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Impact Of Body Mass Index on Osteoporosis Risk Factors: A Meta-Analysis

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ABSTRACT

Objectives: This meta-analysis aimed to evaluate the association between body mass index (BMI) and the risk of osteoporosis.

Methods: Domestic and international databases were systematically searched for case-control studies published between January 1, 1990, and December 31, 2022, using medical subject headings (MeSH) and relevant keywords. Statistical analyses were conducted with Review Manager 5.3. A fixed-effects model was applied when heterogeneity was low ($I^2 < 50\%$), and a random-effects model was used when heterogeneity was high ($I^2 > 50\%$).

Results: A total of 18 case-control studies comprising 9,078 participants were included. Pooled analysis revealed that low BMI is a significant risk factor for osteoporosis in individuals with type 2 diabetes and for primary osteoporosis. High BMI was identified as a risk factor for osteoporosis among postmenopausal women. In addition, BMI was a risk factor for osteoporosis in patients with frequent glucocorticoid use or chronic obstructive pulmonary disease (COPD). However, no clear association was established between BMI and primary osteoporosis at normal or high levels, nor between BMI and osteoporosis risk in stroke patients.

Conclusions: This meta-analysis demonstrates that low BMI increases the risk of osteoporosis in patients with type 2 diabetes and those with primary osteoporosis, while high BMI contributes to osteoporosis risk among postmenopausal women. Furthermore, BMI is a risk factor in patients with frequent glucocorticoid use or COPD. These findings provide important theoretical evidence to support the prevention and management of osteoporosis in clinical practice.

INTRODUCTION

Osteoporosis (OP) is a metabolic bone disease characterized by reduced bone mass, increased bone fragility, and a higher risk of fractures. (2001). It is particularly common among the elderly and represents a major public health concern. Globally, more than 9 million osteoporotic fractures occur annually, with hip fractures carrying especially serious consequences-the one-year mortality rate after such fractures is approximately 23%. For this reason, osteoporosis is often referred to as a "silent killer."

In some regions of China, the detection rate of OP reaches 294–589 per 10,000 individuals. Elderly patients with OP are more likely to suffer fractures following minor falls, and the annual fracture incidence in China is estimated to be around 9.6% Majumdar SR et al. (2018). These fractures frequently necessitate hospitalization, surgical intervention, and prolonged bed rest, placing a substantial burden on patients, families, and healthcare systems Wang et al. (2018).

With changes in lifestyle and an aging population, the prevalence of OP continues to rise. Importantly, early-stage osteoporosis is typically asymptomatic and thus easily overlooked. By the time patients present with pain or fractures caused by bone fragility, the disease has usually progressed to a severe stage Zeng Q et al. (2019)-Tebé C et al. (2019). Consequently, early prevention and timely management of osteoporosis have become critical priorities in reducing its clinical and societal impact.

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Osteoporosis can be classified into primary and secondary forms. Primary osteoporosis mainly includes postmenopausal osteoporosis and osteoporosis in elderly men, while secondary osteoporosis arises from other underlying conditions such as type 2 diabetes, COPD, stroke, or spinal cord injury. Clinical evidence indicates that factors such as aging, excessive alcohol consumption, smoking, menopause, and a family history of osteoporosis increase the risk of developing the disease. Conversely, regular physical activity, daily sun exposure, and adequate milk intake serve as protective factors.

The relationship between body mass index (BMI) and osteoporosis, however, remains controversial. Some studies suggest that a higher BMI may protect against osteoporosis in elderly Chinese men, while others report no significant association between BMI and osteoporosis risk. To address these conflicting findings and provide useful insights for osteoporosis prevention, the present study conducted a comprehensive meta-analysis of relevant domestic and international literature to clarify the correlation between BMI and osteoporosis.

MATERIALS AND METHODS

This meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Page et al. 2021). The study protocol was prospectively registered in the International Prospective Register of Systematic Reviews (PROSPERO).

Data Sources and Search Strategy

We systematically searched PubMed, Web of Science, Springer Link, China National Knowledge Infrastructure (CNKI), China Biomedical Literature Database (CBM), Wan fang, and VIP databases for relevant cohort studies published from database inception to December 31, 2022.

The search strategy combined Me SH terms and keywords. For English databases, the terms included "BMI", "osteoporosis" or "bone loss", and "risk factors", "association factor", "dangerous factors", or "related factors" combined with "case-control trial". Additionally, references from published meta-analyses were reviewed to identify further eligible studies. The literature screening process is illustrated in Figure 1.

Eligibility Criteria

Studies were included if they met the following criteria:

Design: Case-control studies.

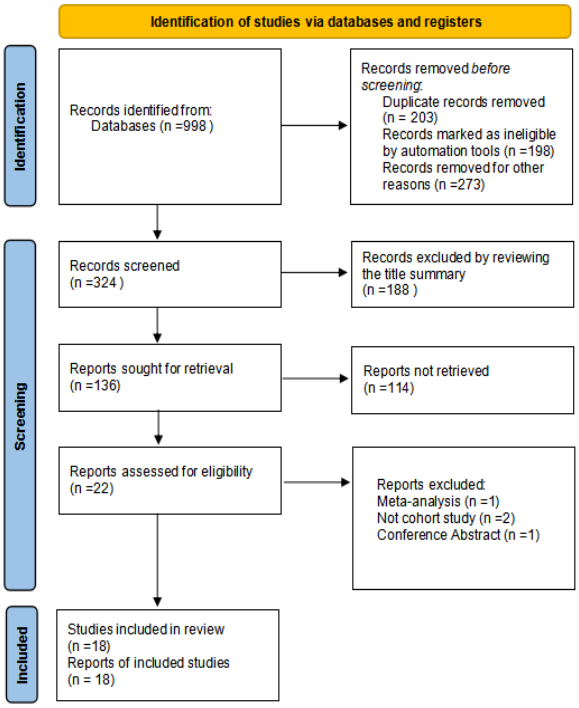
Population: Cases were patients diagnosed with osteoporosis in medical institutions; controls were individuals from the same region or hospital, admitted during the same period, and with comparable conditions.

Publication period: January 1, 1990, to December 31, 2022.

Exposure and outcome: Studies investigating risk factors including BMI.

Data availability: Reported or convertible to odds ratio (OR), 95% confidence interval (CI), and standard error (SE).

Figure 1: Study Screening Process



Exclusion criteria:

- Duplicate publications.
- Non-English or non-chinese articles.
- Studies from the same region and year.
- Studies lacking a control group, with incomplete data, or high loss to follow-up.
- Review articles.
- Studies with definitions of risk factors inconsistent with standard or widely accepted criteria.

Study Selection

Two reviewers independently screened the titles and abstracts to remove duplicates and irrelevant studies. Full texts of potentially eligible studies were then assessed against inclusion criteria. Discrepancies were resolved through discussion with a third reviewer.

Data Extraction

Data extraction was carried out independently by the

same two reviewers using a predefined form, collecting: author, country, year of publication, study design, number of cases and controls, type of osteoporosis, BMI classification, ORs, 95% CIs, and SEs. Disagreements were resolved by consensus with the third reviewer.

Quality Assessment

The Newcastle-Ottawa Scale (NOS) was applied to evaluate study quality. Case-control studies were rated on three domains: selection (up to 4 stars), comparability (up to 2 stars), and exposure/outcome assessment (up to 3 stars), with a maximum of 9 stars. Studies scoring 0–3, 4–6, and 7–9 were categorized as low, moderate, and high quality, respectively.

Statistical Analysis

The association between BMI and osteoporosis was analysed using adjusted ORs with 95% CIs and SEs. Heterogeneity was assessed using the χ^2 test and the I^2 statistic. If $P > 0.1$ and $I^2 \leq 50\%$, a fixed-effects model was used; otherwise, a random-effects model was applied. Sensitivity analyses were performed by excluding one study at a time to test the robustness of pooled results. All analyses were conducted using Review Manager 5.3.

Literature Search

A systematic search of case-control studies published between January 1, 1990, and December 31, 2022, initially identified 998 articles. Following title and abstract screening, 18 studies were deemed potentially relevant. After full-text review, 18 studies were included in the final analysis (Zou Dong Mei et al., 2020; Jin Yong et al., 2016; Xiu Shuang Ling et al., 2020; Ceng Feng et al., 2022; Zhao Ying et al., 2018; Zhu Bing et al., 2005; Gu Qiao Ping et al., 2020; Zhao Yu et al., 2022; Wen Hai Zhao et al., 2022; Xiong Jian et al., 2016; Can-Chen Ma et al., 2017; Yu Mor et al., 2020; Chun-Wei Lin et al., 2015; Lidwien Graat-Verboom et al., 2012; Wang Kai et al., 2020; Li Hui Lan et al., 2008; Cao Ying et al., 2014; T. Suzuki et al., 1997). The study selection process is illustrated in Figure 1.

Study Characteristics

This meta-analysis incorporated 18 case-control studies comprising 9,078 participants published between 1990 and 2022. All studies applied clear diagnostic criteria to distinguish primary osteoporosis (older men and postmenopausal women) from secondary osteoporosis. Odds ratios (OR), 95% confidence intervals (CI), and standard errors (SE) for the association between body mass index (BMI) and osteoporosis were extracted. Two studies assessed BMI by category (Lidwien Graat-Verboom et al., 2012; Cao Ying et al., 2014). Key study characteristics are summarized in Figure 2.

Figure 2: Basic characteristics of the included studies

Author	Country	Publi	Research des	Number of cases	Types of OP	Number of controls	BMI gradation	OR	95%CI	SE	NOSscore
Zoudongmei	China	2020	case control	Type2 diabetesOP 46 cases	Type2 diabetesOP	Type2 diabetes no OP45cases	BMI descend	2.025	1.214~3.694	0.2611	7
Jinyong	China	2016	case control	Type2 diabetesOP133 cases	Type2 diabetesOP	Type2 diabetes no OP133cases	low BMI	2.232	1.323~3.698	0.2668	8
XiuShuangLing	China	2020	case control	Type2 diabetesOP 97 cases	Type2 diabetesOP	Type2 diabetes no OP204cases	low BMI	0.84	0.76~0.91	0.0511	8
Zengfeng	China	2022	case control	Type2 diabetesOP 40 cases	Type2 diabetesOP	Type2 diabetes no OP30cases	low BMI	1.902	1.0389~2.2075	0.076	7
Zhaoying	China	2018	case control	Type2 diabetesOP100 cases	Type2 diabetesOP	Type2 diabetes no OP130cases	low BMI	0.86	1.001~1.139	0.033	7
Zhubing	China	2005	case control	postamenopausal OP101cases	postamenopausal OP	no OP normal women102cases	>25kg/m2	0.53	0.318~0.882	0.2606	9
Guqiaoping	China	2020	case control	postamenopausal OP535cases	postamenopausal OP	normalandreducedBMIafteramenopausal1027cases	high BMI	0.421	0.1819~0.9422	0.4282	8
Zhaoyu	China	2022	case control	postamenopausal OP96cases	postamenopausal OP	postamenopausal no OP105cases	>25kg/m2	2.252	1.198~5.316	0.322	7
Wenhaizhao	China	2022	case control	osteoporosis998cases	osteoporosis	no OP1632cases	low BMI	1.225	0.4085~3.7523	0.597	8
XiongJian	China	2016	case control	osteoporosis120cases	osteoporosis	no OP120cases	low BMI	0.5152	0.303~0.876	0.2708	8
Can-chen Ma	U.S.A	2017	case control	OPcaused byGC 481cases	OPcaused byGC	not usingGC309cases	no	0.86	0.814~0.908	0.028	8
Yu Mor	Japan	2020	case control	OPcaused byGC 225 cases	OPcaused byGC	postamenopausal OP72cases	low BMI	0.844	0.736~0.968	0.0699	8
Chun-Wei Lin	Taiwan	2015	case control	COPDosteoporosis90cases	COPDosteoporosis	COPD no osteoporosis75cases	NO	0.824	0.727~0.933	0.0639	9
Lidwien Graat	U.S.A	2012	case control	COPDosteoporosis49cases	COPDosteoporosis	COPD no osteoporosis49cases	>25 ~ 30 kg/m2	0.277	0.096~0.806	0.5407	7
							>30 kg/m2	0.113	0.039~0.413	0.6721	
Wangkai	China	2020	case control	stroke osteoporosis192cases	stroke osteoporosis	stroke no osteoporosis49cases	lowBMI<18.5kg/m2	2.427	1.579~3.342	0.2191	8
Lihuilan	China	2008	case control	stroke osteoporosis96cases	stroke osteoporosis	stroke no osteoporosis310cases	low BMI	0.75	0.66~0.84	0.0652	8
Caoying	China	2014	case control	elderlyosteoporosis97cases	elderlyosteoporosis	reduced bonemass22cases normal32cases	≤18.5	2.214	0.4563~9.7949	0.7832	7
							18.5~24.0	1.018	0.4459~2.3247	0.4213	
							24.0~28.0	0.897	0.4077~1.9735	0.4023	
T. suzuki	Japan	1997	case control	elderlyosteoporosis249cases	elderlymaleosteoporosi	reduced bonemass200cases normal398cases	18.5~20.7	0.39	0.21	0.3158	9
							20.8~23.0	0.46	0.25~0.84	0.3111	
							23.1 Or more	0.18	0.09 0.35	0.3537	

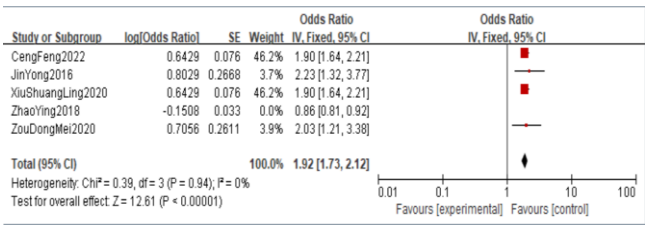
Quality Assessment

Based on the Newcastle–Ottawa Scale (NOS), the average score across all included studies was 7.8. Each study scored ≥7, indicating high methodological quality. Detailed scores are presented in Figure 2.

BMI and Risk of Osteoporosis in Patients with Type 2 Diabetes

Five studies (Zou Dong Mei et al., 2020; Jin Yong et al., 2016; Xiu Shuang Ling et al., 2020; Ceng Feng et al., 2022; Zhao Ying et al., 2018) examined the relationship between BMI and osteoporosis in patients with type 2 diabetes mellitus. Considerable heterogeneity was observed ($I^2 = 98\%$). Sensitivity analysis using stepwise exclusion revealed that removal of Zhao Ying et al. (2018) reduced heterogeneity ($I^2 = 0\%$). The pooled analysis of the remaining four studies demonstrated that low BMI significantly increased the risk of osteoporosis in patients with type 2 diabetes (OR = 1.92; 95% CI: 1.73–2.21; $P < 0.00001$; Figure 3). In contrast, Zhao Ying et al. (2018) reported an OR of 0.85 ($P = 0.045$), suggesting a potential protective role of low BMI.

Figure 3: Meta-analysis of BMI and risk factors for osteoporosis

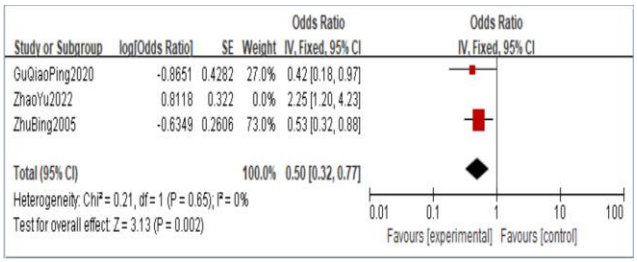


BMI and Risk of Postmenopausal Osteoporosis

Three studies (Zhu Bing et al., 2005; Gu Qiao Ping et al., 2020; Zhao Yu et al., 2022) explored the association between BMI and postmenopausal osteoporosis. Substantial heterogeneity was detected ($I^2 = 87\%$). Excluding Zhao Yu et al. (2022) reduced heterogeneity to 0%. The pooled results of the remaining two studies indicated that higher BMI was associated with a lower risk of postmenopausal osteoporosis (OR = 0.50; 95% CI: 0.32–0.77; P = 0.002; Figure 4). However, Zhao Yu

et al. (2022) reported an opposite association (OR = 2.25; P = 0.0431), suggesting that higher BMI might increase the risk of osteoporosis in this population.

Figure 4: Meta-analysis of BMI and risk factors for postmenopausal osteoporosis in women



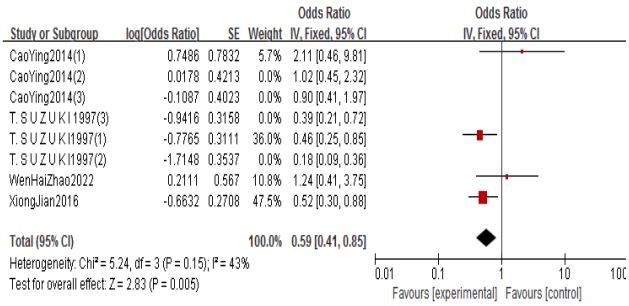
BMI and Risk Factors for Primary Osteoporosis

Four case-control studies (Xiong Jian et al., 2016; Wen Hai Zhao et al., 2022; Cao Ying et al., 2014; Suzuki et al., 1997) investigated the association between BMI and the risk of primary osteoporosis, contributing data from a total of eight datasets. The pooled meta-analysis indicated substantial heterogeneity (I^2 = 65%), prompting a subgroup analysis based on BMI categories (low, normal, high).

- Low BMI: Analysis of four studies (Xiong Jian et al., 2016; Wen Hai Zhao et al., 2022; Cao Ying et al., 2014; Suzuki et al., 1997) showed a significant association between low BMI and increased risk of primary osteoporosis (OR = 0.59, 95% CI: 0.41–0.85; I^2 = 43%; P = 0.005).
- Normal BMI: Two studies (Cao Ying et al., 2014; Suzuki et al., 1997) demonstrated high heterogeneity (I^2 = 90%). Individual analyses revealed inconsistent findings: Cao Ying et al. (2014) reported no association (OR = 1.018, P = 0.9664), while Suzuki et al. (1997) found that normal BMI was protective (OR = 0.46, P < 0.05).
- High BMI: Two studies (Cao Ying et al., 2014; Suzuki et al., 1997) also showed considerable heterogeneity (I^2 = 62%). Cao Ying et al. (2014) reported no significant association (OR = 0.897, P = 0.7874), whereas Suzuki et al. (1997) suggested high BMI was protective against osteoporosis (OR = 0.18, P < 0.001).

Overall, the results indicate that low BMI is consistently associated with a higher risk of primary osteoporosis, while findings for normal and high BMI remain inconclusive.

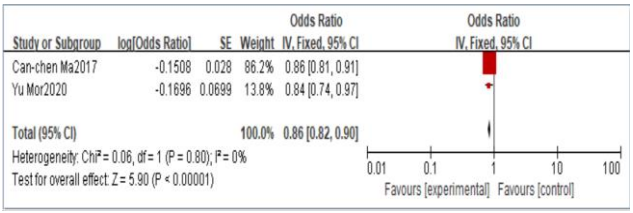
Figure 5: Meta-analysis of low BMI and risk factors for primary osteoporosis



BMI and Risk Factors for Glucocorticoid-Induced Osteoporosis

Two case-control studies (Can-Chen Ma et al., 2017; Yu Mor et al., 2020) assessed the role of BMI in glucocorticoid-induced osteoporosis. Meta-analysis demonstrated a significant association (OR = 0.86, 95% CI: 0.82–0.90; I^2 = 0%; P < 0.00001), indicating that BMI is a protective factor in patients receiving long-term glucocorticoid therapy (Figure 6).

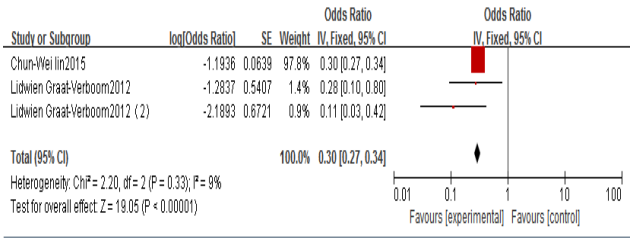
Figure 6: Meta-analysis of BMI and risk factors for glucocorticoid-induced osteoporosis



BMI and Risk Factors for COPD with Osteoporosis

Two studies (Chun-Wei Lin et al., 2015; Lidwien Graat-Verboom et al., 2012), providing three datasets, evaluated the relationship between BMI and osteoporosis in COPD patients. Pooled results showed a strong association (OR = 0.30, 95% CI: 0.27–0.34; I^2 = 9%; P < 0.00001), indicating that BMI is an important protective factor against osteoporosis in COPD patients.

Figure 7: Meta-analysis of BMI and risk factors for COPD combined with osteoporosis



BMI and Risk Factors for Stroke with Osteoporosis

Two case-control studies (Wang Kai et al., 2020; Li Hui Lan et al., 2008) investigated the link between BMI and osteoporosis among stroke patients. The meta-analysis revealed extreme heterogeneity ($I^2 = 96\%$), preventing a firm conclusion. Individual studies, however, suggested an association: Wang Kai et al. (2020) reported low BMI as a risk factor (OR = 2.427, P = 0.043), while Li Hui Lan et al. (2008) also found low BMI associated with higher risk (OR = 0.75, $P < 0.01$).

Publication Bias

As the number of included studies in each subgroup was fewer than seven, publication bias could not be formally assessed.

DISCUSSION

Main Findings

Previous meta-analyses conducted both in China and internationally have examined the link between BMI and osteoporosis risk. Liu X et al. (2023) reported that low BMI is a risk factor for osteoporosis in patients with type 2 diabetes, aligning with the present study. A plausible explanation is that individuals with low BMI exert reduced mechanical load on their bones, which may enhance bone resorption and promote osteoporosis development Liang M et al (2006) Additionally, obesity may have protective effects on bone density through hormonal mechanisms, including the peripheral conversion of testosterone to oestradiol and androstenedione to estrone in adipose tissue, which stimulates osteoblast activity via insulin-like growth factor-1.

Grattan C et al (2004) confirmed that BMI is a protective factor against postmenopausal osteoporosis. However, that study did not differentiate BMI categories. Our analysis demonstrated that high BMI increases the risk of postmenopausal osteoporosis, suggesting that while an appropriate BMI supports bone health Peker N et al (2018) excessive fat mass may disrupt bone cell function through inflammatory mediators, contributing to bone loss Cacciatore S et al (2023).

Regarding primary osteoporosis, previous studies have shown mixed results. Xia Xia-Mei et al. found BMI to be protective in elderly men, whereas Wang Yu-He et al. reported no association. The inconsistency may be due to varying BMI classifications and failure to account for different BMI categories. Our analysis indicates that low BMI increases the risk of primary osteoporosis, while associations with normal and high BMI remain uncertain. Mechanistically, BMI reflects nutritional status and correlates positively with bone mineral density (BMD). Lower body weight reduces skeletal loading, leading to decreased bone mineralization and persistent low BMD, thereby predisposing to osteoporosis.

For comorbid conditions, Zhang N et al (2022) reported that BMI is a risk factor for COPD-related osteoporosis, consistent with our findings. Low BMI in COPD patients may result from abnormal bone metabolism associated with elevated TNF-α, cytokines, and oxidative stress Remels AH et al (2013) However, the precise mechanisms underlying the BMI–osteoporosis relationship in COPD require further investigation Okazaki R et al (2016).

In contrast, evidence regarding stroke patients remains scarce, with no prior studies confirming BMI as a determinant of stroke-related osteoporosis. Our results, showing high heterogeneity and inconsistent findings, do not yet support a definitive association.

LIMITATIONS

The results of this meta-analysis should be interpreted with caution. Several limitations must be acknowledged

1. BMI categorization: Many included studies did not clearly distinguish between BMI categories, potentially obscuring the differential effects of low versus high BMI.

2. Inconsistent BMI criteria: Even when BMI categories were reported, the definitions of “low,” “normal,” and “high” BMI varied across studies, limiting comparability.

3. Limited literature: The number of studies available for some subgroups was small, and high heterogeneity prevented firm conclusions regarding normal and high BMI in primary osteoporosis and BMI in stroke-related osteoporosis.

Future research should focus on collecting larger, high-quality datasets with standardized BMI classifications. Such studies would help clarify the specific roles of low, normal, and high BMI in the development of osteoporosis, thereby offering stronger theoretical support for clinical prevention strategies.

CONCLUSIONS

This meta-analysis demonstrates that

- Low BMI is a risk factor for osteoporosis in type 2 diabetes and primary osteoporosis.

- High BMI is a risk factor for osteoporosis in postmenopausal women.
- BMI is a risk factor for osteoporosis in patients with chronic glucocorticoid use or COPD.

However, no definitive association was established between normal or high BMI and primary osteoporosis, or between BMI and osteoporosis in stroke patients. Further well-designed studies are needed to validate these findings. The results of this analysis may provide valuable guidance for early identification of at-risk populations and for the development of targeted strategies to prevent osteoporosis.

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