

Preplanned Studies

Trends in Low Bone Density-Related Fall Burden and Mendelian Randomization Evidence on Waist Circumference and Bone Density — China, 1990–2023

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Summary

What is already known about this topic?

Low bone mineral density increases fall risk in older adults; however, the age-specific effects of abdominal obesity remain unclear.

What is added by this report?

In China, from 1990 to 2023, deaths due to low bone density-related falls and disability-adjusted life-years increased by 3.66-fold and 3.01-fold, respectively. Mendelian randomization analysis suggested an inverse association between genetically predicted waist circumference and bone density in the 30–44- and ≥ 60 -year groups.

What are the implications for public health practice?

Age- and sex-specific bone health screenings and weight-related metabolic management may help reduce the low bone density-related fall burden.

ABSTRACT

Introduction: Low bone density (LBD)-related falls impose a growing public health burden in China; however, the age-specific impact of abdominal obesity on bone density remains unclear.

Methods: Using data from the Global Burden of Disease 2023, we analyzed trends in mortality and disability-adjusted life-years (DALYs) due to LBD-related falls in China (1990–2023). Joinpoint regression assessed temporal trends and age-stratified two-sample Mendelian randomization (MR) examined the association between genetically predicted waist circumference and bone density.

Results: From 1990 to 2023, deaths increased 3.66-fold, and DALYs increased 3.01-fold. When age standardized, mortality increased slightly and DALY rates increased. In 2023, the burden was concentrated in adults ≥ 60 years old. MR showed that genetically predicted waist circumference was inversely associated

with bone density in the 30–44-year [$\beta = -0.24$, 95% confidence interval (CI): -0.39 , -0.07 , $P = 0.004$] and ≥ 60 -year groups ($\beta = -0.24$, 95% CI: -0.37 , -0.12 , $P < 0.001$).

Conclusion: LBD-related falls impose an increasing burden on older adults in China. This growing burden highlights the need for age- and sex-specific preventive measures. MR findings based on European genome-wide association study data suggested an inverse association between genetically predicted waist circumference and total-body bone density, which requires validation in Chinese populations.

Falls are the second leading cause of unintentional injury-related death worldwide (1–2). In 2021, the Global Burden of Disease (GBD) reported 555,539 fall-related deaths and 16,952,767 disability-adjusted life-years (DALYs) among adults aged 65 years and older worldwide (2). In China, nearly 40 million older adults experience falls annually, with the direct medical costs exceeding 5 billion Chinese Yuan (3).

Low bone mineral density (LBMD) increases the risk of fracture, disability, and premature death after a fall. In China, osteoporosis affects 32.0% of adults aged 65 years and older, while LBMD affects 46.4% of adults aged 50 years and older (4). Previous studies have described the burden of LBMD-related falls using GBD data; however, evidence on the upstream risk factors remains limited. Existing research on adiposity and bone health has mainly focused on the body mass index (BMI), whereas Mendelian randomization (MR) evidence specifically concerning waist circumference remains scarce.

Using GBD 2023 data, this study examined trends in mortality and DALYs due to LBMD-related falls in China from 1990 to 2023 and evaluated the association between genetically predicted waist circumference and bone density using age-stratified

two-sample MR. By combining GBD burden estimates with MR evidence on waist circumference and bone density, this study provides complementary evidence for bone health promotion. GBD analysis quantified the LBMD-related fall burden in China, whereas MR analysis examined bone density rather than falls, mortality, or DALYs.

Using GBD 2023 data, descriptive analyses by age and sex were conducted and Joinpoint regression was used to calculate the average annual percentage change (AAPC) in mortality and DALYs. The Joinpoint Regression Program (version 4.9.0.0; National Cancer Institute, Bethesda, MD, USA) was used to analyze trends in mortality and DALYs from 1990 to 2023, with $P < 0.05$ considered statistically significant. All analyses and visualizations were performed using R software (version 4.5.0; R Foundation for Statistical Computing, Vienna, Austria).

Waist circumference genome-wide association study (GWAS) data were obtained from the Genetic Investigation of Anthropometric Traits (GIANT) Consortium ($n=231,353$) (5). Total-body bone mineral density data were derived from a meta-analysis of 30 GWASs ($n=53,116$) and stratified by age (30–44, 45–59, and ≥ 60 years old) (6). Detailed information on the included studies and consortia is provided in [Supplementary Table S1](#) (available at <https://weekly.chinacdc.cn/>).

Independent single nucleotide polymorphisms (SNPs) associated with waist circumference at genome-wide significance ($P < 5 \times 10^{-8}$, $r^2 < 0.001$) were selected as instrumental variables. All selected SNPs had F-statistics > 10 . Palindromic and ambiguous SNPs were excluded from the analysis.

Two-sample MR analysis was performed using the inverse variance weighted (IVW) method as the primary approach, with MR-Egger, weighted median, and MR-PRESSO as sensitivity analyses to assess pleiotropy. Heterogeneity was evaluated using Cochran's Q test, and a leave-one-out analysis was conducted to assess the influence of individual SNPs (7).

From 1990 to 2023, LBMD-related fall deaths increased from 15,045 to 55,055 (3.66-fold) and DALYs increased from 1,454,283 to 4,379,665 (3.01-fold). During the same period, the age-standardized mortality rate (ASMR) increased slightly from 2.88 to 2.92 per 100,000 people, whereas the age-standardized DALY rate (ASDR) increased from 185.9 to 206.38 per 100,000 people. In 2023, 93.2% of all deaths occurred in individuals aged ≥ 60 years. Females had more deaths (29,747 *vs.* 25,308), more DALYs (2,407,591 *vs.* 1,972,074), and a higher ASDR (215.71 *vs.* 195.2 per 100,000) than males, although the increase in burden over time was greater in males (Table 1).

In 2023, the burden of LBMD-related falls was concentrated in older adults, particularly those aged ≥ 60 years (Figure 1). Age-specific mortality and DALY rates increased with age and reached their highest levels in the 95-and-above age group. In contrast, the absolute number of deaths peaked in the 85–89 age group, whereas DALYs were highest in the 70–74 age group.

From 1990 to 2023, the ASMR showed a non-significant increase [AAPC=0.08%, 95% confidence interval (CI): -0.16, 0.32], whereas the ASDR increased significantly (AAPC=0.94%, 95% CI: 0.63,

TABLE 1. Deaths, DALYs, and mortality and DALY rates of falls attributable to low bone density in 1990 and 2023, by sex and age group.

Characteristic	1990				2023			
	Deaths	ASMR (per 100,000)	DALYs	ASDR (per 100,000)	Deaths	ASMR (per 100,000)	DALYs	ASDR (per 100,000)
Total and sex-specific estimates (age-standardized rates)								
Male	6,374	2.64	631,296	163.43	25,308	3.05	1,972,074	195.2
Female	8,671	2.97	822,987	203.51	29,747	2.78	2,407,591	215.71
Age-group estimates (age-specific rates)								
30–44	384	0.57	119,250	177.22	383	0.42	166,887	182.1
45–59	1,900	3.61	452,895	964.99	3,381	2.98	1,135,910	1,001.04
≥ 60	12,761	446.1	882,138	5,659.73	51,291	811.47	3,076,868	9,444.32
Total	15,045	2.88	1,454,283	185.9	55,055	2.92	4,379,665	206.38

Note: All rates in the total and sex rows are age-standardized per 100,000 individuals. The rates in the age group rows are age specific. Abbreviation: ASMR=age-standardized mortality rate; ASDR=age-standardized DALY rate; DALYs=disability-adjusted life years.

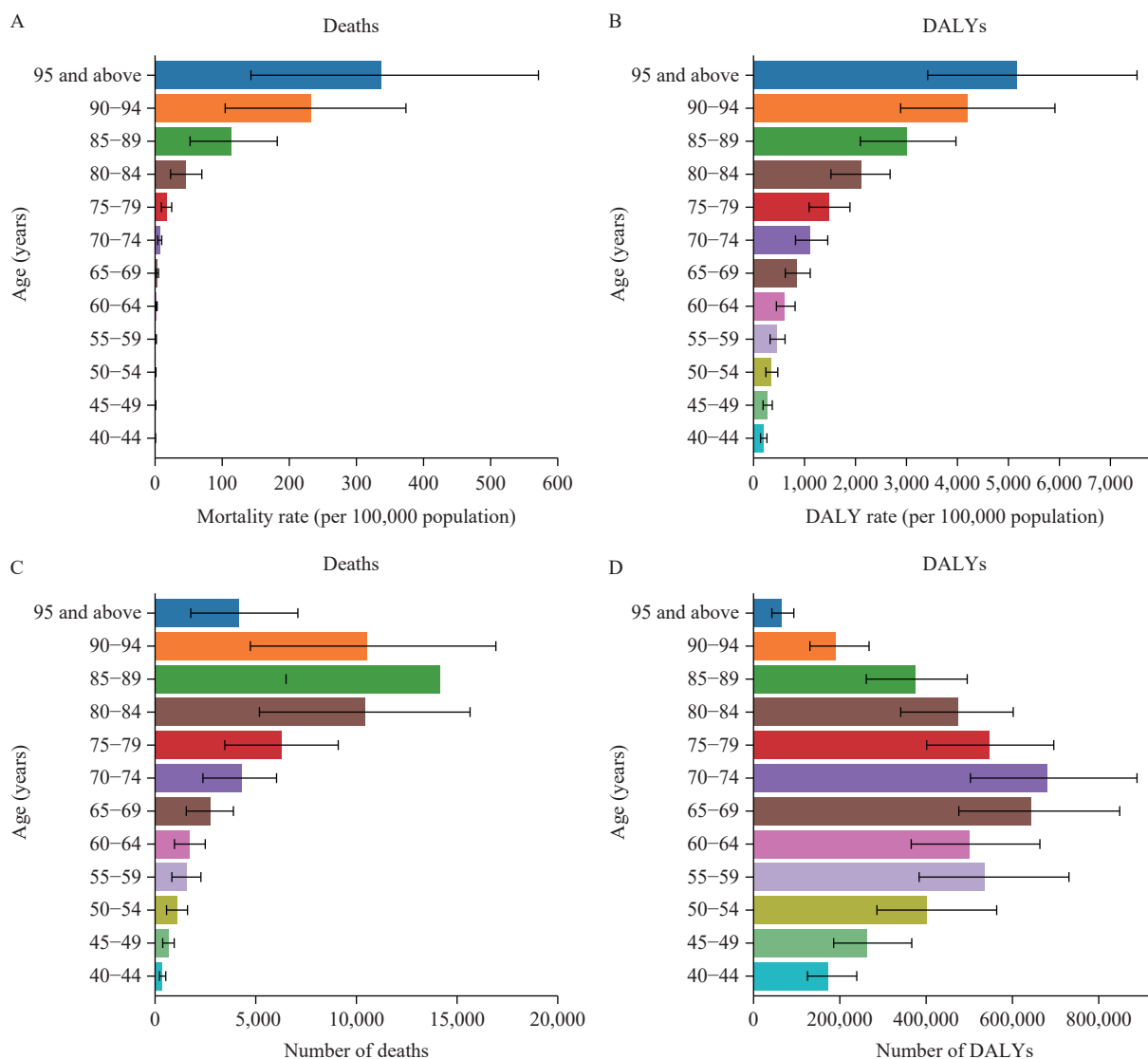


FIGURE 1. Age-specific mortality, DALYs, and corresponding rates of falls attributable to low bone density in 2023. (A) Age-specific mortality rate (per 100,000 population); (B) age-specific DALYs (per 100,000 population); (C) number of deaths; (D) number of DALYs.

Note: Bars represent estimates and error bars indicate 95% uncertainty intervals.

Abbreviation: DALYs=disability-adjusted life years.

1.25). Figure 2 shows that mortality rates declined during 2004–2014 in the 30–44-year group and during 2004–2013 in the 45–59-year group, whereas DALY rates fluctuated over time; in contrast, both mortality and DALY rates in the ≥ 60 -year group showed an overall upward trend.

After LD clumping, proxy SNP identification, and confounder screening using the PhenoScanner database, 63 SNPs were retained as instrumental variables for waist circumference, all with F-statistics >10 . Using IVW as the primary analysis, genetically predicted waist circumference was inversely associated with total-body bone mineral density in the 30–44-

year group ($\beta = -0.24$, 95% CI: -0.39 , -0.07 , $P = 0.004$) and the ≥ 60 -year group ($\beta = -0.24$, 95% CI: -0.37 , -0.12 , $P < 0.001$), but not in the 45–59-year group ($\beta = -0.04$, 95% CI: -0.20 , 0.11 , $P = 0.618$). The results of the MR-Egger, weighted median, simple mode, and weighted mode analyses were generally consistent with the IVW estimates (Supplementary Figure S1, available at <https://weekly.chinacdc.cn/>). Although no clear directional pleiotropy or single-SNP influence was detected, heterogeneity was observed in the 45–59 and ≥ 60 -year groups; therefore, the MR findings should be interpreted with caution (Supplementary Table S2, available at <https://weekly.chinacdc.cn/>).

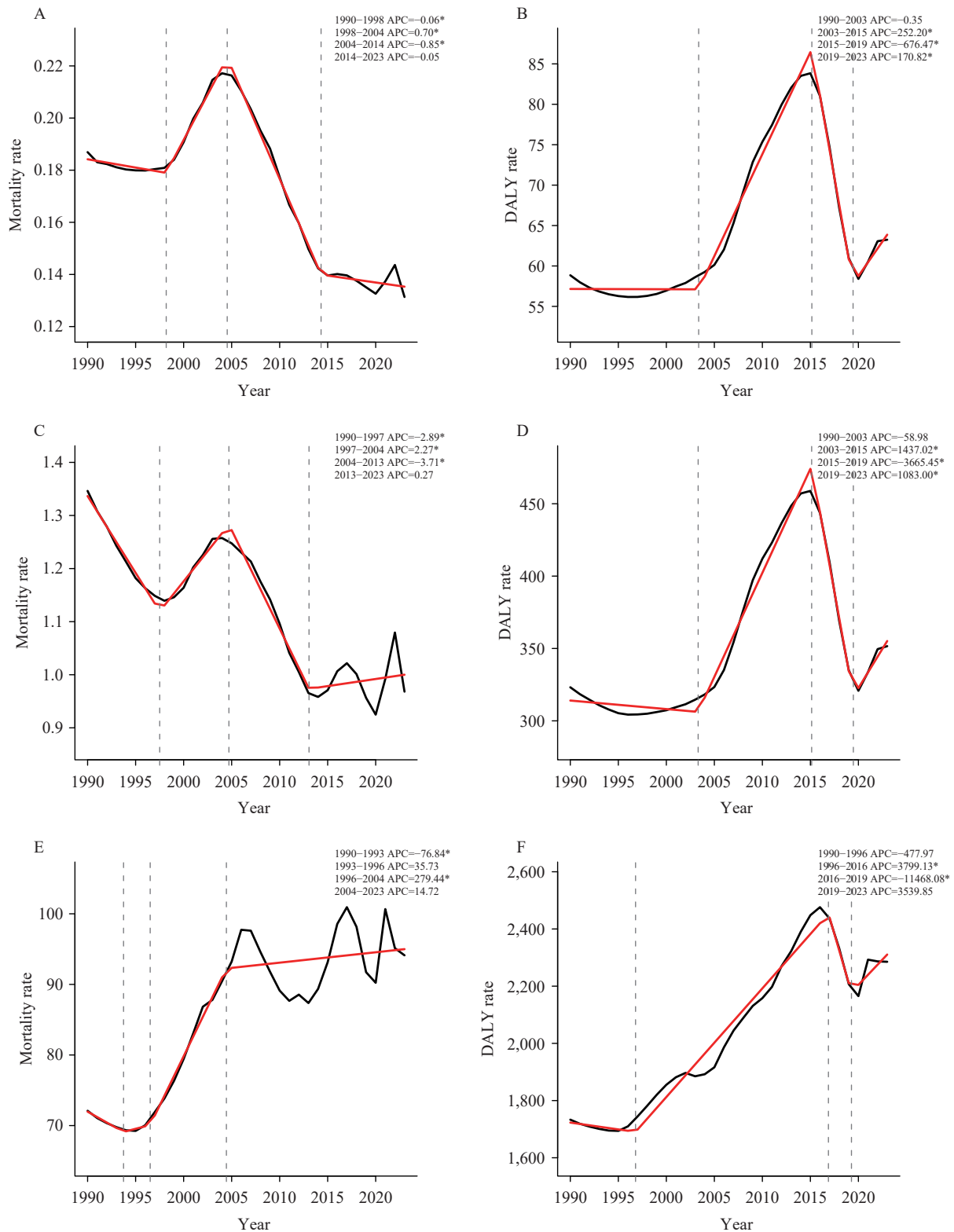


FIGURE 2. Joinpoint regression analysis of age-specific mortality and DALY rates of falls attributable to low bone density, 1990–2023. (A–B) Mortality rate and DALY rate trends in the 30–44-year age group; (C–D) mortality rate and DALY rate trends in the 45–59-year age group; and (E–F) mortality rate and DALY rate trends in the ≥60-year age group.

Note: Black lines indicate observed rates, red lines indicate fitted trends, and dashed vertical lines indicate joinpoints.

Abbreviation: DALYs=disability-adjusted life years.

* APC was significantly different from zero at alpha=0.05. Final selected model: 3 Joinpoints.

DISCUSSION

From 1990 to 2023, the burden of LBMD-related falls in China increased substantially, with deaths rising 3.66-fold and DALYs rising 3.01-fold. This burden was concentrated on older adults, particularly those aged ≥ 60 years, highlighting the growing public health impact of LBMD-related falls in the context of population aging. Although women bore a higher absolute burden in 2023, men showed a greater increase over time, highlighting sex-specific differences in bone health and fall-related burdens.

The higher burden in women may partly reflect postmenopausal bone loss and a higher prevalence of osteoporosis in older women (8), whereas the more rapid increase in men may reflect the under-recognition of osteoporosis and insufficient bone health screening in men (9). These findings suggest that prevention strategies should address not only the high burden among older women but also the growing burden among men.

Beyond descriptive burden analysis, this study used age-stratified MR to explore waist circumference as a potential upstream correlate of bone density. Genetically predicted waist circumference was inversely associated with total-body bone density in the 30–44- and ≥ 60 -year groups, but not in the 45–59-year group. This age-specific pattern should be interpreted cautiously as it may reflect changes in sex hormones, body composition, metabolism, and lifestyle, as well as differences in statistical power, SNP heterogeneity, or instability in age-stratified GWAS estimates. The observed heterogeneity in the 45–59- and ≥ 60 -year groups and the borderline MR-Egger intercept in the ≥ 60 -year group further suggest that potential pleiotropy cannot be fully excluded. Therefore, these MR findings provide complementary evidence on the association between waist circumference and bone density but should not be directly generalized to Chinese populations without validation in Chinese or East Asian datasets.

The conceptual pathways considered in this study were waist circumference, total-body bone density, LBMD-related falls, and deaths/DALYs. However, only the association between waist circumference and bone density was directly examined using MR, whereas subsequent links were interpreted based on established epidemiological evidence and the GBD attribution framework. Therefore, the GBD and MR components should be viewed as complementary evidence rather than as a fully demonstrated causal chain.

The findings in this report are subject to at least four limitations. First, the GBD estimates may be affected by data quality and model assumptions. Second, the MR analysis used GWAS data of European ancestry from GIANT and GEFOS, limiting direct generalization to Chinese populations. Therefore, validation using Chinese or East Asian GWAS data is required. Third, the MR analysis was age but not sex stratified because suitable sex-specific GWAS summary statistics were unavailable, limiting its ability to explain sex-specific differences in LBMD-related fall burden. Finally, BMI was not adjusted for in the MR analysis. Given the close correlation between waist circumference and BMI, the observed association may reflect central adiposity, overall body size, or shared adiposity-related genetic pathways; thus, future BMI-adjusted multivariable MR studies are needed.

Age- and sex-specific interventions are required to reduce the incidence of LBMD-related falls in China. Priority actions include bone health screening and fall prevention in older adults, osteoporosis awareness in men, and weight-related metabolic management in younger and middle-aged adults as part of broader bone health promotion efforts, while recognizing that this MR did not directly assess fall-related outcomes. These actions are consistent with Healthy China 2030 and may support healthy aging in China.

Conflicts of interest: No conflicts of interest.

Ethical statement: Used publicly available, de-identified GBD data and GWAS summary statistics; no additional ethical approval or informed consent was required.

doi: [10.46234/ccdcw2026.159](https://doi.org/10.46234/ccdcw2026.159)

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Submitted: March 23, 2026

Accepted: July 13, 2026

Issued: July 31, 2026

REFERENCES

1. WHO. Falls. 2021. (2021-04-26). <https://www.who.int/news-room/factsheets/detail/falls>. [2026-03-23].
2. Chen Y, Dai FF, Huang SL, Qi DD, Peng CY, Zhang AJ, et al. Global,

- regional, and national burden of falls among older adults: findings from the Global Burden of Disease Study 2021 and projections to 2040. *npj Aging* 2025;11(1):85. <https://doi.org/10.1038/s41514-025-00275-4>.
3. Chen XD, Lin ZT, Gao R, Yang JJ, Li LP. Prevalence and associated factors of falls among older adults between urban and rural areas of Shantou City, China. *Int J Environ Res Public Health* 2021;18(13):7050. <https://doi.org/10.3390/ijerph18137050>.
 4. Chinese Society of Osteoporosis and Bone Mineral Research. Epidemiological survey of osteoporosis in China and results of special action “Healthy Bones”. *Chin J Osteopor Bone Miner Res* 2019;12(4):317-8. <http://dx.doi.org/10.3969/j.issn.1674-2591.2019.04.001>. (In Chinese).
 5. Shungin D, Winkler TW, Croteau-Chonka DC, Ferreira T, Locke AE, Mägi R, et al. New genetic loci link adipose and insulin biology to body fat distribution. *Nature* 2015;518(7538):187 – 96. <https://doi.org/10.1038/nature14132>.
 6. Medina-Gomez C, Kemp JP, Trajanoska K, Luan J, Chesi A, Ahluwalia TS, et al. Life-course genome-wide association study meta-analysis of total body BMD and assessment of age-specific effects. *Am J Hum Genet* 2018;102(1):88 – 102. <https://doi.org/10.1016/j.ajhg.2017.12.005>.
 7. Burgess S, Small DS, Thompson SG. A review of instrumental variable estimators for Mendelian randomization. *Stat Methods Med Res* 2017;26(5):2333 – 55. <https://doi.org/10.1177/0962280215597579>.
 8. Eastell R, O'Neill TW, Hofbauer LC, Langdahl B, Reid IR, Gold DT, et al. Postmenopausal osteoporosis. *Nat Rev Dis Primers* 2016;2(1):16069. <https://doi.org/10.1038/nrdp.2016.69>.
 9. Rinonapoli G, Ruggiero C, Meccariello L, Bisaccia M, Ceccarini P, Caraffa A. Osteoporosis in men: a review of an underestimated bone condition. *Int J Mol Sci* 2021;22(4):2105. <https://doi.org/10.3390/ijms22042105>.

SUPPLEMENTARY MATERIAL

SUPPLEMENTARY TABLE S1. Information on included studies and consortia.

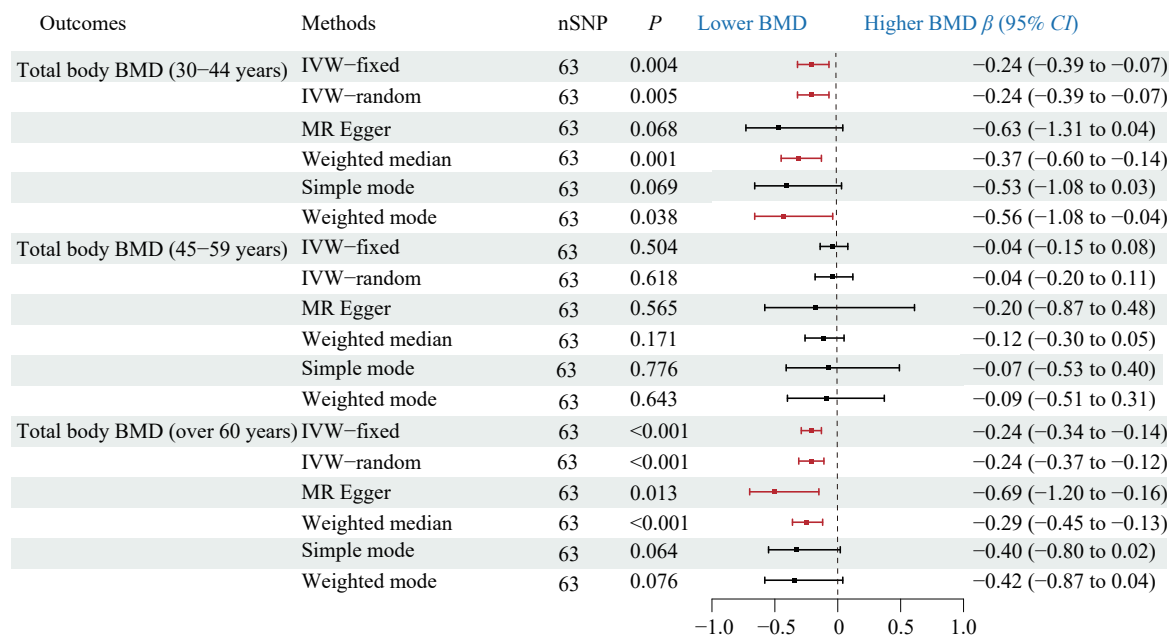
Exposure or outcomes	Consortia	Sample size	Number of SNPs	Ancestry
Waist circumference	GIANT	231,353	2,546,074	European
Total-body bone mineral density (age 30–44)	GEFOS	10,062	9,656,698	European
Total-body bone mineral density (age 45–59)	GEFOS	18,805	10,304,110	European
Total-body bone mineral density (age over 60)	GEFOS	22,504	11,932,096	European

Abbreviation: SNP=single-nucleotide polymorphism; GIANT=genetic investigation of anthropometric traits; GEFOS=genetic factors for osteoporosis.

SUPPLEMENTARY TABLE S2. Heterogeneity and horizontal pleiotropy assessments for the associations between waist circumference and total-body BMD.

Exposure	Outcomes	Heterogeneity test				Horizontal pleiotropy test			
		MR Egger		Inverse variance weighted		MR Egger intercept	SE	P	MR-PRESSO-P
		Rucker's Q	P	Cochran's Q	P				
Waist circumference	Total-body BMD (age 30–44)	63.653	0.383	65.227	0.365	0.011	0.009	0.224	0.308
Waist circumference	Total-body BMD (age 45–59)	111.258	< 0.001	111.675	< 0.001	0.004	0.009	0.634	0.532
Waist circumference	Total-body BMD (age over 60)	89.071	0.011	93.318	0.006	0.011	0.007	0.093	0.666

Abbreviation: BMD=bone mineral density; MR=Mendelian randomization; SE=standard error; MR-PRESSO=Mendelian randomization pleiotropy residual sum and outlier test.



SUPPLEMENTARY FIGURE S1. Mendelian randomization association between genetically predicted waist circumference and total-body bone mineral density across different age groups.

Abbreviation: BMD=bone mineral density; IVW=inverse variance weighted; nSNP=number of single-nucleotide polymorphisms; β =beta coefficient; CI=confidence interval.