Open Access

The effects of resveratrol in animal models of primary osteoporosis: a systematic review and meta-analysis

Rongxian An^{1†}, Qian Luo^{2†}, Lei Li¹, Dinglu Cui¹ and Jingchun Jin^{1*}

Abstract

Background There is still a lack of sufficient evidence-based medical data on the effect of resveratrol (Res) on primary osteoporosis (OP). This meta-analysis aimed to comprehensively evaluate the role of Res in animal models of primary OP.

Methods The PubMed, Cochrane Library, Web of Science and Embase databases were searched up to August 2023. The risk of bias was assessed by the SYRCLE RoB tool. Random- or fixed-effects models were used to determine the 90% confidence interval (CI) or standardized mean difference (SMD). Statistical analysis was performed with Rev-Man 5.4 and Stata 14.0.

Results A total of 24 studies containing 714 individuals were included. Compared with those in the control group, the bone mineral density (BMD) (P < 0.00001), bone volume/total volume (BV/TV) (P < 0.001), trabecular thickness (Tb. Th) (P < 0.00001), and trabecular number (Tb.N) (P < 0.00001) were markedly greater, and the trabecular separation (Tb.Sp) (P < 0.00001) was significantly greater. Compared with the control group, the Res group also exhibited marked decreases in alkaline phosphatase (ALP) (P < 0.00001), tartrate-resistant acid phosphatase 5b (TRAP5b) (P < 0.001), and type I collagen strong carboxyl peptide (CTX-1) (P < 0.00001) and a marked increase in osteoprotegerin (OPG) (P < 0.00001).

Conclusion In summary, we concluded that Res can markedly increase BMD, improve morphometric indices of trabecular microstructure and serum bone turnover markers (BTMs), and exert a protective effect in animal models of primary osteoporosis. This study can supply experimental reference for Res in primary osteoporosis treatment.

Keywords Primary osteoporosis, Resveratrol, Animal models

Introduction

Osteoporosis (OP) is a systemic bone disease characterized by damage to the bone microstructure and decreased bone mass, resulting in bone fragility and easy fracture [1, 2]. Primary osteoporosis, as a major part of

[†]Joint first authors: Rongxian An and Qian Luo.

¹ Yanbian University Hospital, Yanji, China

² Baoji Traditional Chinese Medicine Hospital, Baoji, China

OP, is currently a major public health problem facing patients and medical practitioners globally. A decreasing BMD not only increases the incidence of fractures but also has an incalculable impact on patients' financial status and personal and even whole-family quality of life, given that most patients with primary OP are elderly patients (postmenopausal OP and senile OP) [3, 4]. Clinically, anti-OP drugs are categorized into anti-absorptive and pro-synthetic drugs. Widely used options include bisphosphonates (BP), selective estrogen receptor modulators (SERM), and RANK-ligand inhibitors. Despite their popularity, these drugs are associated with various adverse effects. For example, Denosumab, a type of



© The Author(s) 2024. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.go/licenses/by/4.0. The Creative Commons Public Domain Dedication waiver (http://creativecommons.go/licenses/by/4.0. The Creative Commons Public Domain Dedicated in a credit line to the data.

^{*}Correspondence:

Jingchun Jin

jingchun680928@163.com

BP, significantly increases BMD in the spine and hip of postmenopausal women with OP. However, due to severe gastrointestinal reactions such as acid reflux, nausea, and vomiting, many patients opt for intravenous administration over oral, potentially impacting treatment compliance of patients [5–8]. For another example, although oestrogen replacement treatment has a significant effect on treating postmenopausal OP [9], studies have shown that this therapy may increase the risk of breast and uterine cancer. Thus, there is a critical need to identify drugs that are more effective, convenient, and safer for primary OP.

Resveratrol (Res) is a polyphenolic phytoestrogen that is present in the skin of red grapes, peanuts and various other fruits [10, 11] and has potent antioxidant, antiinflammatory, antiageing, neuroprotective, anticarcinogenic and cardioprotective effects [12, 13]. In vitro evidence has shown that Res can improve the activity of osteoblasts and inhibit the differentiation of osteoclasts [14, 15]. For example, in vitro, Res increases ALP in a dose-dependent manner by promoting the differentiation of osteoblasts [16]. In vivo studies have shown that Res can improve BMD and prevent bone loss in young rats subjected to tail suspension, in ovariectomized (OVX) rats and in old rats subjected to hind limb suspension [17-19]. However, a large number of existing studies have not yet systematically summarized and analyzed the topic. Therefore, this review aims to comprehensively explore the role of Res in an animal model of primary OP through the use of a meta-analysis of animal experiments for the first time.

Methods

The meta-analysis was performed in accordance with PRISMA guidelines (Additional file 1) and registered on the PROSPERO platform of the International Register of Systematic Evaluations (No. CRD42023478041).

Data sources and search

Cochrane Library, PubMed, Web of Science and EMBASE were searched for studies of Res in animal models of primary OP up to August 2023.

Study selection

The inclusion criteria were as follows: (1) The animal model was primary OP; (2) The animal models of primary OP were established by all kinds of methods, such as age-related OP, orchiectomy and ovariectomy; (3) The treatment group was given Res only, while the control group was given either no treatment or saline treatment; (4) The main results were bone mineral density (BMD); the second outcomes were morphometric indices of trabecular microstructure, including bone volume/total

volume (BV/TV), trabecular number (Tb.N), trabecular thickness (Tb.Th), and trabecular separation (Tb.Sp); and serum bone turnover markers (BTMs), including osteocalcin (OC), alkaline phosphatase (ALP), serum osteoprotegerin (OPG), bone alkaline phosphatase (bALP), type I collagen strong carboxyl peptide (CTX-1), and tartrateresistant acid phosphatase 5b (TRAP5b). The exclusion criteria were as follows: (1) reviews, cases, clinical trials, cell studies or other studies; (2) other animal models; and (3) other medicines.

Data extraction

Two authors independently extracted the study characteristics (publication year, first author and sample size), method of modeling, basic characteristics, intervention, and outcome information. All the data were acquired, and several subgroup analyses were carried out for different dosages, modeling-established standards or patient positions. Disputes between the two radiologists were resolved by talking with a third person.

The risk of bias assessment

The risk of bias of the included studies was evaluated by the SYRCLE risk of bias tool [20] (Fig. 2); the risk of bias was classified as "high", "low" or "unclear". Disagreements between An and Luo were resolved by Dr. Jin.

Subgroup and sensitivity analysis

Because of the limited sample size, the number of female animals was greater than the number of male animals, the data on age and weight were incomplete, and the methods of modeling were different. In this review, a subgroup analysis was conducted even though it was difficult. If there was obvious heterogeneity in the primary outcome ($I^2 > 50\%$), this study was subjected to sensitivity analysis. Moreover, the stability of all outcomes was evaluated by ignoring each study in sequence.

Data synthesis

Excel 2016, Stata 14.0, and RevMan 5.4 were used to perform this analysis. When the data were reported as the mean \pm SEM (standard error of the mean), we transformed the SEM into the standard deviation (SD) using the formula δ SEM = SD/square root of the sample size to avoid obfuscating the distinctive usage between the SD and SEM. Statistical heterogeneity was assessed by the chi-square test and the I² test. A fixed-effects model was selected if I^2 was < 50%; otherwise, the random-effects model was selected. Several independent groups in a study (e.g., various doses) were considered separate datasets. P < 0.05 indicated statistical significance.

Results

A total of 714 studies were selected. After removing duplicates, 351 studies remained. Sixty studies were left for full-text screening after screening the titles and abstracts. Finally, 24 studies were analyzed. The basic characteristics of the final 24 studies [15, 17, 19, 21–41] are shown in Table 1. The search process is shown in Fig. 1.

The risk of bias and publication bias

Several studies (Fig. 2) were thought to have an "unclear risk of bias", for example, random sequence generation, random housing and random outcome assessment. A low risk of bias was observed for incomplete outcome data, baseline characteristics and selective reporting in all studies except one [19]. Moreover, the funnel plot (n > ten papers) showed that the stability of the results was not affected by publication bias (Additional file 1).

Effectiveness

Primary outcomes-BMD (Figs. 3 and 4)

Analysis of 45 studies [17, 19, 23–26, 28–32, 34, 36, 39, 40] showed that, compared with the control group, the Res group had a markedly greater BMD (n=587; SMD, 1.59; 95% confidence interval (CI), 1.22 to 1.96; $I^2=60\%$, P<0.00001). Due to the high heterogeneity, we analyzed the BMD subgroups according to the methods of modeling, test methods and test positions (Fig. 4). Subgroup analysis according to the above several points showed no significant reduction in heterogeneity, which may remind us to search for other more suitable points (Additional file 1).

Secondary outcomes

Morphometric indices of the trabecular microstructure (Figs. 5, 6, 7, 8)

1. BV/TV

Analysis of 18 studies [15, 25–27, 30, 33, 35–38, 40, 41] showed that, compared with those in the control group, the BV/TV in the Res group was markedly greater (n=252; SMD, 1.44; 95% CI, 0.68 to 2.19; l^2 =80%, P<0.001).

2. Tb.N

Analysis of 18 studies [19, 25–27, 33, 35–38, 40, 41] showed that, compared with the control group, the Res group had markedly greater total bilirubin (Tb.N) (n=242; SMD, 1.68; 95% CI, 0.95 to 2.42; l^2 =74%, P<0.00001).

3. Tb.Th

Analysis of 18 studies [19, 25, 26, 30, 33, 35–37, 40, 41] showed that, compared with that in the control group, the Tb.Th in the Res group was markedly greater (n=248; SMD, 1.73; 95% CI, 1.09 to 2.37; l^2 =71%, P<0.00001).

4. Tb.Sp

Analysis of 20 studies [19, 25–27, 30, 33, 35–38, 40, 41] showed that, compared with that in the control group, the Tb.Sp in the Res group was markedly lower (n=278; SMD, -1.76; 95% CI, -2.35 to -1.16; I^2 =70%, P<0.00001).

Serum BTM concentrations (Figs. 9, 10, 11, 12, 13 and 14)

1. ALP

Analysis of 16 studies [15, 19, 22, 24, 25, 31, 39, 40] showed that, compared with that in the control group, ALP was markedly lower in the Res group (n=198; SMD, -1.69; 95% CI, -3.01 to -0.37; I^2 =87%; P<0.05).

2. bALP

Analysis of 3 studies [21, 36, 37] showed that, compared with those in the control group, the bALP levels in the Res group were markedly greater (n=52; SMD, 4.11; 95% CI, -0.77 to 8.99; I^2 =95%, P>0.05).

3. OC

Analysis of 10 studies [15, 22, 25, 31, 33] showed that, compared with that in the control group, the OC in the Res group was markedly lower (n=134; SMD, -0.86; 95% CI, -2.11 to 0.39; I^2 =86%, P>0.05).

4. Serum OPG

Analysis of 8 studies [22, 31, 35, 36, 40] showed that, compared with the control group, the Res group had markedly greater OPG levels (n=108; SMD, 2.49; 95% CI, 1.45 to 3.53; l^2 =68%, P<0.00001).

5. CTX-1

Analysis of 9 studies [24, 27, 36, 39, 40] showed that, compared with the control group, the Res group had markedly lower CTX-1 levels (n=100; SMD, -1.81; 95% CI, -2.41 to -1.21; I^2 =37%, P<0.00001).

6. TRAP5b

Analysis of 7 studies [22, 31, 36, 37, 40] showed that, compared with the control group, the Res group had markedly lower TRAP5b levels (n = 100; SMD, -2.78; 95% CI, -4.44 to -1.12; $I^2 = 85\%$, P < 0.01).

Discussion

This review assessed the protective effects of Res in animal models of primary osteoporosis. Twenty-four articles were analyzed, and eleven results were obtained. This review showed that Res can markedly increase BMD,

Study	Species	Sex	Weight (g)	Age	N (T/no-T)	Model (establish; modeling standard)	Treatment group (administration;dose; course of treatment)	Outcome index
Chen [23]	Rat	Female	AA	器 NA	8/8	Ovariectomy	Two weeks after OVX proce- dures; intragastric administration of 0.2 µM RES once;about 10 weeks	Bmd
Jing Feng [25]	Rat	Female	280–350	3 3 months	8/8(low-dose)/8(middle)/8(high)	Ovariectomy	Orally administrated at the dos- age of 5, 25and 45 mg/kg/d, respectively, 7 days after operation for 8 weeks	Bmd,BWTV, Tb.Th,Tb.N, Tb.Sp, alp.oc
Omnia Ameen [21]	Rat	Male	350-400	18-20 months	10/10	Aging- dependent male osteo- porosis	Receiving resveratrol; 20 mg/kg/ day for 6 weeks	Balp
Wei Wan [34]	Rat	Female	250±10	10-12 weeks	10/10(low- dose)/10(middle)/10(high)	Ovariectomy	Res dissolved in 5 ml of normal saline and administered at the dos- age of 10, 20, and 40 mg/kg/d to rats intragastrically for 8 weeks	Bmd
Liwei Wei [36]	Rat	Female	NA	6 months	8/8	Ovariectomy	Two weeks after ovariectomy, rats in OVX and Res groups were received, respectively, Res solution at 10 mg/kg body weight by daily intraperitoneal injection or saline for 12 weeks	Bmd,BV/TV, Tb.Th,Tb.N, Tb.Sp, balp, pg, TRACP-5b, CTX-1
Alka Khera [28]	Rat	Female	A	3 months	6/6	Ovariectomy	The diet was mixed with resvera- trol (625 µg/Kg body weight/day) and administered orally to experi- mental animals as diet pellets for 4 weeks	Bmd
Zamai et al. [38]	Rat	Female	ЧZ	4 months	10/10	Ovariectomy	The administration of Res (10 mg/ Kg) and placebo was performed via gavage during all experiment period after ovariectomy surgery; 22 weeks	Tb.N,Tb.Sp, BV/TV
Qian Lin [29]	Rat	Female	254.91 ± 18.01	3 months	8/8	Ovariectomy	OVX rats with Res 5 mg, 15 mg, 45 mg ×kgbw-1 × day-1, respec- tively, for 13 weeks	Bmd
Yan-Ling Feng [26]	Rat	Female	220±19.27	3 months	10/10	Ovariectomy	RES solution (40 mg/kg body weight, once daily; 10 weeks	Bmd,BV/TV, Tb.Th,Tb.N, Tb.Sp
Elseweidy et al. [24]	Rat	Female	200-220	3 months	6/6	Ovariectomy	OVX rats that received 80 mg/kg/ day of Res orally for 8 weeks (Res)	Bmd, CTX-1, alp
Yixuan Jiang [27]	Mice	Female	NA	8 weeks	4/4	Ovariectomy	RES (40 mg/kg body weight) was performed intraperitoneally once every day for 8 weeks	BV/TV,Tb.N, Tb.Sp, CTX-1

 Table 1
 Characteristics of the included studies in the meta-analysis

\sim
5
ă
5
2
·=
Ę
5
0
9
9
<u> </u>
0
e 1
ole 1 (o
ible 1 (O
Table 1 (C
Table 1 (O

Study	Species	Sex	Weight (g)	Age	N (T-on/T) N	Model (establish; modeling standard)	Treatment group (administration;dose; course of treatment)	Outcome index
Liu et al. [17]	Rat	Female	220–250	Ч Ч	11/11	Ovariectomy	RES group treated with 0.7 mg/ kg of body weight of res- veratrol. Tested materials were given by gavage for 12 weeks after ovariectomy	Bmd
Haifeng Zhao [19]	Rat	Female	200-220	3-4 months	10/10(low- dose)/10(middle)/10(high)	Ovariectomy	Res(20, 40, 80 mg/kg/day) was orally administered, respec- tively, through a custom-made stomach tube for 12 weeks	Bmd,Tb.Th, Tb.N, Tb.Sp, alp
Lee et al. [15]	Rat	Male	NA	6 months	7/7	Ageing rats	20 mg/kg/day; 3 months	BV/TV,OC,alp, CTX-1
Tresguerres et al. [33]	Rat	Male	AN	22 months	10/10	Ageing rats	Treated with Res at dosages of 10 mg/kg per day; 10 weeks	BV/TV,Tb.Th, Tb.N,Tb.Sp, CTX-1, OC
Sehmisch et al. [32]	Rat	Female	220-260	3 months	11/11(low-dose)/11(high)	Ovariectomy	The rats received daily doses of 5 mg/kg bw for RES low and 50 mg/kg bw for RES high; 3 months	Bmd
Ye Zhang [39]	Rat	Female	NA	NA	8/8(low-dose)/8(middle)/8(high)	Ovariectomy	Given orally with RES (50, 100, and 200 mg/day); 12 weeks	Bmd,balp, opg, TRAP-5b, CTX-1, alp,BV/TV, Tb.Th, Tb.N, Tb.Sp
Yujin Zhang [40]	Rat	Female	220±18	3 months	8/8(low-dose)/8(middle)/8(high)	Ovariectomy	RES-L, RES-M and RES-H treatment group were, respectively, given RES (dimethyl sulfoxide, DWSO), the concentration of DWSO in the solution was 0.5% of 5 mg/ (kg.d), 15 mg/(kg.d) and 45 mg/ (kg.d) by gavage; 12 weeks	Bmd,oc,alp, CTX-1
Wang(35)	Rat	Female	300	12 weeks	8/8(low-dose)/8(high)	Ovariectomy	Resveratrol(5 mg/kg/day)/ (45 mg/ kg/day) was administered orally, respectively, to rats for 10 weeks	Bmd,BV/TV, Tb.Th,Tb.N, Tb.Sp. opg
Yuquan Shi[<mark>37</mark>]	Mice	Female	AA	8 weeks	8/8	Ovariectomy	The mice received treatment with Res (7 mg/kg) on the second day after OVX surgery; 6 weeks	BV/TV,Tb.Th, Tb.N,Tb.Sp, balp, TRAP- 5b
Sakr et al. [31]	Rat	Male	300±25	14 weeks	8/8	Orchiectomy	Res time-release pellets (50 mg, Cat. No. NX-999) were implanted subcutaneously (one pellet/ani- mal) to release the whole concen- tration of Res over 90 days	Bmd,opg,TRAP-5b, OC, alp
Osturk et al. [30]	Rat	Female	200–250	3 months	12/12(low-dose)/12(high)	Ovariectomy	Res was administered by oral gav- age (40 and 80 mg/kg/day) for ten weeks	Bmd, Alp, OC, BV/TV,Tb.Th, Tb.Sp

(continued)	
-	
Ð	
9	
Ta	

Study	Species	Sex	Weight (g)	Age	N (T/no-T)	Model (establish; modeling standard)	Treatment group (administration;dose; course of treatment)	Outcome index
Zuozhong Liu [41]	Mice	Female	NA	8 weeks	6/6	Ovariectomy	The mice received treatment with Res (7 mg/kg) on the second day after OVX surgery; 6 weeks	BV/TV,Tb.Th, Tb.N, Tb.Sp
Basem [22]	Rat	Female	365 ± 10	12–14 weeks	10/10	Ovariectomy	45 μg/kg/day, orally by gavage; 16 weeks	Bmd,opg,TRAP-5b, OC, alp







Study cs tubercour Mean SD Total SD <th< th=""><th></th><th>Exp</th><th>erimental</th><th></th><th>0</th><th>Control</th><th></th><th>1</th><th>Std. Mean Difference</th><th>Std. Mean Difference</th></th<>		Exp	erimental		0	Control		1	Std. Mean Difference	Std. Mean Difference
Alka Khera 2018 0.068 0.011 6 0.061 0.070 6 3.0% 0.70 0.74 0.48 1.12 5.00 Halfeng Zhao 2014 at 0.15175 0.02183 10 0.0147764 0.031948 3 2.8% 0.56 0.75 1.81 Halfeng Zhao 2014 at 0.1617740 0.031948 3 2.8% 0.56 0.57 1.81 Hussein 2023 at 0.16038 0.00275 6 0.21875 0.018625 8 3.1% 1.34 0.22.87 Jing Feng 2014 at 0.16038 0.00275 6 0.148513 0.01525 8 3.1% 1.34 0.22.87 Jing Feng 2014 at 0.1603 0.165 0.5 3 2.6% 0.171 1.6 1.00 <th>Study or Subgroup</th> <th>Mean</th> <th>SD</th> <th>Total</th> <th>Mean</th> <th>SD</th> <th>Total</th> <th>Weight</th> <th>IV, Random, 95% Cl</th> <th>IV, Random, 95% Cl</th>	Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl
Basem H 2021 0128384 0013837 10 0.0490695 0012915 10 0.30% 2.31 [1:12, 30] Hafferg Zhao 2014 a1 0.1575 00.22163 10 0.314764 0.031946 3 2.8% 0.56 [0.76, 187] Hafferg Zhao 2014 a2 0.0143 0.160525 8 0.221675 00.015625 8 3.0% 1.70 [0.51, 288] Hussein 2023 a1 0.25 0.016625 8 0.14631 30.0125 8 3.0% 1.70 [0.51, 288] Jing Ferg 2014 a2 0.020 10 0.041 8 0.165 0.005 3 2.8% 0.17 [1:16, 150] Jing Ferg 2014 a2 0.020 10 0.33 8 0.165 0.005 2 2.4% 0.84 [0.72, 246] Jing Ferg 2014 a2 0.020 10 0.33 8 0.165 0.005 2 2.4% 0.84 [0.72, 246] Jing Ferg 2014 a2 0.020 10 32 8 152 42 3 1.7% 3.26 [1:10, 247] Jing Ferg 2014 a2 0.020 10 32 8 152 42 3 1.7% 3.26 [1:10, 248] Jing Ferg 2014 a2 0.020 10 32 8 0.07536 0.0091653 8 1.0% 3.26% 1.19 [1.27, 246] Jing Ferg 2014 b3 0.157 0.01837 8 0.0091653 8 1.0% 3.26% 1.19 [1.27, 246] Jing Ferg 2014 b3 0.157 0.01837 8 0.0091653 8 1.0% 3.26% 1.19 [1.27, 246] Jing Ferg 2014 b3 0.157 0.01837 8 0.0091653 8 1.0% 3.26% 1.19 [1.27, 246] Jing Ferg 2014 b3 0.157 0.01837 8 0.0091653 8 1.0% 4.26% 1.19 [1.27, 246] Jing Ferg 2014 b3 0.157 0.01837 8 0.0091653 8 1.0% 4.278 [1.26, 3.28] Jing Ferg 2014 b3 0.157 0.01837 8 0.0091653 8 1.0% 4.26% 1.19 [1.27, 246] Jing Ferg 2014 b3 0.157 0.01837 8 0.0091653 8 1.0% 4.26% 1.19 [1.27, 246] Jing Ferg 2014 b3 0.157 0.01837 8 0.0091653 8 1.0% 4.26% 1.19 [1.27, 246] Jing Ferg 2014 b3 0.157 0.01837 8 0.0091653 8 1.0% 4.26% 1.19 [1.27, 246] Jing Ferg 2014 0.011 8 0.22 0 0 3 Not estimable Olan Li 2005 b1 0.23 0 0 8 0.22 0 0 1 3 2.8% 0.94 [1.65, 0.32] Jing Ling 2005 1 0.23 0 0 8 0.22 0 1 3 2.6% 0.94 [1.65, 0.32] Jing Ling 2005 1 0.23 0 0 8 0.22 0 0 1 3 2.6% 0.94 [1.65, 0.32] Jing Ling 2005 1 0.23 0.01 8 0.22 0.01 3 2.6% 0.94 [1.65, 0.32] Jing Ling 2005 2 0.24 0.01 8 0.22 0.01 3 2.6% 0.94 [1.65, 0.32] Jing Ling 2005 2 0.24 0.01 8 0.22 0.01 3 2.6% 0.94 [1.65, 0.32] Jing Ling 2005 2 0.24 0.01 8 0.22 0.01 3 2.6% 0.94 [1.65, 0.32] Jing Ling 2005 2 0.24 0.01 8 0.22 0.01 3 2.6% 0.94 [1.65, 0.32] Jing Ling 2005 2 0.24 0.01 8 0.023 0.01185 3 3.2% 0.06 [1.65, 0.32] Ji	Alka Khera 2018	0.068	0.011	6	0.061	0.007	6	3.0%	0.70 [-0.48, 1.88]	+
Halfeng Zhao 2014 a1 0.151757 0.023163 10 0.147764 0.031948 3 2.8% 0.15[+1.4,1.4] Halfeng Zhao 2014 a2 0.16355 0.028754 10 0.147764 0.031948 4 2.9% 1.20[+0.08,1.47] Halfeng Zhao 2014 a2 0.16053 0.02875 8 0.221675 0.015525 8 3.1% 1.20[+0.08,2.47] Hussein 2023 a2 0.160938 0.00375 8 0.145313 0.0125 8 3.1% 1.20[+0.08,2.47] Hussein 2023 a2 0.025 0.023 8 0.1665 0.05 3 2.8% 0.17[+1.16,1.50] Jing Feng 2014 a3 0.214 0.053 8 0.0166 0.05 3 2.8% 0.17[+1.16,1.50] Jing Feng 2014 b2 330 52 8 152 42 3 2.5% 1.30[+0.18,2.48] Jing Feng 2014 b2 330 52 8 152 42 2 3 1.7% 3.26[+1.0,5.41] Jing Feng 2014 b2 330 50 8 0.007029 0.0091603 8 1.6% 5.32[0,7,74] Hussein 2023 0.152672 0.01832 8 0.007029 0.0091603 8 1.6% 5.32[0,7,74] Mohamed M 2021 0.117627 0.000676 6 0.097166 0.00136 6 0.2% 1.764[8,95,2.32] Olar Lin 2005 a3 0.24 0.011 8 0.21 0.011 3 2.3% 1.83[0,19,3.48] Olar Lin 2005 b3 0.24 0.011 8 0.22 0 3 Notestimable Olar Lin 2005 b3 0.24 0.011 8 0.22 0 3 Notestimable Olar Lin 2005 b3 0.24 0.011 8 0.22 0 3 Notestimable Olar Lin 2005 b1 0.23 0 8 0.22 0 3 Notestimable Olar Lin 2005 b1 0.23 0 8 0.22 0 3 Notestimable Olar Lin 2005 b1 0.23 0 8 0.22 0 3 Notestimable Olar Lin 2005 b1 0.23 0 8 0.22 0 3 Notestimable Olar Lin 2005 b1 0.23 0 8 0.22 0 3 Notestimable Olar Lin 2005 b2 0.24 0.011 8 0.22 0 2 Notestimable Olar Lin 2005 b1 0.23 0 8 0.22 0 3 Notestimable Olar Lin 2005 b1 0.23 0 8 0.22 0 3 Notestimable Olar Lin 2005 b1 0.23 0 8 0.22 0 3 Notestimable Olar Lin 2005 b1 0.23 0 8 0.22 0 3 Notestimable Olar Lin 2005 b1 0.23 0 0 8 0.22 0 3 Notestimable Olar Lin 2005 b1 0.23 0 0 8 0.22 0 3 Notestimable Olar Lin 2005 b1 0.23 0 0 8 0.22 0 3 Notestimable Olar Lin 2005 b1 0.23 0 0 8 0.22 0 3 Notestimable Olar Lin 2005 b1 0.23 0 0.04 8 0.22 0 0.13 2.6% 0.91[+0.50,230] Heterogenety Table 50 0.2566 10 0.160075 0.2568 0 3.27% 0.68[+0.48, 1.20,08] Heterogenety Table 50 0.2566 10 0.160075 0.01855 3 2.2% 0.41[+0.50,530] Heterogenety Table 50.2566 10 0.221893 0.023689 3 2.8% 0.68[+0.48, 2.23] Heterogenety Table 50.2566 0.10 0.1045	Basem H 2021	0.126384	0.013837	10	0.0940959	0.0129151	10	3.0%	2.31 [1.12, 3.50]	
Haifeng Zhao 2014 a2 0.0165335 0.029754 10 0.147764 0.031949 3 2.8% 0.56 [4.76, 187] Hussein 2023 a1 0.25 0.016525 8 0.021875 0.015625 8 3.0% 1.70 [0.51, 289] Hussein 2023 a1 0.025 0.009375 8 0.014551 0.0255 8 3.0% 1.70 [0.51, 289] Hussein 2023 a2 0.160938 0.009375 8 0.014551 0.025 8 3.0% 1.70 [0.51, 289] Jing Feng 2014 a2 0.205 0.023 8 0.165 0.05 3 2.8% 0.17 [F1.16, 150] Jing Feng 2014 a2 0.205 0.023 8 0.165 0.05 2 2.4% 0.84 [4.078, 2.46] Jing Feng 2014 b1 2.01 32 8 152 42 3 1.7% 3.26 [1.15, 51] Jing Feng 2014 b3 350 40 8 152 42 2 3 1.7% 3.26 [1.15, 51] Jing Feng 2014 b3 350 40 8 152 42 2 3 1.7% 3.26 [1.15, 51] Liwei Wei 2023 0.152872 0.01932 8 0.0091560 8 1.6% 5.38 [3.02, 7.4] Mohamed M 2020 0.176270 0.00067 6 0.0971560 0.00136 8 1.6% 5.38 [3.02, 7.4] Mohamed M 2020 0.17627 0.000676 0 0.0971560 0.00136 8 1.6% 5.38 [3.02, 7.4] Mohamed M 2020 0.17627 0.000676 8 0.0971560 0.0136 8 1.6% 5.38 [3.02, 7.4] Jing Feng 2014 b3 350 40 8 0.21 0.011 3 Notestimable Olan Lin 2005 a1 0.23 0 8 0.22 0 3 Notestimable Olan Lin 2005 b1 0.23 0 8 0.22 0 3 Notestimable Olan Lin 2005 b1 0.23 0 8 0.22 0 3 Notestimable Olan Lin 2005 c1 0.21 0.011 8 0.22 0 1 3 2.6% 0.91 [1.650, 3.23] Olan Lin 2005 c1 0.21 0.011 8 0.22 0 1 2 1.7% 1.81 [1.05, 3.2] Olan Lin 2005 c1 0.21 0.011 8 0.22 0 1 2 2.1% 1.81 [1.05, 3.2] Olan Lin 2005 c1 0.221 0.011 8 0.22 0.01 2 2.1% 1.81 [1.05, 3.2] Olan Lin 2005 c1 0.221 0.011 8 0.22 0.01 2 2.1% 1.81 [1.05, 3.2] Olan Lin 2005 c1 0.221 0.011 8 0.22 0.01 2 2.1% 1.81 [1.05, 3.2] Olan Lin 2005 c1 0.221 0.011 8 0.22 0.01 2 2.1% 1.81 [1.05, 3.2] Olan Lin 2005 c1 0.221 0.011 8 0.22 0.01 2 2.1% 1.81 [1.05, 3.2] Olan Lin 2005 c1 0.221 0.011 8 0.22 0.01 3 2.6% 0.91 [1.50, 3.2] Olan Lin 2005 c1 0.221 0.011 8 0.22 0.01 3 2.6% 0.91 [1.50, 3.2] Olan Lin 2005 c1 0.221 0.011 8 0.22 0.01 3 2.6% 0.91 [1.50, 3.2] Olan Lin 2005 c1 0.224 0.0101 8 0.22 0.01 3 2.6% 0.91 [1.50, 3.2] Olan Lin 2005 c1 0.224 0.0101 8 0.22 0.01 3 2.6% 0.91 [1.50, 1.2] Hereoreal 2002 0.20 (2.00240 0.00000); F = 50% Ye Zhang 2020	Haifeng Zhao 2014 a1	0.151757	0.023163	10	0.147764	0.031948	3	2.8%	0.15 [-1.14, 1.44]	+
Haleng Zhao 2014 a3 0.180511 0.023163 10 0.147764 0.03146 4 2.9% 1.2010.08,2.47] Hussein 2023 a2 0.16038 0.00875 8 0.124756 0.015625 8 3.3% 1.70 [0.51,2.89] Hussein 2023 a2 0.16038 0.00875 8 0.14531 0.0125 8 3.3% 1.34 [0.22,2.45] Jing Feng 2014 a3 0.205 0.023 8 0.166 0.05 3 2.2% 0.41778,2.46] Jing Feng 2014 a3 0.214 0.053 8 0.166 0.05 3 2.2% 0.41078,2.46] Jing Feng 2014 b1 201 32 8 152 42 3 2.5% 1.30 [0.18,2.78] Jing Feng 2014 b2 330 52 8 152 42 3 1.7% 3.326[1:10,5.41] Jing Feng 2014 b2 330 52 8 0.0091603 8 1.66 % 0.53 3.28% 0.44 [0.78,2.46] Jing Feng 2014 b2 330 52 8 0.0722 0.0091603 8 1.6% 5.33 [3.02,7.74] Jing Feng 2014 b2 330 52 8 0.0091603 8 0.166 % 0.53 3.23% 1.320 [1.13,5.46] Jing Feng 2014 b2 330 52 8 0.0722 0.009163 8 1.6% 5.33 [3.02,7.74] Jing Feng 2014 b2 3.26 4.0 18 0.221 0.001 3 Not estimable Olan Lin 2005 a1 0.22 0 8 0.22 0 3 Not estimable Olan Lin 2005 b1 0.23 0 8 0.22 0 3 Not estimable Olan Lin 2005 b1 0.23 0 8 0.22 0 3 Not estimable Olan Lin 2005 b1 0.23 0 8 0.22 0 3 Not estimable Olan Lin 2005 b1 0.23 0.01 8 0.22 0 3 Not estimable Olan Lin 2005 b1 0.23 0.01 8 0.22 0 3 Not estimable Olan Lin 2005 b1 0.24 0.01 8 0.22 0 3 Not estimable Olan Lin 2005 b1 0.22 0.01 8 0.22 0 3 Not estimable Olan Lin 2005 b1 0.23 0.04 8 0.22 0 3 Not estimable Olan Lin 2005 b1 0.24 0.01 8 0.22 0 3 Not estimable Olan Lin 2005 b1 0.24 0.01 8 0.22 0 3 Not estimable Olan Lin 2005 b1 0.24 0.01 8 0.22 0 3 Not estimable Olan Lin 2005 b1 0.24 0.01 8 0.22 0 3 Not estimable Olan Lin 2005 b1 0.24 0.01 8 0.22 0.01 3 2.5% 0.01 [1.50,2.32] Olan Lin 2005 c2 0.21 0.01 8 0.22 0.01 3 2.5% 0.01 [1.50,2.32] Olan Lin 2005 c2 0.21 0.01 8 0.22 0.01 3 2.5% 0.01 [1.50,2.32] Olan Lin 2005 c3 0.24 0.01 8 0.22 0.01 3 2.5% 0.01 [1.50,2.34] Heterogravity A1 0.2404 0.02486 10 0.108473 0.01133 3 2.7% 0.68 [0.48,2.23] Heterogravity A1 0.24086 10 0.021803 0.024686 3 3.2% 0.56 [0.41,1.8] Wei Wang 2020 a1 0.218046 0.02867 10 0.22183 0.023668 3 2.8% 0.56 [0.44,2.23] Heterogravity A1 0.24086 0.01 0.010473 0.01133 3 2.7% 0.68	Haifeng Zhao 2014 a2	0.165335	0.028754	10	0.147764	0.031948	3	2.8%	0.56 [-0.76, 1.87]	+-
Hussein 2023 at 0.1508 0.009375 & 0.021875 0.015625 8 0.30% 1.70[0.51, 2.89] Jing Feng 2014 at 0.073 0.041 8 0.165 0.005 3 2.8% 0.177.116, 1.50] Jing Feng 2014 a2 0.026 0.023 8 0.166 0.005 3 2.8% 0.177.116, 1.50] Jing Feng 2014 b1 0.214 0.053 8 0.166 0.005 2 2.4% 0.84 [0.78, 2.46] Jing Feng 2014 b1 0.214 0.053 8 0.165 0.005 2 2.4% 0.84 [0.78, 2.46] Jing Feng 2014 b1 0.214 0.053 8 0.165 0.005 2 2.4% 0.84 [0.78, 2.46] Jing Feng 2014 b1 0.201 0.32 8 0.152 42 2 1.1% 4.62 [1.56, 7.65] Jing Feng 2014 b3 356 40 8 0.52 42 2 1.1% 4.62 [1.56, 7.65] Liwei Wei 2023 0.152672 0.01832 8 0.070229 0.0091603 8 1.6% 5.38 [3.07, 7.4] Mohamed M.201 0.117672 0.00076 8 0.02135 6 0.23% 17.44 [8.95, 2.37] Olan Lin 2005 at 0.23 00 8 0.22 0.03 Not estimable Olan Lin 2005 at 0.23 00 8 0.22 0 3 Not estimable Olan Lin 2005 b1 0.23 00 8 0.22 0 3 Not estimable Olan Lin 2005 c1 0.21 0.001 8 0.22 0 3 Not estimable Olan Lin 2005 c1 0.21 0.001 8 0.22 0 3 Not estimable Olan Lin 2005 c1 0.21 0.001 8 0.22 0 3 Not estimable Olan Lin 2005 c1 0.21 0.001 8 0.22 0.01 3 2.6% 0.91 [-56, 3.23] Olan Lin 2005 c1 0.221 0.001 8 0.22 0.01 3 2.6% 0.91 [-56, 3.23] Olan Lin 2005 c1 0.21 0.001 8 0.22 0.01 2 2.1% 1.81 [-0.05, 3.68] Serwal 2023 a 1.3844 0.45783 12 0.903614 0.168676 6 3.3% 1.019 [0.3, 2.14] Serwal 2023 a 1.3844 0.45783 12 0.903614 0.168676 6 3.3% 1.019 [0.3, 2.14] Wei Wang 2020 a 2 0.51479 0.029686 10 0.180473 0.011335 3 2.7% 0.88 [-0.48, 2.23] Vei Wang 2020 a 0.251470 0.029686 10 0.180473 0.011335 3 2.7% 0.88 [-0.48, 2.23] Wei Wang 2020 a 0.251470 0.029686 10 0.180473 0.011335 3 2.7% 0.88 [-0.48, 2.23] Wei Wang 2020 a 0.251470 0.029686 10 0.180473 0.011335 3 2.7% 0.88 [-0.48, 2.23] Wei Wang 2020 a 0.251470 0.029686 10 0.180473 0.011335 3 2.7% 0.88 [-0.48, 2.23] Wei Wang 2020 a 0.25668 0.025668 10 0.221893 0.023669 3 2.4% 0.58 [-0.41, 1.80] Wei Wang 2020 a 0.25668 0.025686 10 0.221893 0.023669 3 2.4% 0.58 [-0.41, 1.80] Wei Wang 2020 a 0.25668 0.025676 10 0.221893 0.023669 3 2.4% 0.58 [-0.41, 1.80] Wei Wang 2020 a 0.25686 0.	Haifeng Zhao 2014 a3	0.180511	0.023163	10	0.147764	0.031948	4	2.9%	1.20 [-0.08, 2.47]	
Hussein 2023 a2 0.16038 0.00875 8 0.145313 0.0125 8 3.1% 1.34 (0.22.44) Jing Feng 2014 a1 0.0173 0.041 8 0.165 0.05 3 2.8% 0.1711.15, 1.50 Jing Feng 2014 a3 0.205 0.023 8 0.165 0.05 3 2.8% 0.41078, 2.44) Jing Feng 2014 b1 201 32 8 152 42 3 2.5% 1.30 (0.13, 2.78) Jing Feng 2014 b2 330 52 8 152 42 3 1.7% 3.2611.10, 5.41 Jing Feng 2014 b2 330 52 8 0.0702.20 0.0091603 4 1.680, 7.651 Jing Feng 2014 b2 330 52 8 0.0702.20 0.0091603 4 1.680, 7.651 Jing Feng 2014 b2 330 52 8 0.0702.20 0.0091603 4 1.680, 7.653 0 1.000 Olan Lin 2005 a1 0.223 0 8 0.221 0.01 3 2.3% 1.83 (0.13, 8.61) Olan Lin 2005 a2 0.23 0.01 8 0.221 0.01 3 2.3% 1.83 (0.13, 8.61) Olan Lin 2005 b1 0.23 0 8 0.22 0 3 Not estimable Olan Lin 2005 b1 0.23 0 8 0.22 0 3 Not estimable Olan Lin 2005 b1 0.23 0 8 0.22 0 3 Not estimable Olan Lin 2005 b1 0.23 0 8 0.22 0 3 Not estimable Olan Lin 2005 b1 0.23 0 8 0.22 0 3 Not estimable Olan Lin 2005 b1 0.23 0 8 0.22 0 3 Not estimable Olan Lin 2005 b1 0.23 0 8 0.22 0 3 Not estimable Olan Lin 2005 b1 0.22 0.01 8 0.22 0 2 Not estimable Olan Lin 2005 b1 0.24 0.01 8 0.22 0 2 Not estimable Olan Lin 2005 b1 0.22 0.01 8 0.22 0.01 3 2.5% 0.01 [1.50,5.362] Olan Lin 2005 c1 0.21 0.01 8 0.22 0.01 3 2.5% 0.01 [1.50,5.362] Olan Lin 2005 c1 0.21 0.01 8 0.22 0.01 3 2.5% 0.01 [1.50,5.362] Olan Lin 2005 c2 0.21 0.01 8 0.22 0.01 3 2.5% 0.01 [1.50,5.362] MetWag 2020 a1 0.21 0.001 8 0.02 0.01 3 2.7% 0.08 [1.40,0.2,2.41] MetWag 2020 a1 0.21 0.003 0 0.01647 0.01133 3 2.7% 0.08 [1.40,0.2,2.41] MetWag 2020 a1 0.21 0.003 0 0.012 (1.83 0.02.866 3 3.% -0.16 [1.1,0.02] MetWag 2020 a1 0.21 0.02 0.01 0.02 (1.83 0.02.866 3 3.% 0.01 [8,1.60] MetWag 2020 a1 0.22 0.01 0 0.01847 0.01133 3 2.7% 0.08 [1.40,0.2,2.41] MetWag 2020 a1 0.23 0.03 0.00 0.02 0.80 0.02 0.03 0.02 0.66 3 3.2% 0.05 [0.41,1.80] MetWag 2020 a1 0.23 0.03 0.00 1.00 0.21 (1.00,0.21 (1.40,0.21,1.80] MetWag 2020 a1 0.23 0.02 0.00 1.00 0.02 0.01 0.22 1.83 0.02 0.66 1.38% 4.2.8% 0.05 [0.41,3.45] MetWag 2020 a1 0.15 0.00 0.00 0.00 0.00 0.00 0.00 0.0	Hussein 2023 a1	0.25	0.015625	8	0.221875	0.015625	8	3.0%	1.70 [0.51, 2.89]	
Jing Feng 2014 a1 0.173 0.041 8 0.165 0.05 3 2.8% 0.175 (1.61, 50) Jing Feng 2014 a2 0.214 0.063 8 0.165 0.05 2 2.4% 0.84 (0.78, 2.46) Jing Feng 2014 b1 330 52 8 152 42 3 1.7% 3.26 (1.54, 76) Jing Feng 2014 b1 330 52 8 152 42 3 1.7% 3.26 (1.54, 76) Jing Feng 2014 b1 330 52 8 0.070229 0.001603 8 1.8% 5.38 (30, 7.74) Jing Feng 2014 b2 0.117877 0.000876 6 0.027 (1.001 3 2.3% 1.38 (1.9) (3.46) Gian Lin 2005 a1 0.23 0 8 0.21 0.01 3 2.3% 1.39 (1.9) (3.46) Gian Lin 2005 b2 0.24 0.01 8 0.22 0 3 Not estimable Gian Lin 2005 c1 0.21 0.011 8 0.22 0 3 2.6% 0.31 (-0.03, 2.14) Gian Lin 2005 c1 0.21 0.011 8 <td< td=""><td>Hussein 2023 a2</td><td>0.160938</td><td>0.009375</td><td>8</td><td>0.145313</td><td>0.0125</td><td>8</td><td>3.1%</td><td>1.34 [0.22, 2.45]</td><td><u>⊢</u></td></td<>	Hussein 2023 a2	0.160938	0.009375	8	0.145313	0.0125	8	3.1%	1.34 [0.22, 2.45]	<u>⊢</u>
Jing Feng 2014 a2 0.205 0.023 8 0.165 0.05 3 2.8% 1186 028, 22.644 Jing Feng 2014 b1 201 32 8 152 42 3 2.5% 1.30 (b17, 2.78) Jing Feng 2014 b1 330 52 8 152 42 2 2.1% 3.26 [1.10, 5.41] Jing Feng 2014 b2 358 40 8 152 42 2 1.1% 4.62 [1.59, 7.65] Liwei Wei 2023 0.156272 0.01832 8 0.0071686 0.00136 6 0.2% 1.7% (A.89, 5.63) Gian Lin 2005 a1 0.23 0 8 0.21 0.01 3 Not estimable Gian Lin 2005 b1 0.23 0 8 0.22 0 3 Not estimable Gian Lin 2005 b3 0.24 0.01 8 0.22 0.3 Not estimable Gian Lin 2005 c1 0.21 0.01 8 0.22 0.01 3 2.6% 0.31 (b.60, 2.62) 2.21 Gian Lin 2005 c2 0.24 0.01 8 0.22 0.01 2.	Jing Feng 2014 a1	0.173	0.041	8	0.165	0.05	3	2.8%	0.17 [-1.16, 1.50]	+
Jung Feng 2014 a3 0.214 0.063 8 0.165 0.05 2 2.4% 0.84 [078,246] Jung Feng 2014 b1 330 52 8 152 42 3 2.5% 1.30 [0.18,246] Jung Feng 2014 b2 330 52 8 152 42 2 1.1% 3.26 [1.5,41] Jung Feng 2014 b2 330 52 8 152 42 2 1.1% 4.62 [1.5,41] Jung Feng 2014 b3 388 40 8 152 42 2 1.1% 5.38 [2.5,27] Mohamed M 2021 0.117627 0.000876 6 0.001756 0 0.00136 6 0.2% 17.64 [8.65,28] Colan Lin 2005 a1 0.23 0 8 0.21 0.01 3 2.3% 1.89 [0.3,46] Colan Lin 2005 a1 0.23 0 8 0.21 0.01 3 2.3% 1.89 [0.3,46] Colan Lin 2005 b1 0.23 0 8 0.21 0.01 3 2.3% 1.89 [0.3,46] Colan Lin 2005 b2 0.24 0.01 8 0.21 0.01 3 2.5% Notestimable Colan Lin 2005 b2 0.24 0.01 8 0.22 0 3 Notestimable Colan Lin 2005 c1 0.21 0.01 8 0.22 0 2 Notestimable Colan Lin 2005 c2 0.21 0.01 8 0.22 0 2 Notestimable Colan Lin 2005 c2 0.21 0.01 8 0.22 0 2 Notestimable Colan Lin 2005 c3 0.24 0.01 8 0.22 0 2 Notestimable Colan Lin 2005 c3 0.24 0.01 8 0.22 0.01 3 2.6% 0.91 [-05, 2.32] Colan Lin 2005 c1 0.21 0.01 8 0.22 0.01 3 2.6% 0.91 [-05, 2.32] Colan Lin 2005 c2 0.21 1.01 8 0.2 0.01 3 2.6% 0.91 [-05, 2.32] Colan Lin 2005 c3 0.22 0.11 8 0.2 0.01 3 2.6% 0.91 [-05, 2.32] Colan Lin 2005 c3 0.22 0.11 8 0.22 0.01 3 2.6% 0.91 [-05, 2.32] Colan Lin 2005 c3 0.22 0.11 8 0.2 0.01 3 2.6% 0.91 [-05, 2.32] Colan Lin 2005 c3 0.22 0.11 8 0.22 0.01 3 2.6% 0.91 [-05, 2.32] Colan Lin 2005 c3 0.22 0.11 8 0.22 0.01 3 2.6% 0.91 [-05, 2.32] Colan Lin 2005 c3 0.22 0.01 1 8 0.02 0.01 3 2.6% 0.91 [-05, 2.32] Colan Lin 2005 c3 0.22 0.01 1 8 0.02 0.01 3 2.6% 0.91 [-05, 2.32] Colan Lin 2005 c3 0.22 0.01 1 8 0.02 0.01 3 2.6% 0.91 [-05, 2.32] Colan Lin 2005 c3 0.02 (-02.11 0.01 1 8 0.02 0.01 3 2.6% 0.91 [-05, 2.32] Colan Lin 2005 c3 0.02 (-02.14 1 0.01 40 0.18047 3 0.01 135 3 2.2% -0.14 [-1.18, 0.2] Wei Wang 2020 a1 0.20149 0.023669 10 0.180473 0.01 1935 3 2.2% 0.95 [-07, 4.13] Wei Wang 2020 a2 0.201477 0.02366 10 0.21 [-03 0.023669 3 2.4% 0.65 [-07, 4.13] Wei Wang 2020 a2 0.021675 0.03560 8 2.9% 2.66 [0.74, 4.2] Wei Wang 2020 a1 0.020145 0 0.02468 0 1.0380 0 0.0466 3 2.9% 2.66 [0.74,	Jing Feng 2014 a2	0.205	0.023	8	0.165	0.05	3	2.6%	1.18 [-0.29, 2.64]	+
Jung Feng 2014 bl 201 32 8 152 42 3 2,5% 1,30 [10] 2,79] Jung Feng 2014 b2 358 40 8 152 42 2 11% 4,62 [15,9,7,65] Livei Wei 2023 0.152872 0.001822 8 0.070229 0.0091603 6 1.8% 5.38 [3.02,7,74] Wohamed M 2021 0.17527 0.00076 6 0.0971668 0.00132 Notestimable Gian Lin 2005 a1 0.23 0 8 0.21 0.01 3 2.3% 1.154 [8.5, 2.32] Gian Lin 2005 a2 0.23 0.1 8 0.21 0.01 3 2.3% 0.91 [0.54, 4.88] Gian Lin 2005 b1 0.23 0 8 0.22 0 3 Not estimable Gian Lin 2005 b1 0.24 0.01 8 0.22 0 3 Not estimable	Jing Feng 2014 a3	0.214	0.053	8	0.165	0.05	2	2.4%	0.84 [-0.78, 2.46]	+
Jung Feng 2014 b2 330 52 8 152 42 3 17.% 32.9110, 5.411 Livei Viei 2023 0.152672 0.0182 8 0.007229 0.0091603 8 1.8% 5.38 [3.02, 7.74] Mohamed M 2021 0.017627 0.000676 6 0.0971668 0.00366 6 0.2% 17.84 [8.85, 26.32] Gian Lin 2005 a1 0.23 0 8 0.21 0.01 3 Not estimable Gian Lin 2005 a3 0.24 0.01 8 0.22 0 3 Not estimable Gian Lin 2005 b1 0.23 0 8 0.22 0 3 Not estimable Gian Lin 2005 b2 0.24 0.01 8 0.22 0 3 Not estimable Gian Lin 2005 c1 0.24 0.01 8 0.2 0.01 3 2.6% 0.91 [-50, 0.32] Gian Lin 2005 c3 0.22 0.18 0.2 0.01 3 2.6% 0.91 [-50, 0.32] Gian Lin 2005 c3 0.22 0.21 1.01 (-8676 6 3.2% 0.01 [-90, 0.3, 2.14]	Jina Fena 2014 b1	201	32	8	152	42	3	2.5%	1.30 (-0.19, 2.79)	
Jung Feng 2014 b3 388 40 8 152 42 2 1.1% 4.82 [1.50, 7.65] Liwei Wei 2023 0.152672 0.01832 8 0.070229 0.0091603 8 1.8% 5.38 [3.02, 7.74] Mohamed M 2021 0.117627 0.000876 6 0.0211666 0.0133 Not estimable Gian Lin 2005 s2 0.23 0.01 8 0.21 0.01 3 Not estimable Gian Lin 2005 b1 0.23 0 8 0.22 0 3 Not estimable Gian Lin 2005 b1 0.24 0.01 8 0.22 0 3 Not estimable Gian Lin 2005 c1 0.21 0.01 8 0.22 0.01 3 2.6% 0.91 [0.50, 2.32] Gian Lin 2005 c1 0.21 0.01 8 0.22 0.01 2.6% 0.91 [0.50, 2.32] Gian Lin 2005 c1 0.21 0.01 8 0.22 0.01 2.6% 0.91 [0.50, 2.32] Gian Lin 2005 c1 0.21 0.01 8 0.22 0.01 2.2% 1.4 1.4 1.4 1.8 [0.61,	Jina Fena 2014 b2	330	52	8	152	42	3	1.7%	3.26 [1.10, 5.41]	——
Luwei Wei 2022 015267 0.01832 8 0.070220 0.0091603 8 1.65% 5.38 [3.02, 7.74] Mohamed M 2021 0.117627 0.000676 6 0.0971568 0.001366 0.2% 17.64 [8.95, 6.32] Gian Lin 2005 a1 0.23 0 8 0.21 0.01 3 2.3% 1.83 [0.19, 3.46] Gian Lin 2005 a2 0.23 0.01 8 0.21 0.01 2 1.7% 2.71 [0.54, 4.88] Gian Lin 2005 a3 0.24 0.01 8 0.22 0 3 Not estimable Gian Lin 2005 b1 0.23 0 8 0.22 0 3 Not estimable Gian Lin 2005 b2 0.24 0.01 8 0.22 0 2 Not estimable Gian Lin 2005 b2 0.24 0.01 8 0.22 0 2 Not estimable Gian Lin 2005 c1 0.21 0.01 8 0.22 0 2 Not estimable Gian Lin 2005 c1 0.21 0.01 8 0.22 0 2 Not estimable Gian Lin 2005 c1 0.21 0.01 8 0.22 0 2 Not estimable Gian Lin 2005 c1 0.21 0.01 8 0.22 0 2 Not estimable Gian Lin 2005 c3 0.24 0.01 8 0.22 0 2 Not estimable Gian Lin 2005 c3 0.22 0.01 8 0.22 0.01 2 2.1% 1.81 [0.05, 3.66] Sewal 2023 a1 1.3494 0.45783 12 0.903614 0.168676 6 3.2% 1.09 [0.03, 2.14] Sewal 2023 a2 1.30145 0.34939 12 0.903614 0.168676 6 3.2% 1.09 [0.03, 2.14] Sewal 2023 a2 0.251479 0.029566 10 0.180473 0.011835 3 2.2% 0.88 [0.48, 2.33] Wei Vang 2020 a1 0.271453 10 2.21893 0.023668 3 2.4% 1.09 [0.03, 2.14] Wei Vang 2020 a1 0.221647 0.012453 10 0.1080473 0.011835 3 2.2% 0.88 [0.48, 2.33] Wei Vang 2020 a1 0.239645 10 0.180473 0.011835 3 2.2% 0.88 [0.48, 2.33] Wei Vang 2020 b1 0.239645 10 0.221893 0.023668 3 2.4% 1.92 [0.63, 3.49] Wei Vang 2020 b1 0.239645 0.029568 11 0.0221893 0.023669 3 2.4% 0.62 [0.11, 8] X-HCHEN 2019 0.438666 0.03560 8 0.33770 0.035503 8 2.6% 0.65 [0.12, 1.409] X-HCHEN 2019 0.438666 0.31944 8 850 1.388 4 2.9% 0.62 [0.61, 1.86] X Vang 2022 a1 0.129688 0.018775 0.032778 0.035603 8 2.6% 0.65 [0.12, 1.409] Yan-Ling Feng 2018 7 2.206 4.81 10 6.8379 1.1.46 10 2.4% 3.91 [1.23, 0.552] Total (95% C1) 395 192 100.0% 1.59 [1.22, 1.96] Ye Zhang 2020 a1 0.129688 0.019375 0.01875 3 2.0% 0.62 [0.61, 1.86] X Vang 2022 a1 0.802560 2.90 0.93 1.1 0.45 0.03 11 3.3% 1.60 [0.62, 2.59] Total (95% C1) 395 192 100.0% 1.15 [1.22, 1.96] Ye Zhang 2020 a1 0.150040 0.003020 8 0.101466 3 2 1.6% 2.92 [0.66, 5.	Jing Feng 2014 b3	358	40	8	152	42	2	11%	4 62 [1 59 7 65]	——
Mohamed M 2021 0.117627 0.000676 6 0.0071568 0.001356 6 0.2% 17.64 [6.95, 26.32] Glan Lin 2005 a1 0.23 0 8 0.21 0.01 3 Not estimable Glan Lin 2005 a2 0.23 0.01 8 0.21 0.01 3 2.3% 18.80 [0.9, 3.46] Glan Lin 2005 b3 0.24 0.01 8 0.22 0 3 Not estimable Glan Lin 2005 b3 0.24 0.01 8 0.22 0 3 Not estimable Glan Lin 2005 c1 0.21 0.01 8 0.22 0.1 3 2.6% 0.91 [-05.0, 2.32] Glan Lin 2005 c2 0.21 0.01 8 0.2 0.01 2.1% 1.81 [-0.05, 3.66] Sewal 2023 a1 1.3444 0.45783 12 0.903614 0.168676 6 3.2% -0.14 [1.20, 0.91] Wei Wang 2020 a1 0.201183 0.023669 10 0.14825 3.2% -0.14 [1.20, 0.91] - Wei Wang 2020 a2 0.21479 0.023669 10 0.180473 0.011835	Liwei Wei 2023	0.152672	0.01832	8	0.070229	0.0091603	8	1.6%	5.38 [3.02, 7.74]	——
Qian Lin 2005 a1 0.23 0 8 0.21 0.01 3 2.3% Not estimable Qian Lin 2005 a2 0.23 0.01 8 0.21 0.01 3 2.3% 1.83 [0.19, 3.46] Qian Lin 2005 b1 0.23 0 8 0.22 0 3 Not estimable Qian Lin 2005 b2 0.24 0.01 8 0.22 0 3 Not estimable Qian Lin 2005 b2 0.24 0.01 8 0.22 0 2 Not estimable Qian Lin 2005 b2 0.24 0.01 8 0.22 0.01 3 2.6% 0.91 [-0.50, 2.32] Qian Lin 2005 c2 0.21 0.01 8 0.2 0.01 2 1.90 [0.03, 2.14] Sewal 2023 a2 1.36145 0.168676 6 3.7% 1.09 [0.03, 2.14] 4 Stephan 2008 a1 622.11 10.414 11 646.1 86.55 6 3.3% -0.18 [+1.18, 0.82] Wei Wang 2020 a2 0.21479 0.023666 10 0.21839 0.023666 3.24% 0.58 [-0.74, 1.89]	Mohamed M 2021	0 117627	0.000676	6	0.0971568	0.001356	6	0.2%	17 64 18 95 26 321	
Qian Lin 2005 a2 0.23 0.01 8 0.21 0.01 3 2.3% 1.83 [0.19, 3.46] Qian Lin 2005 a3 0.24 0.01 8 0.21 0.01 2 1.7% 2.71 [0.54, 4.88] Qian Lin 2005 b1 0.23 0 8 0.22 0 3 Notestimable Qian Lin 2005 b2 0.24 0.01 8 0.22 0 3 Notestimable Qian Lin 2005 c1 0.21 0.01 8 0.22 0.01 3 2.6% 0.91 [-0.50, 2.32] Qian Lin 2005 c2 0.21 0.01 8 0.2 0.011 3 2.6% 0.91 [-0.50, 2.32] Qian Lin 2005 c3 0.22 0.011 2 2.1% 1.81 [0.05, 3.66] 1.99 [0.03, 2.14] Sewal 2023 a1 1.3494 0.45733 12 0.903614 0.168676 6 3.2% -0.14 [-1.20, 0.91] Stephan 2008 a2 62.71 10.414 11 646.1 88.55 5 3.2% -0.14 [-1.20, 0.91] Wei Wang 2020 a1 0.23669 10 0.1180473 0.011825	Qian Lin 2005 a1	0.23	0.0000.0	8	0.001 1000	0.001000	3	0.270	Not estimable	
Qian Lin 2005 a3 0.24 0.01 8 0.21 0.01 2 1.7% 2.71 [0.54, 4.88] Qian Lin 2005 b1 0.23 0 8 0.22 0 3 Not estimable Qian Lin 2005 b1 0.23 0 8 0.22 0 2 Not estimable Qian Lin 2005 b2 0.24 0.01 8 0.22 0 2 Not estimable Qian Lin 2005 c1 0.21 0.01 8 0.22 0.01 3 2.6% 0.91 [-0.50, 2.32] Qian Lin 2005 c3 0.22 0.01 8 0.2 0.01 2 2.1% 1.81 [-0.05, 3.86] Sewal 2023 a1 1.38145 0.34973 12 0.903614 0.168676 6 3.2% -0.14 [-1.20, 0.91] Stephan 2008 a1 624.9 154.2231 11 646.1 88.55 6 3.2% -0.14 [-1.20, 0.91] Wei Wang 2020 a2 0.251479 0.029568 10 0.180473 0.011835 3 2.2% 2.43 [0.72, 4.13] Wei Wang 2020 b1 0.239658 10 0.21893 0.023669	Qian Lin 2005 a?	0.20	0.01	8	0.21	0.01	3	2.3%	1 83 [0 19 3 46]	
Gian Lin 2005 b1 0.23 0.8 0.22 0 3 Not estimable Gian Lin 2005 b2 0.24 0.01 8 0.22 0 3 Not estimable Gian Lin 2005 b3 0.24 0.01 8 0.22 0 3 Not estimable Gian Lin 2005 c1 0.21 0.01 8 0.22 0.01 3 2.6% 0.91 [0.50, 2.32] Gian Lin 2005 c2 0.21 0.01 8 0.2 0.011 2.1% 1.81 [-0.05, 3.66] Sewal 2023 a1 1.3494 0.45783 12 0.903614 0.168676 6 3.3% -0.14 [-1.20, 0.91] Stephan 2008 a1 624.9 154.2231 11 646.1 88.55 6 3.3% -0.18 [-1.18, 0.82] Wei Wang 2020 a1 0.201835 0.023669 10 0.180473 0.011835 3 2.7% 0.68 [-0.48, 2.23] Wei Wang 2020 b2 0.281065 0.029566 10 0.221893 0.023669 3 2.8% 0.56 [0.74, 1.89] Wei Wang 2020 b2 0.281065 0.029566 10 0.221893	Qian Lin 2005 a2	0.20	0.01	8	0.21	0.01	2	1 7%	2 71 [0 54 4 88]	
Gian Lin 2005 b2 0.24 0.01 8 0.22 0 2 Not estimable Gian Lin 2005 b3 0.24 0.01 8 0.22 0 2 Not estimable Gian Lin 2005 c1 0.21 0.01 8 0.22 0.01 3 2.6% 0.91 [-0.50, 2.32] Gian Lin 2005 c2 0.21 0.01 8 0.2 0.01 2 2.1% 1.81 [-0.05, 3.66] Sewal 2023 a1 1.3449 0.478783 12 0.903614 0.168676 6 3.3% -0.18 [-1.18, 0.02] Sewal 2023 a2 1.36145 0.34939 12 0.903614 0.168676 6 3.3% -0.18 [-1.18, 0.82] Wei Wang 2020 a1 0.201183 0.023669 10 0.180473 0.011835 3 2.7% 0.88 [-0.48, 2.23] Wei Wang 2020 b1 0.236656 10 0.180473 0.011835 3 2.6% 0.56 [-0.74, 1.89] Wei Wang 2020 b1 0.236656 10 0.221893 0.023669 3 2.6% 1.65 [1.21, 4.09]	Qian Lin 2005 b1	0.24	0.01	, s	0.21	0.01	2	1.1 70	Not estimable	
Gian Lin 2005 b2 0.24 0.01 8 0.22 0 2 Not estimable Gian Lin 2005 b3 0.24 0.01 8 0.22 0 3 2.6% 0.91 [-0.50, 2.32] Gian Lin 2005 c1 0.21 0.01 8 0.2 0.01 2.6% 0.91 [-0.50, 2.32] Gian Lin 2005 c2 0.21 0.01 8 0.2 0.01 2.2% 1.81 [-0.05, 3.66] Sewal 2023 a1 1.3494 0.45783 12 0.903614 0.168676 6 3.3% -0.14 [-1.20, 0.91] Stephan 2008 a1 62.49 154.2231 11 646.1 88.55 5 3.3% -0.14 [-1.20, 0.91] Stephan 2008 a2 0.251479 0.029568 10 0.180473 0.011835 3 2.7% 0.88 [-0.48, 2.23] Wei Wang 2020 a1 0.201483 0.021893 0.023669 3 2.4% 0.58 [-0.74, 1.89] Wei Wang 2020 b1 0.239845 0.029566 10 0.221893 0.023669 4 2.3% 2.82 [1.13, 4.51]	Oian Lin 2005 b7	0.23	0.01	0	0.22	0	3		Not estimable	
Gian Lin 2005 G1 0.21 0.01 8 0.22 0.01 3 2.6% 0.091 [0.50, 2.32] Gian Lin 2005 G2 0.21 0.01 8 0.2 0.01 3 2.6% 0.91 [0.50, 2.32] Gian Lin 2005 G2 0.21 0.01 8 0.2 0.01 2 2.1% 1.81 [0.05, 3.66] Sewal 2023 a1 1.3494 0.45783 12 0.903614 0.168676 6 3.2% 1.09 [0.03, 2.14] Stephan 2008 a1 624.9 154.2231 11 646.1 88.55 5 3.2% -0.14 [-1.20, 0.91] Wei Wang 2020 a1 0.201898 10 0.180473 0.011835 3 2.7% 0.88 [0.48, 2.23] Wei Wang 2020 a1 0.2019586 10 0.180473 0.011835 3 2.4% 0.58 [0.74, 1.89] Wei Wang 2020 b1 0.339645 0.0221893 0.023669 3 2.4% 0.58 [0.74, 1.89] Wei Wang 2020 b1 0.238462 10 0.221893 0.023669 3 2.4% 0.58 [0.74, 1.89] Wei Wang 2020 b2 0.281065 0.397276 0.03503	Qian Lin 2005 b2	0.24	0.01		0.22	0	2		Not estimable	
Gian Lin 2005 c1 0.21 0.01 6 0.22 0.01 3 2.08 0.31 [p-00, 2.32] Gian Lin 2005 c2 0.21 0.01 8 0.2 0.01 2 2.1% 1.81 [p-05, 3.66] Sewal 2023 a1 1.3494 0.45783 12 0.903614 0.188676 6 3.2% 1.09 [0.03, 2.14] Sewal 2023 a2 1.8145 0.34939 12 0.903614 0.188676 6 3.3% -0.14 [p-12, 0.91] Stephan 2008 a1 627.1 104.14 11 646.1 88.55 6 3.3% -0.18 [p-18, 0.82] Wei Wang 2020 a1 0.201183 0.023669 10 0.180473 0.011835 3 2.2% 2.43 [0.72, 4.13] Wei Wang 2020 b1 0.239645 0.0221693 0.023669 3 2.4% 1.92 [0.36, 3.49] Wei Wang 2020 b1 0.239645 10 0.221893 0.023669 3 2.4% 1.92 [0.36, 3.49] Wei Wang 2020 b1 0.239645 10 0.221893 0.023669 3 2.4% 1.92 [0.36, 5.2]	Qian Lin 2005 55	0.24	0.01		0.22	0.01	2	200	0.01 0.050 2 221	
Gian Lin 2003 f.2 0.21 0.01 6 0.22 0.01 2 2.05 1.81 [-0.05, 3.66] Sewal 2023 a1 1.3494 0.45783 12 0.903614 0.168676 6 3.2% 1.09 [0.03, 2.14] Sewal 2023 a2 1.36145 0.34939 12 0.903614 0.168676 6 3.2% 0.014 [+1.20, 0.91] Stephan 2008 a1 62.4 154.2231 1 646.1 88.55 5 3.2% 0.018 [+1.20, 0.91] Wei Wang 2020 a1 0.21183 0.023669 10 0.180473 0.011835 3 2.7% 0.88 [-0.48, 2.23] Wei Wang 2020 a2 0.251479 0.029586 10 0.180473 0.011835 3 2.4% 0.58 [-0.74, 1.89] Wei Wang 2020 b1 0.238645 10 0.221893 0.023669 3 2.4% 1.92 [0.36, 3.49] Wei Wang 2020 b1 0.328640 10 0.221893 0.023669 3 2.8% 1.65 [0.74, 1.89]	Qian Lin 2005 c1	0.21	0.01		0.2	0.01	2	2.0%	0.01 [0.00, 2.32]	
Grant Chi 2003 ct 0.22 0.01 0 0.01 0.2 1.01 (2003, 0.00) Serval 2023 at 1.36145 0.34393 12 0.903614 0.168676 6 3.2% 1.09 (0.03, 2.14) Stephan 2008 at 624.9 154.2231 11 646.1 88.55 5 3.2% -0.14 [-1.20, 0.91] Stephan 2008 at 627.1 104.14 1 646.1 88.55 6 3.3% -0.14 [-1.20, 0.91] Wei Wang 2020 at 0.201183 0.023669 10 0.180473 0.011835 3 2.2% 2.43 [0.72, 41.3] Wei Wang 2020 bt 0.032645 10 0.180473 0.011835 4 1.8% .394 [1.87, 6.02] Wei Wang 2020 bt 0.0338462 0.0221893 0.023669 3 2.4% 1.92 [0.36, 3.49] Wei Wang 2020 b1 0.338402 0.038462 10 0.221893 0.023669 4 2.3% 2.65 [1.21, 4.09] X. Hot Hot 200 0.338402 0.038462 10 0.221893 0.023669 4 2.3% 2.65 [1.21, 4.09] X. Wang 2022 at 900	Qian Lin 2005 c2	0.21	0.01		0.2	0.01	2	2.070	1 01 [-0.30, 2.32]	
Serval 2023 a1 1.3494 0.439763 12 0.930314 0.108076 6 3.12% 1.139(0.03, 2.14) Stephan 2008 a1 624.9 154.2231 11 646.1 88.55 6 3.3% -0.14 [+1.20, 0.81] Wei Wang 2020 a1 0.201183 0.023669 10 0.180473 0.011835 3 2.7% 0.88 [-0.48, 2.23] Wei Wang 2020 a2 0.251479 0.029586 10 0.180473 0.011835 3 2.2% 2.43 [0.72, 4.13] Wei Wang 2020 b2 0.281065 0.029586 10 0.21893 0.023669 3 2.4% 1.92 [0.36, 3.49] Wei Wang 2020 b1 0.328402 0.038603 8 0.266 [-1.21, 4.09]	Rowal 2022 of	1 2404	0.01	12	0.002614	0.01	2	2.1%	1.01 [-0.03, 3.00]	
Stephan 2008 a1 624.93 10.303.03 11 60.66.076 5 1.45 [0.32, 2.54] Stephan 2008 a2 627.1 104.14 11 646.1 88.55 6 3.3% -0.18 [-1.18, 0.82] Wei Wang 2020 a1 0.201183 0.023669 10 0.180473 0.011835 3 2.2% 2.43 [0.72, 4.13] Wei Wang 2020 b1 0.236645 0.029586 10 0.180473 0.011835 3 2.9% 0.58 [0.74, 1.89] Wei Wang 2020 b1 0.238645 0.029586 10 0.21893 0.023669 3 2.4% 1.92 [0.36, 3.49] Wei Wang 2020 b2 0.281065 0.029586 10 0.221893 0.023669 4 2.3% 2.82 [1.13, 4.51] X-H.CHEN 2019 0.436686 0.35503 8 0.337278 0.035503 8 2.6% 2.65 [1.21, 4.09] X.Wang 2022 a1 88.065 3.944 8 850 1.389 4 2.9% 0.62 [0.61, 1.86]	Sevial 2023 a1	1.3494	0.40700	12	0.903014	0.100070	0	3.270	1.05 [0.03, 2.14]	
Stephan 2008 a1 024.3 194.4231 11 046.1 88.55 6 3.3% -0.14 [-1.20,03] Wei Wang 2020 a1 0.201183 0.023669 10 0.180473 0.011835 3 2.7% 0.88 [-0.48 [-1.20,03] Wei Wang 2020 a2 0.251479 0.029586 10 0.180473 0.011835 3 2.2% 2.43 [0.72,413] Wei Wang 2020 b1 0.239645 10 0.180473 0.011835 4 1.8% 3.94 [1.87, 6.02] Wei Wang 2020 b1 0.239645 10 0.221893 0.023669 3 2.4% 1.92 [0.36, 3.49] Wei Wang 2020 b2 0.281065 0.029586 10 0.221893 0.023669 4 2.3% 2.82 [1.13, 4.51]	Sevial 2023 az	1.30143	154 0004	12	0.903014	0.100070	5	3.170	1.43 [0.32, 2.34]	_
Stephan 2008 a2 627.1 104.14 11 646.1 58.33 -0.16[1.16, 0.52] Wei Wang 2020 a1 0.201183 0.201835 3 2.7% 0.88 [0.48, 2.23] Wei Wang 2020 a2 0.251479 0.029586 10 0.180473 0.011835 3 2.2% 2.43 [0.72, 4.13] Wei Wang 2020 a3 0.301775 0.032545 10 0.180473 0.011835 4 1.8% 3.94 [1.87, 6.02] Wei Wang 2020 b1 0.239645 0.0221893 0.023669 3 2.8% 0.58 [-0.74, 1.89] Wei Wang 2020 b3 0.328402 0.038462 10 0.221893 0.023669 4 2.3% 2.82 [1.13, 4.51] XH.CHEN 2019 0.436686 0.337278 0.035503 8 2.6% 2.65 [1.21, 4.09] - X. Wang 2022 a1 0.86.056 31.944 8 850 1.389 4 2.9% 0.62 [-0.61, 1.86] Y. Wang 2020 a1 0.129688 0.019375 0.01875 3 2.7% 0.88 [-0.53, 2.28] - Ye Zhang 2020 a1 0.129688 0.109375 0.01875 3 <td< td=""><td>Stephan 2008 al</td><td>624.9</td><td>104.2231</td><td>11</td><td>040.1</td><td>00.00</td><td>5</td><td>3.270</td><td>-0.14 [-1.20, 0.91]</td><td></td></td<>	Stephan 2008 al	624.9	104.2231	11	040.1	00.00	5	3.270	-0.14 [-1.20, 0.91]	
Wei Wang 2020 a1 0.201183 0.023699 10 0.180473 0.011835 3 2.7% 0.088 [-0.48, 2.25] Wei Wang 2020 a2 0.251479 0.029586 10 0.180473 0.011835 4 1.8% 3.94 [1.87, 6.02] Wei Wang 2020 b1 0.239645 0.029586 10 0.221893 0.023669 3 2.4% 1.92 [0.36, 3.49] Wei Wang 2020 b2 0.281405 0.029586 10 0.221893 0.023669 4 2.3% 2.85 [1.21, 4.61] X-H.CHEN 2019 0.436686 0.035503 8 0.337278 0.035503 8 2.6% 2.65 [1.21, 4.09] X-Wang 2022 a1 868.056 31.944 8 850 1.389 4 2.9% 0.62 [-0.61, 1.86] Yan-Ling Feng 2018 72.9.66 4.81 10 693.79 11.46 10 2.4% 3.91 [2.30, 5.52]	Stephan 2008 az	027.1	104.14	11	040.1	88.00	0	3.3%	-0.18[-1.18, 0.82]	<u> </u>
Wei Wang 2020 a2 0.251479 0.029586 10 0.180473 0.011835 3 2.2% 2.43 [0.72, 41.3] Wei Wang 2020 a2 0.30175 0.32845 10 0.180473 0.011835 4 1.8% 3.94 [1.87, 6.02] Wei Wang 2020 b2 0.281065 0.029586 10 0.221893 0.023669 3 2.4% 1.92 [0.36, 3.49] Wei Wang 2020 b3 0.328402 0.038462 10 0.221893 0.023669 4 2.3% 2.82 [1.13, 4.51] X-H.CHEN 2019 0.436686 0.035503 8 0.337278 0.035503 8 2.6% 1.65 [0.21, 3.10] X.Wang 2022 a2 900 33.333 8 850 1.389 4 2.6% 1.65 [0.21, 3.10] Ya Zhang 2020 a1 0.129688 0.019375 0.01875 3 2.7% 0.88 [-0.53, 2.28]	Wei Wang 2020 at	0.201183	0.023009	10	0.180473	0.011835	3	2.1%	0.88 [-0.48, 2.23]	
Wei Wang 2020 b1 0.301775 0.032545 10 0.18473 0.01355 4 1.8% 3.34 [1.87, 0.02] Wei Wang 2020 b1 0.281065 0.0221893 0.023669 3 2.4% 1.92 [0.36, 3.49] Wei Wang 2020 b3 0.328402 0.03862 10 0.221893 0.023669 4 2.3% 2.82 [1.13, 4.51] XH.CHEN 2019 0.436686 0.035503 8 0.387278 0.035603 8 2.6% 2.65 [1.21, 4.09] X.Wang 2022 a2 900 33.33 8 850 1.389 4 2.6% 1.65 [0.21, 3.10] Yan-Ling Feng 2018 729.66 4.81 10 693.79 11.46 10 2.4% 3.91 [2.30, 5.52] Ye Zhang 2020 a1 0.129688 0.019375 0.01875 3 2.7% 0.88 [-0.53, 2.28]	Wei Wang 2020 az	0.201479	0.029580	10	0.180473	0.011835	3	2.2%	2.43 [0.72, 4.13]	
wei Wang 2020 b1 0.239645 0.029586 10 0.221893 0.023669 3 2.8% 0.036[-0.74, 1.89] Wei Wang 2020 b2 0.238645 0.021893 0.023669 3 2.4% 1.92[0.36, 3.49] Wei Wang 2020 b3 0.328402 0.038462 10 0.221893 0.023669 4 2.3% 2.82[1.13, 4.51] X-H.CHEN 2019 0.436686 0.035503 8 0.337278 0.035603 8 2.6% 2.65[1.21, 4.09] X.Wang 2022 a1 868.056 31.944 8 850 1.389 4 2.9% 0.62[-0.61, 1.86] Y.Wang 2022 a2 900 3.333 8 850 1.389 4 2.9% 0.62[-0.61, 1.86] Yan-Ling Feng 2018 729.66 4.81 10 693.79 11.46 10 2.4% 3.91[2.30, 5.52] Ye Zhang 2020 a1 0.129688 0.021875 8 0.109375 0.01875 3 2.0% 2.69 [0.76, 4.62]	Wei Wang 2020 a3	0.301775	0.032545	10	0.180473	0.011835	4	1.8%	3.94 [1.87, 6.02]	
Wei Wang 2020 b2 0.2810b5 0.029586 10 0.221893 0.023669 3 2.4% 1.92 [0.36, 3.49] Wei Wang 2020 b3 0.328402 0.038662 10 0.221893 0.023669 4 2.3% 2.82 [1.13, 4.51] X-H.CHEN 2019 0.436686 0.035503 8 0.035703 8 2.6% 2.65 [1.21, 4.09] X.Wang 2022 a1 868.056 31.944 8 850 1.389 4 2.9% 0.62 [-0.61, 1.86] X.Wang 2022 a2 900 33.333 8 850 1.389 4 2.4% 3.91 [2.30, 5.52] Ye Zhang 2020 a1 0.129688 0.019375 0.01875 3 2.7% 0.88 [-0.53, 2.28] Ye Zhang 2020 a2 0.190625 0.029688 8 0.109375 0.01875 3 2.0% 2.69 [0.76, 4.62] Ye Zhang 2020 a3 0.220312 0.035938 8 0.109375 0.01875 3 2.6% 0.95 [-0.47, 2.36] Yujin Zhang 2020 a3 0.150049 0.010465 8 0.120063 0.010465 1.9% 2.79 [0.82, 4.77]	Wel Wang 2020 bi	0.239645	0.029586	10	0.221893	0.023669	3	2.8%	0.58 [-0.74, 1.89]	
Wei Wang 2020 b3 0.328402 0.03462 10 0.221893 0.035603 4 2.3% 2.82 [1.31, 4.51] XH.CHEN 2019 0.436686 0.035503 8 0.035503 8 2.6% 2.65 [1.21, 4.09] X.Wang 2022 a1 868.056 31.944 8 850 1.389 4 2.6% 1.65 [0.21, 3.10] Y.Wang 2022 a2 900 33.333 8 850 1.389 4 2.6% 1.65 [0.21, 3.10] Ye Zhang 2020 a1 0.129688 0.021875 8 0.109375 0.01875 3 2.7% 0.88 [-0.53, 2.28] Ye Zhang 2020 a2 0.190625 0.029688 8 0.109375 0.01875 3 2.0% 2.69 [0.76, 4.62]	Wei Wang 2020 b2	0.281065	0.029586	10	0.221893	0.023669	3	2.4%	1.92 [0.36, 3.49]	
XH.CHEN 2019 0.436686 0.035503 8 0.337278 0.0355033 8 2.6% 2.65 [1.21, 4.09] X. Wang 2022 a1 868.056 31.944 8 850 1.389 4 2.9% 0.62 [-0.61, 1.86] X. Wang 2022 a2 900 33.333 8 850 1.389 4 2.9% 0.62 [-0.61, 1.86] Y. Wang 2022 a2 900 33.333 8 850 1.389 4 2.6% 1.65 [0.21, 3.10] Yan-Ling Feng 2018 729.66 4.81 10 693.79 11.46 10 2.4% 3.91 [2.30, 5.52] Ye Zhang 2020 a1 0.129688 0.021875 3 2.7% 0.88 [-0.53, 2.28]	Wei Wang 2020 b3	0.328402	0.038462	10	0.221893	0.023669	4	2.3%	2.82 [1.13, 4.51]	
X. Wang 2022 a1 868.056 31.944 8 850 1.389 4 2.9% 0.62 [-0.61, 1.86] X. Wang 2022 a2 900 33.333 8 850 1.389 4 2.6% 1.65 [0.21, 3.10] Yan-Ling Feng 2018 729.66 4.81 10 693.79 11.46 10 2.4% 3.91 [2.30, 5.52] Ye Zhang 2020 a1 0.129688 0.021875 8 0.109375 0.01875 3 2.7% 0.88 [-0.53, 2.28] Ye Zhang 2020 a2 0.190625 0.029688 8 0.109375 0.11875 3 2.0% 2.69 [0.76, 4.62] Ye Zhang 2020 a3 0.220312 0.035938 8 0.120063 0.010465 3 2.9% 0.95 [-0.47, 2.36] Yujin Zhang 2020 a2 0.152049 0.010465 3 1.9% 2.79 [0.82, 4.77]	XH.CHEN 2019	0.436686	0.035503	8	0.337278	0.035503	8	2.6%	2.65 [1.21, 4.09]	
X. Wang 2022 a2 900 33.333 8 850 1.389 4 2.6% 1.65 [0.21, 3.10] Yan-Ling Feng 2018 729.66 4.81 10 693.79 11.46 10 2.4% 3.91 [2.30, 5.52] Ye Zhang 2020 a1 0.129688 0.029688 8 0.109375 0.01875 3 2.7% 0.88 [-0.53, 2.28] Ye Zhang 2020 a2 0.190625 0.029688 8 0.109375 0.01875 3 2.0% 2.69 [0.76, 4.62] Ye Zhang 2020 a3 0.220312 0.035938 8 0.109375 0.11875 3 2.6% 0.95 [-0.47, 2.36] Yujin Zhang 2020 a1 0.152049 0.010465 8 0.120063 0.010465 3 1.9% 2.79 [0.82, 4.77] Yujin Zhang 2020 a2 0.151081 0.009302 8 0.120063 0.010465 2 1.6% 2.96 [0.69, 5.24] Z.P 2005 0.5 0.03 11 0.45 0.03 11 3.3% 1.60 [0.62, 2.59] Heterogeneity: Tau"= 0.80; Chi"= 99.92, df = 40 (P < 0.00001); I"= 60%	X. Wang 2022 a1	868.056	31.944	8	850	1.389	4	2.9%	0.62 [-0.61, 1.86]	T
Yan-Ling Feng 2018 729.66 4.81 10 693.79 11.46 10 2.4% 3.91 [2.30, 5.52] Ye Zhang 2020 a1 0.129688 0.021875 8 0.109375 0.01875 3 2.7% 0.88 [-0.53, 2.28] Ye Zhang 2020 a2 0.190625 0.029688 8 0.109375 0.01875 3 2.0% 2.86 [0.76, 4.62] Ye Zhang 2020 a3 0.220312 0.035938 8 0.109375 0.01875 2 1.6% 2.92 [0.66, 5.19] Yujin Zhang 2020 a1 0.130923 0.010465 8 0.120063 0.010465 3 2.6% 0.95 [-0.47, 2.36] Yujin Zhang 2020 a2 0.152049 0.010465 8 0.120063 0.010465 1.9% 2.79 [0.82, 4.77] Yujin Zhang 2020 a3 0.151081 0.009302 8 0.120063 0.010465 2 1.6% 2.95 [0.69, 5.24] Z.P 2005 0.5 0.03 11 0.33 1.60 [0.62, 2.59] + Total (95% CI) 395 192 100.0% 1.59 [1.22, 1.96] + - Heterogeneity: Tau ² = 0.80; C	X. Wang 2022 a2	900	33.333	8	850	1.389	4	2.6%	1.65 [0.21, 3.10]	
Ye Zhang 2020 a1 0.129688 0.021875 8 0.109375 0.01875 3 2.7% 0.88 [-0.53, 2.28] Ye Zhang 2020 a2 0.190625 0.029688 8 0.109375 0.01875 3 2.0% 2.69 [0.76, 4.62] Ye Zhang 2020 a3 0.220312 0.035938 8 0.109375 0.01875 2 1.6% 2.92 [0.66, 5.19] Yujin Zhang 2020 a1 0.130923 0.010465 8 0.120063 0.010465 3 2.6% 0.95 [-0.47, 2.36] Yujin Zhang 2020 a2 0.152049 0.010465 8 0.120063 0.010465 3 1.9% 2.79 [0.82, 4.77] Yujin Zhang 2020 a3 0.151081 0.009302 8 0.120063 0.010465 2 1.6% 2.96 [0.69, 5.24] Z.P 2005 0.5 0.03 11 0.45 0.03 11 3.3% 1.60 [0.62, 2.59] Total (95% Cl) 395 192 100.0% 1.59 [1.22, 1.96] Heterogeneity: Tau ² = 0.80; Chi ² = 99.92, df = 40 (P < 0.00001); P = 60% Test for overall effect: Z = 8.50 (P < 0.00001)	Yan-Ling Feng 2018	729.66	4.81	10	693.79	11.46	10	2.4%	3.91 [2.30, 5.52]	
Ye Zhang 2020 a2 0.190625 0.029688 8 0.109375 0.1875 3 2.0% 2.69 [0.76, 4.62] Ye Zhang 2020 a3 0.220312 0.035938 8 0.109375 0.01875 2 1.6% 2.92 [0.66, 5.19] Yujin Zhang 2020 a1 0.130923 0.010465 8 0.120063 0.010465 3 2.9% 0.95 [0.47, 2.36] Yujin Zhang 2020 a2 0.152049 0.010465 8 0.120063 0.010465 2 1.6% 2.96 [0.69, 5.24] Z.P 2005 0.5 0.03 11 0.45 0.03 11 3.3% 1.60 [0.62, 2.59] Total (95% Cl) 395 192 100.0% 1.59 [1.22, 1.96]	Ye Zhang 2020 a1	0.129688	0.021875	8	0.109375	0.01875	3	2.7%	0.88 [-0.53, 2.28]	
Ye Zhang 2020 a3 0.220312 0.035938 8 0.109375 0.01875 2 1.6% 2.92 [0.66, 5.19] Yujin Zhang 2020 a1 0.130923 0.010465 8 0.120063 0.010465 3 2.6% 0.95 [-0.47, 2.36] Yujin Zhang 2020 a2 0.152049 0.010465 8 0.120063 0.010465 2 1.6% 2.98 [0.69, 5.24] Yujin Zhang 2020 a3 0.151081 0.009302 8 0.120063 0.010465 2 1.6% 2.98 [0.69, 5.24] Z.P 2005 0.5 0.03 11 0.45 0.03 11 3.3% 1.60 [0.62, 2.59] Total (95% Cl) 395 192 100.0% 1.59 [1.22, 1.96]	Ye Zhang 2020 a2	0.190625	0.029688	8	0.109375	0.01875	3	2.0%	2.69 [0.76, 4.62]	
Yujin Zhang 2020 a1 0.130923 0.010465 8 0.120063 0.010465 3 2.6% $0.95 [0.47, 2.36]$ Yujin Zhang 2020 a2 0.152049 0.010465 8 0.120063 0.010465 3 $2.79 [0.82, 4.77]$ Yujin Zhang 2020 a3 0.151081 0.009302 8 0.120063 0.010465 2 1.6% $2.96 [0.69, 5.24]$ Z.P 2005 0.5 0.03 11 0.45 0.03 11 3.3% $1.60 [0.62, 2.59]$ Total (95% Cl) 395 192 100.0% $1.59 [1.22, 1.96]$ -20 -10 0 10 20 Heterogeneity: Tau ² = 0.80; Chi ² = 99.92, df = 40 (P < 0.00001); P = 60\% Test for overall effect: Z = 8.50 (P < 0.00001); P = 60\% $159 [1.22, 1.96]$ -20 -10 0 10 20 Test for overall effect: Z = 8.50 (P < 0.00001) $P < 0.00001$	Ye Zhang 2020 a3	0.220312	0.035938	8	0.109375	0.01875	2	1.6%	2.92 [0.66, 5.19]	
Yujin Zhang 2020 a2 0.152049 0.010465 8 0.120063 0.010465 3 1.9% 2.79 [0.82, 4.77] Yujin Zhang 2020 a3 0.151081 0.009302 8 0.120063 0.010465 2 1.6% 2.96 [0.69, 5.24] Z.P 2005 0.5 0.03 11 0.45 0.03 11 3.3% 1.60 [0.62, 2.59] Total (95% Cl) 395 192 100.0% 1.59 [1.22, 1.96] + Heterogeneity: Tau ² = 0.80; Chi ² = 99.92, df = 40 (P < 0.00001); I ² = 60% 1.59 [1.22, 1.96] + -20 Test for overall effect: Z = 8.50 (P < 0.00001)	Yujin Zhang 2020 a1	0.130923	0.010465	8	0.120063	0.010465	3	2.6%	0.95 [-0.47, 2.36]	
Yujin Zhang 2020 a3 0.151081 0.009302 8 0.120063 0.010465 2 1.6% 2.96 [0.69, 5.24] Z.P 2005 0.5 0.03 11 0.45 0.03 11 3.3% 1.60 [0.62, 2.59] Total (95% Cl) 395 192 100.0% 1.59 [1.22, 1.96] + Heterogeneity: Tau ² = 0.80; Chi ² = 99.92, df = 40 (P < 0.00001); i ² = 60% 1.59 [1.22, 1.96] + - Test for overall effect: Z = 8.50 (P < 0.00001)	Yujin Zhang 2020 a2	0.152049	0.010465	8	0.120063	0.010465	3	1.9%	2.79 [0.82, 4.77]	
Z.P. 2005 0.5 0.03 11 0.45 0.03 11 3.3% 1.60 [0.62, 2.59] Total (95% Cl) 395 192 100.0% 1.59 [1.22, 1.96] ↓ Heterogeneity: Tau ² = 0.80; Chi ² = 99.92, df = 40 (P < 0.00001); I ² = 60% 1.59 [1.22, 1.96] ↓ ↓ Test for overall effect: Z = 8.50 (P < 0.00001)	Yujin Zhang 2020 a3	0.151081	0.009302	8	0.120063	0.010465	2	1.6%	2.96 [0.69, 5.24]	——
Total (95% Cl) 395 192 100.0% 1.59 [1.22, 1.96] Heterogeneity: Tau ² = 0.80; Chi ² = 99.92, df = 40 (P < 0.00001); i ² = 60% 1.59 [1.22, 1.96] -20 -10 0 10 20 Test for overall effect: Z = 8.50 (P < 0.00001)	Z.P 2005	0.5	0.03	11	0.45	0.03	11	3.3%	1.60 [0.62, 2.59]	+
Heterogeneity: Tau ² = 0.80; Chi ² = 99.92, df = 40 (P < 0.00001); l ² = 60% Test for overall effect: Z = 8.50 (P < 0.00001) Favours for overall effect: Z = 8.50 (P < 0.00001)	Total (95% CI)			395			192	100.0%	1.59 [1.22, 1.96]	•
Test for overall effect: Z = 8.50 (P < 0.00001) 10 20 Fayours favorerimentall Favours forontroll	Heterogeneity: Tau ² = 0.	80; Chi² = 99	9.92, df = 40	(P < 0.	.00001); I ² = 6	60%				
	Test for overall effect: Z =	= 8.50 (P < 0	.00001)							-20 -10 0 10 20 Favours (experimental) Favours (control)

Fig. 3 The meta-analysis results of the Res for BMD

	Number	of	SMD	P for	I2	P for subgroup
	group		[95%CI]	subgroup		interactions
	compariso	ns		outcomes		
Models						
Orchiectomy	3		1.76[1.09,2.44]	P<000001	0%	P<000001
Ovariectomy	42		1.59[1.19,1.99]	P<000001	62%	
Test Methods						
Micro-CT	9		1.72[0.67,2.78]	P<001	79%	P<000001
X-ray	36		1.56[1.19,1,93]	P<00001	49%	
Text Positions						
femur	21		1.73[1.23,2,24]	P<00001	59%	P<000001
lumbar spine	12		1.81[1.07,2.54]	P<00001	50%	
tibia	12		1.38[0.66,2.10]	P<001	68%	

Fig. 4 Subgroup analysis of Res for BMD

	Exp	erimental		C	Control			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl
Alice 2014	19.186	0.969	7	22.2868	0.5814	7	5.2%	-3.63 [-5.53, -1.73]	
Isabel F 2014	31.044	3.8461	10	25	3.8462	10	6.7%	1.51 [0.49, 2.52]	
Jing Feng 2014 a1	15	3	8	10	3	3	5.8%	1.52 [-0.02, 3.07]	<u>⊢</u>
Jing Feng 2014 a2	28	3	8	10	3	3	3.3%	5.49 [2.33, 8.64]	
Jing Feng 2014 a3	33	4	8	10	3	2	3.0%	5.34 [1.96, 8.72]	
Liwei Wei 2023	25.0382	2.4427	8	9.16031	1.83209	8	3.5%	6.95 [4.01, 9.90]	
Sewal 2023 a1	9.20455	1.19315	12	8.86364	1.10795	6	6.8%	0.28 [-0.71, 1.26]	
Sewal 2023 a2	9.54545	1.10795	12	8.86364	1.10795	6	6.8%	0.59 [-0.42, 1.59]	+
X. Wang 2022 a1	0.270456	0.14069	8	0.230122	0.124138	4	6.4%	0.27 [-0.93, 1.48]	
X. Wang 2022 a2	0.310768	0.211034	8	0.230122	0.124138	4	6.4%	0.39 [-0.82, 1.61]	
Yan-Ling Feng 2018	36.14	8.62	10	20.88	7.53	10	6.7%	1.81 [0.73, 2.88]	_
Ye Zhang 2020 a1	0.2013	0.074	8	0.2528	0.034	3	6.1%	-0.70 [-2.08, 0.68]	
Ye Zhang 2020 a2	0.361	0.042	8	0.2528	0.034	3	5.3%	2.45 [0.61, 4.29]	
Ye Zhang 2020 a3	0.3629	0.033	8	0.2528	0.034	2	4.5%	3.00 [0.71, 5.29]	
Yixuan Jiang 2020	0.306087	0.045217	4	0.156522	0.048695	4	4.4%	2.77 [0.41, 5.12]	
Yuquan Shi 2022	8.51064	1.06383	8	5.53191	1.06383	8	6.0%	2.65 [1.21, 4.09]	
ZAMA 2020	39.7163	11.9149	11	36.7376	9.9291	11	7.0%	0.26 [-0.58, 1.10]	
Zuozhong Liu 2021	8.2	1.2	6	6.6	0.2	6	6.1%	1.72 [0.31, 3.13]	
Total (95% CI)			152			100	100.0%	1.44 [0.68, 2.19]	
Heterogeneity: Tau ² = 1	.92; Chi ² = 8	33.53, df = 1	7 (P < I	0.00001); l²	= 80%				-10 -5 0 5 10
rest for overall effect: Z	= 3.73 (P =	0.0002)							Favours [experimental] Favours [control]

Fig. 5 The meta-analysis results of Res for BV/TV

	Exp	erimental		0	Control			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl
Haifeng Zhao 2014 a1	5.18	0.74	10	5	0	3		Not estimable	
Haifeng Zhao 2014 a2	6.24	1.12	10	5	0	3		Not estimable	
Haifeng Zhao 2014 a3	6.43	0.86	10	5	0	4		Not estimable	
Isabel F 2014	10.1573	1.7079	10	8.35955	0.62921	10	8.2%	1.34 [0.35, 2.33]	
Jing Feng 2014 a1	2.5	0.5	8	1.8	0.6	3	6.9%	1.22 [-0.25, 2.69]	+
Jing Feng 2014 a2	3.3	0.5	8	1.8	0.6	3	5.8%	2.62 [0.71, 4.52]	
Jing Feng 2014 a3	3.8	0.6	8	1.8	0.6	2	4.9%	3.01 [0.71, 5.31]	
Liwei Wei 2023	4.45802	0.61068	8	2.25954	0.24428	8	5.5%	4.47 [2.43, 6.50]	
X. Wang 2022 a1	3.50336	1.61073	8	3.02013	1.32886	4	7.6%	0.29 [-0.92, 1.50]	<u>-</u>
X. Wang 2022 a2	3.42282	1.85235	8	3.02013	1.32886	4	7.6%	0.22 [-0.99, 1.42]	
Yan-Ling Feng 2018	4.79	0.26	10	2.94	0.79	10	7.2%	3.01 [1.65, 4.37]	
Ye Zhang 2020 a1	3.446	0.858	8	3.178	0.179	3	7.3%	0.32 [-1.02, 1.66]	
Ye Zhang 2020 a2	3.967	0.695	8	3.178	0.179	3	6.9%	1.17 [-0.29, 2.63]	+
Ye Zhang 2020 a3	4.065	0.715	8	3.178	0.179	2	6.4%	1.19 [-0.50, 2.88]	+
Yixuan Jiang 2020	4.17391	0.76522	4	1.98261	0.73043	4	5.1%	2.55 [0.31, 4.78]	
Yuquan Shi 2022	3.19149	0.19149	8	2.17021	0.25532	8	5.7%	4.28 [2.31, 6.25]	
ZAMA 2020	11.2035	2.2341	11	12.0325	2.766	11	8.5%	-0.32 [-1.16, 0.52]	
Zuozhong Liu 2021	0.052973	0.0064865	6	0.0367568	0.0054054	6	6.4%	2.51 [0.84, 4.17]	
T-4-1 (05%) (0)			454				100.0%	4 60 10 05 0 401	
Total (95% CI)			151			91	100.0%	1.68 [0.95, 2.42]	
Heterogeneity: Tau* = 1.4	46; Chi* = 53	30, αf = 14 (P < 0.0	0001); P= 74	1%				-4 -2 0 2 4
rest for overall effect: Z =	= 4.49 (P < U	.00001)							Favours [experimental] Favours [control]

Fig. 6 The meta-analysis results of Res for Tb.N

improve morphometric indices of the trabecular microstructure and serum BTMs concentration, and exert a protective effect on animal models of primary OP.

BMD, a gold standard for diagnosing OP, can be detected via dual-energy X-ray (DXA) or micro-CT. Mizutani K et al. reported that Res can alleviate the decrease in femoral BMD induced by ovariectomy in rats [18, 42], while Li YT et al. suggested that inhibiting bone resorption may be related to the ability of Res to increase BMD because Res can inhibit the production of prostaglandin e2 and interleukin-6 [43]. Kenny reported that the serum testosterone concentration is positively correlated with the BMD, and Res may ameliorate bone loss caused by male hypogonadism by maintaining the balance between RANK and OPG [31]. Therefore, our study evaluated the ability of Res to improve BMD in primary OP patients. This study showed that the BMD in the Res group increased significantly. In addition, the subgroup analysis according to the modeling methods, detection methods or detection positions also yielded significant results. In addition, due to the high heritability of BMD, one study had explored the reason why individual differences exist in the effectiveness of bisphosphonates (a first-line anti-OP drug at present) from the genetics. The findings revealed that, in contrast to rs1544410 A/G, another variant, rs2228570 C/T associated with the vitamin D receptor, exhibited a correlation with a favorable response to antiresorptive therapy. This study prompts us to explore

	Exp	erimental		C	ontrol			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl
Haifeng Zhao 2014 a1	42.96	3.12	10	43.29	2.06	3	6.3%	-0.10 [-1.39, 1.19]	
Haifeng Zhao 2014 a2	52.36	2.14	10	43.29	2.06	3	4.2%	3.97 [1.73, 6.21]	
Haifeng Zhao 2014 a3	58.71	1.24	10	43.29	2.06	4	1.7%	9.70 [5.31, 14.10]	
Isabel F 2014	0.648543	0.13299	10	0.605437	0.127064	10	7.3%	0.32 [-0.57, 1.20]	+-
Jing Feng 2014 a1	61	10	8	47	11	3	5.8%	1.25 [-0.23, 2.73]	
Jing Feng 2014 a2	83	9	8	47	11	3	4.2%	3.47 [1.23, 5.72]	
Jing Feng 2014 a3	86	12	8	47	11	2	4.1%	2.97 [0.69, 5.24]	
Liwei Wei 2023	0.0278626	0.0030534	8	0.0167939	0.0022901	8	5.0%	3.88 [2.05, 5.71]	
Sewal 2023 a1	0.909836	0.040984	12	0.893443	0.040983	6	7.1%	0.38 [-0.61, 1.37]	+-
Sewal 2023 a2	0.92623	0.04918	12	0.893443	0.040983	6	7.0%	0.67 [-0.34, 1.68]	+
X. Wang 2022 a1	0.092069	0.0051724	8	0.0848276	0.0051724	4	6.1%	1.29 [-0.06, 2.65]	
X. Wang 2022 a2	0.105517	0.01138	8	0.0848276	0.0051724	4	5.7%	1.92 [0.40, 3.45]	
Yan-Ling Feng 2018	78.67	14.76	10	51.8	3.74	10	6.5%	2.39 [1.19, 3.60]	
Ye Zhang 2020 a1	0.0712	0.027	8	0.0627	0.015	3	6.2%	0.31 [-1.02, 1.65]	
Ye Zhang 2020 a2	0.0946	0.016	8	0.0627	0.015	3	5.5%	1.85 [0.21, 3.49]	
Ye Zhang 2020 a3	0.1072	0.049	8	0.0627	0.015	2	5.5%	0.87 [-0.75, 2.50]	
Yuquan Shi 2022	0.0421053	0.0025263	8	0.0311579	0.0042105	8	5.7%	2.98 [1.44, 4.52]	
Zuozhong Liu 2021	3.22078	0.62338	6	2.38961	0.31169	6	6.1%	1.56 [0.19, 2.92]	
Total (95% Cl) Heterogeneity: Tau ² = 1.2	26; Chi ² = 58.	15, df = 17 (P	160 • < 0.00	001); I² = 719	6	88	100.0 %	1.73 [1.09, 2.37]	-10 -5 0 5 10
l est for overall effect: Z =	: 5.30 (P < 0.0	0001)							Favours [experimental] Favours [control]

Fig. 7 The meta-analysis results of Res for Tb.Th

	Exp	erimental		0	Control		9	Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl
Haifeng Zhao 2014 a1	167.24	8.28	10	179.06	9.38	3	5.3%	-1.30 [-2.72, 0.13]	
Haifeng Zhao 2014 a2	132.44	10.63	10	179.06	9.38	3	3.6%	-4.16 [-6.48, -1.85]	
Haifeng Zhao 2014 a3	117.24	9.54	10	179.06	9.38	4	2.7%	-6.09 [-9.00, -3.19]	
Isabel F 2014	0.075887	0.0131154	10	0.100782	0.020984	10	6.3%	-1.36 [-2.36, -0.37]	
Jing Feng 2014 a1	0.44	0.04	8	0.49	0.07	3	5.4%	-0.95 [-2.36, 0.47]	
Jing Feng 2014 a2	0.28	0.08	8	0.49	0.07	3	4.4%	-2.47 [-4.31, -0.62]	<u> </u>
Jing Feng 2014 a3	0.25	0.06	8	0.49	0.07	2	3.2%	-3.53 [-6.06, -1.01]	<u> </u>
Liwei Wei 2023	0.122137	0.016103	8	0.169466	0.016794	8	5.2%	-2.72 [-4.18, -1.26]	
Sewal 2023 a1	3.91813	0.32164	12	4.06433	0.2924	6	6.3%	-0.45 [-1.44, 0.55]	
Sewal 2023 a2	3.74269	0.23392	12	4.06433	0.2924	6	6.1%	-1.21 [-2.28, -0.13]	
X. Wang 2022 a1	0.310067	0.15302	8	0.374497	0.1651	4	5.8%	-0.38 [-1.59, 0.83]	
X. Wang 2022 a2	0.326174	0.165101	8	0.374497	0.1651	4	5.8%	-0.27 [-1.48, 0.94]	
Yan-Ling Feng 2018	0.13	0.02	10	0.24	0.04	10	5.3%	-3.33 [-4.78, -1.88]	
Ye Zhang 2020 a1	0.326	0.047	8	0.3691	0.024	3	5.4%	-0.92 [-2.33, 0.49]	
Ye Zhang 2020 a2	0.1641	0.054	8	0.3691	0.024	3	3.4%	-3.83 [-6.23, -1.43]	
Ye Zhang 2020 a3	0.1528	0.075	8	0.3691	0.024	2	3.7%	-2.76 [-4.96, -0.57]	
Yixuan Jiang 2020	0.410949	0.066373	4	0.719168	0.181421	4	4.2%	-1.96 [-3.90, -0.03]	
Yuquan Shi 2022	0.238298	0.025532	8	0.285106	0.017022	8	5.7%	-2.04 [-3.31, -0.77]	
ZAMA 2020	0.0515	0.008	11	0.048	0.0095	11	6.7%	0.38 [-0.46, 1.23]	+
Zuozhong Liu 2021	0.261333	0.032	6	0.309333	0.010667	6	5.3%	-1.86 [-3.31, -0.41]	
Total (95% CI)			175			103	100.0%	-1.76 [-2.35, -1.16]	◆
Heterogeneity: Tau ² = 1.1	19; Chi ² = 64	.04. df = 19 (P < 0.0	0001); I ² = 7	70%			-	
Test for overall effect: Z =	= 5.80 (P < 0.	.00001)							-4 -2 U 2 4
									Favours (experimental) Favours (control)

Fig. 8 The meta-analysis results of Res for Tb.Sp

whether the genetic characteristics of diverse primary OP conditions influence the efficacy of resveratrol in improving BMD, given its promising results [44].

It is well-known that the morphometric indices of the trabecular microstructure play a vital role in the diagnosis of osteoporosis [45]. The BV/TV is one of the key indices of trabecular microstructure, and an increase in this parameter indicates that bone anabolism is more common than catabolism and that the bone mass is greater, and vice versa. Ozturk S et al. reported that Res (80 mg/kg/day) can reduce the BV/TV, Tb.N and Tb.Th and prevent a sharp decrease in bone mass caused by ovariectomy by improving the microstructure and

biophysical and chemical properties of bone [27]. Therefore, our study evaluated the BV/TV in an animal model of primary OP and revealed that Res can improve bone mass and bone metabolism by increasing the BV/TV. In addition, Tb.Th, Tb.N, and Tb.Sp are the primary parameters used to evaluate the spatial morphological structure of trabecular bone. Once osteoporosis occurs, the Tb.Sp increases, while the Tb.N and Tb.Th decrease. Therefore, by evaluating the above three indices, this study revealed that Res can increase the Tb.Th and Tb.N while reducing the Tb.Sp, thus improving bone loss in an animal model of OP.

	Exp	erimental		0	Control			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl
Alice 2014	113.298	7.979	7	90.1596	0	7		Not estimable	
Basem H 2021	278.967	11.07	10	241.328	59.779	10	8.3%	0.84 [-0.08, 1.76]	
Haifeng Zhao 2014 a1	289.3	17.35	10	290.5	17.29	3	8.0%	-0.06 [-1.35, 1.23]	
Haifeng Zhao 2014 a2	236	9.38	10	290.5	17.29	3	6.7%	-4.51 [-6.96, -2.07]	
Haifeng Zhao 2014 a3	231.3	11.47	10	290.5	17.29	4	7.0%	-4.21 [-6.38, -2.03]	
Hussein 2023 a1	431.25	65.625	8	262.5	46.875	8	7.8%	2.80 [1.31, 4.28]	
Jing Feng 2014 a1	194.3	42.6	8	237.1	39.2	3	7.9%	-0.93 [-2.35, 0.48]	
Jing Feng 2014 a2	171.8	47.4	8	237.1	39.2	3	7.8%	-1.31 [-2.80, 0.19]	
Jing Feng 2014 a3	160.8	39.6	8	237.1	39.2	2	7.4%	-1.74 [-3.58, 0.09]	
Mohamed M 2021	516.7	10.19	6	707.7	12.27	6	2.2%	-15.63 [-23.35, -7.92]	←
Ye Zhang 2020 a1	58.3486	12.1101	8	55.0459	12.1101	3	8.0%	0.25 [-1.08, 1.58]	_
Ye Zhang 2020 a2	83.6697	18.7153	8	55.0459	12.1101	3	7.8%	1.50 [-0.04, 3.04]	
Ye Zhang 2020 a3	85.8716	18.7154	8	55.0459	12.1101	2	7.5%	1.54 [-0.23, 3.32]	+
Yujin Zhang 2020 a1	114.362	4.371	8	149.152	10.68	3	6.1%	-5.02 [-7.95, -2.08]	
Yujin Zhang 2020 a2	79.0096	3.8834	8	149.152	10.68	3	3.3%	-10.53 [-16.18, -4.88]	<
Yujin Zhang 2020 a3	86.3719	6.3112	8	149.152	10.68	2	4.0%	-8.09 [-12.90, -3.28]	←
Total (95% CI)			133			65	100.0%	-1.69 [-3.01, -0.37]	•
Heterogeneity: Tau ² = 5.1	19; Chi ² = 1	09.10, df=	= 14 (P	< 0.00001); l² = 87%				-4 -2 0 2 4
Test for overall effect: Z =	: 2.52 (P =	0.01)							Favours (experimental) Favours (control)

Fig. 9 The meta-analysis results of Res for ALP

	Exp	erimental		C	Control			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl
Liwei Wei 2023	9.64885	1.09925	8	6.10687	0.85496	8	35.7%	3.40 [1.73, 5.07]	-
Omnia Ameen 2020	464.73	380.5232	10	771.784	275.55	10	36.8%	-0.89 [-1.81, 0.04]	-
Yuquan Shi 2022	0.349296	0.014084	8	0.174648	0.014084	8	27.5%	11.72 [6.94, 16.50]	_
Total (95% CI)			26			26	100.0%	4.11 [-0.77, 8.99]	-
Heterogeneity: Tau² = 1 Test for overall effect: Z	6.60; Chi² = := 1.65 (P =	41.25, df= 0.10)	2 (P < I	0.00001); I ^z	= 95%				-20 -10 0 10 20 Favours (experimental) Favours (control)

Fig. 10 The meta-analysis results of Res for bALP

	Expe	rimental		0	Control			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl
Alice 2014	0.0734375	0.00625	7	0.146875	0.010938	7	6.2%	-7.72 [-11.25, -4.19]	←
Basem H 2021	323.247	26.568	10	232.472	33.211	10	10.7%	2.89 [1.56, 4.22]	
Hussein 2023 a1	412.5	84.375	8	276.563	56.25	8	11.0%	1.79 [0.58, 3.01]	
Isabel F 2014	5.80645	3.46774	10	8.54839	5.08061	10	11.5%	-0.60 [-1.50, 0.30]	
Jing Feng 2014 a1	45.5	10.8	8	49.7	9.1	3	10.7%	-0.37 [-1.71, 0.97]	
Jing Feng 2014 a2	40.5	16.4	8	49.7	9.1	3	10.7%	-0.56 [-1.92, 0.80]	
Jing Feng 2014 a3	37.1	10.9	8	49.7	9.1	2	10.0%	-1.06 [-2.73, 0.60]	
Yujin Zhang 2020 a1	2.26471	0.11764	8	2.5	0.08824	3	10.0%	-1.92 [-3.59, -0.26]	
Yujin Zhang 2020 a2	2.08824	0.17647	8	2.5	0.08824	3	9.7%	-2.34 [-4.14, -0.54]	
Yujin Zhang 2020 a3	2.17647	0.14706	8	2.5	0.08824	2	9.4%	-2.07 [-4.01, -0.13]	
Total (95% CI)			83			51	100.0%	-0.86 [-2.11, 0.39]	
Heterogeneity: Tau ² = 3.33; Chi ² = 63.67, df = 9 (P < 0.00001); I ² = 86%									
Test for overall effect: Z	C = 1.35 (P = 0).18)							Favours (experimental) Favours (control)

Fig. 11 The meta-analysis results of Res for OC

Intermediate metabolites or enzymes produced during bone turnover are called serum BTMs. BTMs can be classified as bone formation or bone resorption markers. The former indicates osteoblast activity and bone formation, such as ALP, bALP and OC, while the latter reflects osteoclast activity and bone resorption, such as CTX-1 and TRAP5b. BTMs play a role in diagnosing various bone diseases, determining bone turnover types, predicting the risk of fracture, monitoring treatment compliance and evaluating drug efficacy [22, 36, 40]. The level of BTMs in primary OP is usually normal or slightly elevated. Feng J et al. reported that Res inhibits the generation of osteoclasts in OVX rats by decreasing RANKL and TRAP5b and increasing OPG. This difference may be related to the antiapoptotic, antioxidative and antiinflammatory effects of Res [26]. Elesawy reported that chronic administration of Res can significantly improve the BMD of the tibia, and the protective mechanism

	Exp	erimental			Control			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl
Basem H 2021	176.852	11.111	10	96.2963	37.9627	10	14.8%	2.76 [1.46, 4.05]	
Hussein 2023 a1	191.406	17.578	8	95.7031	19.5309	8	10.5%	4.87 [2.69, 7.05]	
Liwei Wei 2023	1.64122	0.19084	8	1.22137	0.13359	8	14.4%	2.41 [1.04, 3.78]	
X. Wang 2022 a1	0.4	0.076923	8	0.3	0.069231	4	14.6%	1.24 [-0.11, 2.58]	
X. Wang 2022 a2	0.653846	0.084615	8	0.3	0.069231	4	9.9%	4.07 [1.75, 6.39]	
Ye Zhang 2020 a1	77.3289	10	8	76.2426	11.6592	3	14.7%	0.10 [-1.23, 1.42]	+
Ye Zhang 2020 a2	133.713	18.333	8	76.2426	11.6592	3	10.9%	3.08 [0.99, 5.16]	_ →
Ye Zhang 2020 a3	136.756	20	8	76.2426	11.6592	2	10.2%	2.85 [0.62, 5.08]	
Total (95% CI) 66 4								2.49 [1.45, 3.53]	•
Heterogeneity: Tau ² = 1.47; Chi ² = 21.71, df = 7 (P = 0.003); l ² = 68%									
Test for overall effect: Z = 4.68 (P < 0.00001)									Foregran Foregran Foregran Foregran
									Favou's (experimental) Favou's (control)

Fig. 12 The meta-analysis results of Res for OPG

	Experimental			Control				Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% Cl	IV, Fixed, 95% CI
Liwei Wei 2023	21.0687	2.1374	8	28.7023	3.3588	8	18.1%	-2.56 [-3.98, -1.15]	
Mohamed M 2021	4.238	0	6	6.4	0.6099	6		Not estimable	
Ye Zhang 2020 a1	566.667	83.333	8	666.667	100	3	17.6%	-1.05 [-2.48, 0.39]	
Ye Zhang 2020 a2	358.333	50	8	666.667	100	3	5.2%	-4.37 [-7.00, -1.73]	
Ye Zhang 2020 a3	350	50	8	666.667	100	2	3.6%	-4.88 [-8.03, -1.72]	
Yixuan Jiang 2020	26.25	3	4	33.25	3	4	9.4%	-2.03 [-4.00, -0.06]	
Yujin Zhang 2020 a1	367.647	34.314	8	406.863	24.51	3	17.3%	-1.11 [-2.55, 0.34]	
Yujin Zhang 2020 a2	348.039	44.118	8	406.863	24.51	3	16.2%	-1.33 [-2.82, 0.17]	
Yujin Zhang 2020 a3	348.039	44.118	8	406.863	24.51	2	12.5%	-1.26 [-2.96, 0.44]	
Total (95% CI)			66			34	100.0%	-1.81 [-2.41, -1.21]	•
Heterogeneity: Chi ² = 1	1.18, df = 7	7 (P = 0.1	3); I² =	37%				-	
Test for overall effect: Z = 5.88 (P < 0.00001)									Favours [experimental] Favours [control]

Fig. 13 The meta-analysis results of Res for CTX-1

	Exp	erimental		0	Control		:	Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl
Basem H 2021	13.9453	1.4444	10	22.1452	3	10	16.7%	-3.34 [-4.78, -1.89]	-
Hussein 2023 a1	13.125	2.1094	8	20.625	4.6875	8	17.2%	-1.95 [-3.20, -0.70]	
Liwei Wei 2023	1.80916	0.16031	8	2.54198	0.20611	8	15.6%	-3.75 [-5.54, -1.96]	
Ye Zhang 2020 a1	640.347	95.575	8	698.813	103.54	3	16.9%	-0.55 [-1.91, 0.81]	
Ye Zhang 2020 a2	224.83	39.823	8	698.813	103.54	3	9.1%	-7.21 [-11.19, -3.22]	
Ye Zhang 2020 a3	191.615	39.823	8	698.813	103.54	2	6.7%	-8.77 [-13.95, -3.60]	
Yuquan Shi 2022	11.3028	0.6338	8	11.1972	0.6338	8	17.9%	0.16 [-0.82, 1.14]	+
Total (95% CI) 58 42							100.0%	-2.78 [-4.44, -1.12]	▲
Heterogeneity: Tau ² = 3.75; Chi ² = 40.95, df = 6 (P < 0.00001); l ² = 85%									-20 -10 0 10 20
Test for overall effect: Z = 3.29 (P = 0.001)									Favours (experimental) Favours (control)

Fig. 14 The meta-analysis results of Res for TRAP5b

may involve increasing the levels of OC, OPG and ALP [22]. Therefore, the present study showed that ALP, CTX-1 and TRAP5b in the Res group were significantly decreased, and OC tended to decrease. In addition, bALP showed an opposite trend to that of the other indicators, which may be due to the small amount of data. OPG is a metabolite secreted by osteoblasts and can inhibit the formation of osteoclasts by competitively binding with RANK [22, 36, 40]. Our results showed that the OPG in the Res group increased significantly, which improved the state of primary OP. In addition to the above markers,

there are other bone metabolic intermediates, including p1np, p1cp, LCa/Cr, dpyr, and ntx [45, 46]. Unfortunately, this review did not pursue further investigation due to challenges in acquiring adequate data.

The study limitations were as follows: (1) Language bias; (2) the reliability of the risk of bias assessment was limited to low-quality included studies; and (3) most of the results were highly heterogeneous; however, we performed a subgroup analysis. The results of the sensitivity analysis were robust (Additional file 1).

Conclusions

Res can markedly increase BMD, improve morphometric indices of the trabecular microstructure and serum BTM concentration, and exert a protective effect on animal models of primary osteoporosis. This study can provide an experimental reference for Res in primary OP. In the future, additional studies are needed to evaluate the effects of Res as an anti-primary OP drug.

Abbreviations

Res	Resveratrol
OP	Osteoporosis
BMD	Bone mineral density
BP	Bisphosphonates
SERM	Estrogen receptor modulators
CI	Confidence interval
SMD	Standardized mean difference
BV/TV	Bone volume/total volume
Tb.N	Trabecular number
Tb.Th	Trabecular thickness
Tb.Sp	Trabecular separation
OC	Osteocalcin
ALP	Alkaline phosphatase
OPG	Serum osteoprotegerin
bALP	Bone alkaline phosphatase
CTX-1	Type I collagen strong carboxyl peptide
TRAP5b	Tartrate-resistant acid phosphatase 5b
BTMs	Bone turnover markers
OVX	Ovariectomized
SEM	Standard error of the mean
SD	Standard deviation

Supplementary Information

The online version contains supplementary material available at https://doi. org/10.1186/s13018-024-04595-1.

Additional file 1. PRISMA checklist.

Author contributions

RA and QL designed the study. RA drafted the manuscript. RA, QL, LL, and DC were responsible for the collection and analysis of the research information. LL, DC and JJ carefully revised the manuscript. All the authors read and approved the final manuscript.

Funding

This research was supported by the National Natural Science Foundation of China (No. 82360441) and by projects funded by the Science and Technology Department of Jilin Province (No. 20200201492JC and YDZJ202201ZYTS161).

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Received: 14 November 2023 Accepted: 28 January 2024 Published online: 13 February 2024

References

- Liang H, Xiong C, Luo Y, Zhang J, Huang Y, Zhao R, et al. Association between serum polyunsaturated fatty acids and bone mineral density in US adults: NHANES 2011–2014. Front Endocrinol (Lausanne). 2023;14:1266329.
- Yang Y, Liu Z, Wu J, Bao S, Wang Y, Li J, et al. Nrf2 mitigates RANKL and M-CSF induced osteoclast differentiation via ROS-dependent mechanisms. Antioxidants (Basel). 2023;12(12):2094.
- Orsini LS, Rousculp MD, Long SR, Wang S. Health care utilization and expenditures in the United States: a study of osteoporosis-related fractures. Osteoporos Int. 2005;16(4):359–71.
- Roche JJ, Wenn RT, Sahota O, Moran CG. Effect of comorbidities and postoperative complications on mortality after hip fracture in elderly people: prospective observational cohort study. BMJ. 2005;331(7529):1374.
- Migliorini F, Colarossi G, Eschweiler J, Oliva F, Driessen A, Maffulli N. Antiresorptive treatments for corticosteroid-induced osteoporosis: a Bayesian network meta-analysis. Br Med Bull. 2022;143(1):46–56.
- Migliorini F, Maffulli N, Colarossi G, Eschweiler J, Tingart M, Betsch M. Effect of drugs on bone mineral density in postmenopausal osteoporosis: a Bayesian network meta-analysis. J Orthop Surg Res. 2021;16(1):533.
- Migliorini F, Giorgino R, Hildebrand F, Spiezia F, Peretti GM, Alessandri-Bonetti M, et al. Fragility fractures: risk factors and management in the elderly. Medicina (Kaunas). 2021;57(10):1119.
- Migliorini F, Colarossi G, Baroncini A, Eschweiler J, Tingart M, Maffulli N. Pharmacological management of postmenopausal osteoporosis: a level I evidence based - expert opinion. Expert Rev Clin Pharmacol. 2021;14(1):105–19.
- Rossouw JE, Anderson GL, Prentice RL, LaCroix AZ, Kooperberg C, Stefanick ML, et al. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results From the Women's Health Initiative randomized controlled trial. JAMA. 2002;288(3):321–33.
- Baolin L, Inami Y, Tanaka H, Inagaki N, linuma M, Nagai H. Resveratrol inhibits the release of mediators from bone marrow-derived mouse mast cells in vitro. Planta Med. 2004;70(4):305–9.
- Dai Z, Li Y, Quarles LD, Song T, Pan W, Zhou H, et al. Resveratrol enhances proliferation and osteoblastic differentiation in human mesenchymal stem cells via ER-dependent ERK1/2 activation. Phytomedicine. 2007;14(12):806–14.
- Knutson MD, Leeuwenburgh C. Resveratrol and novel potent activators of SIRT1: effects on aging and age-related diseases. Nutr Rev. 2008;66(10):591–6.
- Novakovic R, Ilic B, Beleslin-Cokic B, Radunovic N, Heinle H, Scepanovic R, et al. The effect of resveratrol on contractility of non-pregnant rat uterus: the contribution of K(+) channels. J Physiol Pharmacol. 2013;64(6):795–805.
- Boissy P, Andersen TL, Abdallah BM, Kassem M, Plesner T, Delaissé JM. Resveratrol inhibits myeloma cell growth, prevents osteoclast formation, and promotes osteoblast differentiation. Cancer Res. 2005;65(21):9943–52.
- Lee AM, Shandala T, Nguyen L, Muhlhausler BS, Chen KM, Howe PR, et al. Effects of resveratrol supplementation on bone growth in young rats and microarchitecture and remodeling in ageing rats. Nutrients. 2014;6(12):5871–87.
- Picard F, Kurtev M, Chung N, Topark-Ngarm A, Senawong T, Machado De Oliveira R, et al. Sirt1 promotes fat mobilization in white adipocytes by repressing PPAR-gamma. Nature. 2004;429(6993):771–6.
- Liu ZP, Li WX, Yu B, Huang J, Sun J, Huo JS, et al. Effects of trans-resveratrol from Polygonum cuspidatum on bone loss using the ovariectomized rat model. J Med Food. 2005;8(1):14–9.
- Mizutani K, Ikeda K, Kawai Y, Yamori Y. Resveratrol attenuates ovariectomyinduced hypertension and bone loss in stroke-prone spontaneously hypertensive rats. J Nutr Sci Vitaminol (Tokyo). 2000;46(2):78–83.

- Zhao H, Li X, Li N, Liu T, Liu J, Li Z, et al. Long-term resveratrol treatment prevents ovariectomy-induced osteopenia in rats without hyperplastic effects on the uterus. Br J Nutr. 2014;111(5):836–46.
- Hooijmans CR, Rovers MM, de Vries RB, Leenaars M, Ritskes-Hoitinga M, Langendam MW. SYRCLE's risk of bias tool for animal studies. BMC Med Res Methodol. 2014;14:43.
- Ameen O, Yassien RI, Naguib YM. Activation of FoxO1/SIRT1/RANKL/ OPG pathway may underlie the therapeutic effects of resveratrol on aging-dependent male osteoporosis. BMC Musculoskelet Disord. 2020;21(1):375.
- 22. Basem H, Elesawy HFS, Amr M. Synergistic protective effects of resveratrol and estradiol on estrogen deficiency-induced osteoporosis through attenuating RANK pathway. Int J Pharmacol. 2021;4:217–28.
- Chen XH, Shi ZG, Lin HB, Wu F, Zheng F, Wu CF, et al. Resveratrol alleviates osteoporosis through improving the osteogenic differentiation of bone marrow mesenchymal stem cells. Eur Rev Med Pharmacol Sci. 2019;23(14):6352–9.
- Elseweidy MM, El-Swefy SE, Shaheen MA, Baraka NM, Hammad SK. Effect of resveratrol and mesenchymal stem cell monotherapy and combined treatment in management of osteoporosis in ovariectomized rats: role of SIRT1/FOXO3a and Wnt/β-catenin pathways. Arch Biochem Biophys. 2021;703: 108856.
- Feng J, Liu S, Ma S, Zhao J, Zhang W, Qi W, et al. Protective effects of resveratrol on postmenopausal osteoporosis: regulation of SIRT1-NF-kB signaling pathway. Acta Biochim Biophys Sin (Shanghai). 2014;46(12):1024–33.
- Feng YL, Jiang XT, Ma FF, Han J, Tang XL. Resveratrol prevents osteoporosis by upregulating FoxO1 transcriptional activity. Int J Mol Med. 2018;41(1):202–12.
- Jiang Y, Luo W, Wang B, Wang X, Gong P, Xiong Y. Resveratrol promotes osteogenesis via activating SIRT1/FoxO1 pathway in osteoporosis mice. Life Sci. 2020;246: 117422.
- Khera A, Kanta P, Kalra J, Dumir D, M T. Resveratrol restores the level of key inflammatory cytokines and RANKL/OPG ratio in the femur of rat osteoporosis model. J Women Aging. 2019;31(6):540–52.
- Lin Q, Huang YM, Xiao BX, Ren GF. Effects of resveratrol on bone mineral density in ovarectomized rats. Int J Biomed Sci. 2005;1(1):76–81.
- Ozturk S, Cuneyit I, Altuntas F, Karagur ER, Donmez AC, Ocak M, et al. Resveratrol prevents ovariectomy-induced bone quality deterioration by improving the microarchitectural and biophysicochemical properties of bone. J Bone Miner Metab. 2023;41(4):443–56.
- Sakr HF, Ammar B, AlKharusi A, Al-Lawati I, AlKhateeb M, Elesawy BH. Resveratrol modulates bone mineral density and bone mineral content in a rat model of male hypogonadism. Chin J Integr Med. 2023;29(2):146–54.
- Sehmisch S, Hammer F, Christoffel J, Seidlova-Wuttke D, Tezval M, Wuttke W, et al. Comparison of the phytohormones genistein, resveratrol and 8-prenylnaringenin as agents for preventing osteoporosis. Planta Med. 2008;74(8):794–801.
- Tresguerres IF, Tamimi F, Eimar H, Barralet J, Torres J, Blanco L, et al. Resveratrol as anti-aging therapy for age-related bone loss. Rejuvenation Res. 2014;17(5):439–45.
- Wang W, Zhang LM, Guo C, Han JF. Resveratrol promotes osteoblastic differentiation in a rat model of postmenopausal osteoporosis by regulating autophagy. Nutr Metab (Lond). 2020;17:29.
- Wang X, Lu C, Chen Y, Wang Q, Bao X, Zhang Z, et al. Resveratrol promotes bone mass in ovariectomized rats and the SIRT1 rs7896005 SNP is associated with bone mass in women during perimenopause and early postmenopause. Climacteric. 2023;26(1):25–33.
- Wei L, Chai S, Yue C, Zhang H, Li J, Qin N. Resveratrol protects osteocytes against oxidative stress in ovariectomized rats through AMPK/JNK1dependent pathway leading to promotion of autophagy and inhibition of apoptosis. Cell Death Discov. 2023;9(1):16.
- Yuquan Shi CK, Li Y. Resveratrol inhibits osteoporosis in mice model. Mater Express. 2022;12:939–47.
- Zamai RS, Corrêa MG, Ribeiro FV, Cirano FR, Casati MZ, Messora MR, et al. Does resveratrol favor peri-implant bone repair in rats with ovariectomyinduced osteoporosis? Gene expression, counter-torque and micro-CT analysis. Braz Oral Res. 2023;37: e003.
- Zhang Y, Deng L, Fan J, Zhang Y. Effects of resveratrol on bone metabolism and bone turnover related indexes in ovariectomized osteoporosis rats. Cell Mol Biol Noisy-le-grand. 2020;66(5):92–7.

- Zhang Y, Liu MW, He Y, Deng N, Chen Y, Huang J, et al. Protective effect of resveratrol on estrogen deficiency-induced osteoporosis though attenuating NADPH oxidase 4/nuclear factor kappa B pathway by increasing miR-92b-3p expression. Int J Immunopathol Pharmacol. 2020;34:2058738420941762.
- Zuozhong Liu CS, Huang L, Yiming Qu. Resveratrol facilitates bone marrow mesenchymal stem cells (BMSCs) differentiation to prevent osteoporosis via restraining of secreted frizzled-related protein 1 expression. Mater Express. 2021;11(10):1636–44.
- 42. Mizutani K, Ikeda K, Kawai Y, Yamori Y. Resveratrol stimulates the proliferation and differentiation of osteoblastic MC3T3-E1 cells. Biochem Biophys Res Commun. 1998;253(3):859–63.
- Li YTZM, Deng YJ, Zhu XY, Cheng GF. Expression of interleukin-6 in delayed type hypersensitivity and inhibition effects of resveratrol on interleukin-6 biosynthesis Yao Hsueh Hsueh Pao. ACTA PHARMACEUTICA SINICA. 1999;34:189–91.
- 44. Conti V, Russomanno G, Corbi G, Toro G, Simeon V, Filippelli W, et al. A polymorphism at the translation start site of the vitamin D receptor gene is associated with the response to anti-osteoporotic therapy in postmenopausal women from southern Italy. Int J Mol Sci. 2015;16(3):5452–66.
- Migliorini F, Maffulli N, Spiezia F, Tingart M, Maria PG, Riccardo G. Biomarkers as therapy monitoring for postmenopausal osteoporosis: a systematic review. J Orthop Surg Res. 2021;16(1):318.
- Migliorini F, Maffulli N, Spiezia F, Peretti GM, Tingart M, Giorgino R. Potential of biomarkers during pharmacological therapy setting for postmenopausal osteoporosis: a systematic review. J Orthop Surg Res. 2021;16(1):351.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.