mineral density: a study of 97 811 Danish individuals and a meta-analysis. J Intern Med. 2018; 284 (3): 254–269.
42. *Aslam H., Holloway-Kew K., Mohebbi M., et al.*: Association between dairy intake and fracture in an Australian-based cohort of women: A prospective study. BMJ Open. 2019; 9 (11): e031594.
43. *Nakamura K., Kurahashi N., Ishihara J., et al.*: Calcium intake and the 10-year incidence of self-reported vertebral fractures in women and men: The Japan Public Health Centre-based Prospective Study. Br J Nutr. 2009; 101 (2): 285–294.
44. *Kanis J., Johnell O., Gullberg B., et al.*: Risk factors for hip fracture in men from southern Europe: The MEDOS study. Osteoporos Int. 1999; 9 (1): 45–54.
45. *Slavens M.J.*: Milk Intake in Early and Late Adulthood and Risk of Osteoporotic Hip Fractures in Utah [thesis]. Utah State University. 2006.
46. *Holloway K.L., Bucki-Smith G., Morse A.G., et al.*: Humeral Fractures in South-Eastern Australia: Epidemiology and Risk Factors. Calcif Tissue Int. 2015; 97 (5): 453–465.
47. *Tavani A., Negri E., La Vecchia C.*: Calcium, dairy products, and the risk of hip fracture in women in northern Italy. Epidemiology. 1995; 6 (5): 554–557.
48. *Zhu Y., Liu S., Chen W., et al.*: Epidemiology of low-energy fracture in Chinese postmenopausal women: changing trend of incidence since menopause and associated risk factors, a national population-based survey. Menopause. 2018; 26 (3): 286–292.
49. *Lan T.-Y., Hou S.-M., Chen C.-Y., et al.*: Risk factors for hip fracture in older adults: a case-control study in Taiwan. Osteoporos Int. 2010; 21 (5): 773–784.
50. *Suzuki T., Yoshida H., Hashimoto T., et al.*: Case-control study of risk factors for hip fractures in the Japanese elderly by a Mediterranean Osteoporosis Study (MEDOS) questionnaire. Bone. 1997; 21 (5): 461–467.