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Complete List of Authors:	Jepsen, Ditte; Odense Universitetshospital, Department of Geriatric Medicine; Syddansk Universitet Det Sundhedsvidenskabelige Fakultet, Institute of Clinical Research Thomsen , Katja ; Odense Universitetshospital, Department of geriatric medicine; Syddansk Universitet Det Sundhedsvidenskabelige Fakultet, Institute of Clinical Research Hansen, Stinus; Odense Universitetshospital, Department of Endocrinology; Syddansk Universitet Det Sundhedsvidenskabelige Fakultet, Institute of Clinical Research Jørgensen, Niklas; Syddansk Universitet Det Sundhedsvidenskabelige Fakultet, OPEN- Odense Patient data Explorative Network; Rigshospitalet, Department of Clinical Biochemistry Masud, Tahir ; Nottingham University Hospitals NHS Trust, Department of Geriatric Medicine; Syddansk Universitet Det Sundhedsvidenskabelige Fakultet, Institute of Clinical Research Ryg, Jesper; Odense University Hospital, Department of Geriatric Medicine; Syddansk Universitet Det Sundhedsvidenskabelige Fakultet, Institute of Clinical Research
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The Effect Of Whole Body Vibration Exercise In Preventing Falls And Fractures: A Systematic Review And Meta-analysis

Ditte Beck Jepsen, MD, PhD student[1,2], Ditte.Beck.Jepsen2@syd.dk
Katja Thomsen, MD, PhD, ass. Professor[2,3], Katja.Thomsen@rsyd.dk
Stinus Hansen MD, PhD[2,4], Stinus.Jorn.Hansen@rsyd.dk
Niklas Rye Jørgensen MD, Professor[5,6], Niklas.Rye.Joergensen@regionh.dk
Tahir Masud MD, Professor[1,2,7], Tahir.Masud@nuh.nhs.uk
Jesper Ryg, MD, PhD, ass. Professor[1,2], Jesper.Ryg@rsyd.dk

1: Department of Geriatric Medicine, Odense University Hospital, Denmark

2: Institute of Clinical Research, University of Southern Denmark, Denmark

3: Department of Geriatric Medicine, Odense University Hospital, Svendborg, Denmark

4: Department of Endocrinology, Odense University Hospital, Denmark

5: Department of Clinical Biochemistry, Rigshospitalet, Denmark

6: OPEN- Odense Patient data Explorative Network, Odense University Hospital/ University of Southern Denmark

7: Department of Geriatric Medicine, Nottingham University Hospitals Trust NHS, United Kingdom

Corresponding author
Ditte Beck Jepsen

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Abstract

Objective - To investigate the effect of Whole Body Vibration exercise (WBV) on fracture risk in adults ≥ 50 years of age.

Design - A systematic review and meta-analysis calculating relative risk ratios, fall rate ratio, and absolute weighted mean difference using random effects models. Heterogeneity was estimated using I^2 statistics and Cochrane Collaboration's risk of bias tool and the GRADE approach were used to evaluate quality of evidence and summarize conclusions.

Data sources - the databases PubMed, EMBASE, and the Cochrane Central Register from inception to April 2016, and reference lists of retrieved publications.

Eligibility criteria for selecting studies - randomized controlled trials examining the effect of WBV on fracture risk in adults ≥ 50 years of age. The primary outcomes were fractures, fall rates, and the proportion of participants who fell. Secondary outcomes were bone mineral density (BMD), bone microarchitecture, bone turnover markers, and calcaneal broadband attenuation (BUA).

Results - 15 papers (14 trials) met the inclusion criteria. Only one study had fracture data reporting a non-significant fracture reduction (RR=0.47, 95% CI 0.14-1.57, p=0.22) (Moderate quality of evidence). Four studies (n=746) showed that WBV reduced the rate of falls with a rate ratio of 0.67 (95% CI 0.50-0.89, p=0.0006; I^2=19%) (moderate quality of evidence). Furthermore, data from three studies (n=805) found a trend towards falls reduction (RR=0.76, 95% CI 0.48-1.20, p=0.24; I^2=24%) (low quality of evidence). Finally moderate to low quality of evidence showed no overall effect on BMD and only sparse data were available regarding microarchitecture parameters, bone turnover markers, and BUA.

Conclusions - WBV reduces fall rate, but seems to have no overall effect on BMD or microarchitecture. The impact of WBV on fractures requires further larger adequately powered studies. This meta-analysis suggests that WBV may prevent fractures by reducing falls.

Systematic review registration - PROSPERO ID CRD42016036320.

Key words:
Whole-body vibration, WBV, Exercise, Fractures, Accidental falls, Bone strength, BMD, Meta-analysis

Strengths and limitations of this study

- This is the first systematic review comprehensively conducting a meta-analysis on the effect of Whole Body Vibration exercise (WBV) on the overall risk of fractures, including falls
- An extensive systematic literature search identified all available randomised controlled trials using WBV in adults aged 50 on falls, fractures, and bone parameters
- A risk of selection bias exists due to no inclusion of non-English language literature, grey literature, or adverse effects

Introduction

Fragility fractures are associated with much morbidity, mortality, and cost to society (1, 2). In Europe, the direct medical cost of these fractures has been estimated at 31.7 billion Euros per year, expected to rise to 76.7 billion Euros by 2050 (3). Propensity to fall and osteoporosis are the major determinants of fragility fractures (1, 4, 5).

One third of the population over 65 years of age falls at least once a year (6). Increasing age, frailty, comorbidity, reduced muscle strength, and impaired balance contribute to the risk of falls (4, 6). In Europe 22 million women and 5.5 million men were estimated to have osteoporosis in 2010 (1). WHO criteria for diagnosing osteoporosis is based on measurement of bone mineral density (BMD), but there are also other important aspects of bone fragility including microarchitecture and bone turnover (7, 8). The combination of age-related bone loss and an increased risk of falls, cause a higher incidence of fragility fractures in people aged 50 years or more (1, 9). With an aging population the increased cost caused by fragility fractures poses a significant challenge to healthcare systems (1, 3). Reducing fracture risk with the dual approach of lowering fall risk and enhancing bone strength is therefore desirable (10).

Whole body vibration exercise (WBV) has been proposed as an exercise modality anabolic to bone, capable of enhancing balance, and improving muscle strength (11-14). Animal studies have showed that mechanical signals introduced via vibration stimulate bone formation and suppress bone resorption (15-17). The accelerations from vibration platforms are transmitted from the feet to the adjacent muscles and bones. WBV with high magnitude (high frequency and/or amplitude) has shown to increase muscular activation and this technique has been suggested as an alternative to weight bearing exercise (18). Several studies have investigated the role of WBV on BMD, muscle strength, and balance (11, 12, 14, 19-24). However, the results have been inconsistent perhaps due to differences in types of vibration studied; intervention designs, populations assessed, and study quality. Fewer studies have focused on the effect of WBV on falls and bone strength parameters other than BMD (19, 20, 25-27).

Previous systematic reviews on the effect of WBV on balance and muscle strength in older adults have reported improvement in lower extremity muscle strength or in certain balance measures (28-32). Systematic reviews focusing on BMD have shown inconsistent results (32-35), with some showing no overall effect (32), others a small increase in BMD of the hip (33) or no effect on the hip but an effect on lumbar spine (35), whilst some found a BMD increase in certain subgroups only (34). To the best of our knowledge no systematic review has comprehensively investigated the role of WBV on fragility fractures and overall risk of fragility fractures, including falls and bone quality.

The objectives of this systematic review were to address if WBV in adults over 50 years of age could affect the incidence of fractures, falls, as well as estimates of bone mass, architecture and turnover.

Methods

Data sources and searches

Literature searches were conducted in the following electronic bibliographic databases: PubMed, EMBASE, and The Cochrane Library (Cochrane Central Register of Controlled Trials (CENTRAL)). The searches were conducted from inception to fourth- of April 2016. Additionally we performed manual searches of the reference lists of retrieved publications and earlier reviews (29, 32-35). An updated search was conducted by end of January 2017, to check for any new relevant studies prior to submission.

The search string was structured with librarian assistance using the PICO method: P (population) = adults ≥50 years of age, I (intervention) = whole-body sinusoidal vibration (i.e. constant vibration frequency) from a platform, C (comparison) = no intervention, sham, normal care, or same exercise in both arms, and O (outcome) = fractures, falls, and bone property parameters.

The searches were conducted without filters or restrictions and the search string is available as appendix 1.

Study selection

One author (DJ) screened title and abstracts. Two authors (DJ, KT) independently evaluated the full-text papers and eligibility. Conflicts were resolved by a third author (JR). The selection was conducted using the software Covidence (Covidence systematic review software, Veritas Health Innovation, Melbourne, Australia) and a standardized eligibility form.

Inclusion criteria: randomized controlled trials (RCT) investigating the effect of WBV on fractures, falls, and bone properties within the population ≥ 50 years of age. WBV had to be whole-body sinusoidal vibration (i.e. constant vibration frequency) from a platform that vibrates vertically or side alternating, with no restriction on frequency, amplitude, or magnitude. The participants had to stand during the WBV. The control groups had to have either no intervention, usual care, sham vibration, activity unlikely to influence bone or fall risk parameters, or exercise or interventions identical in both arms (where WBV was an add on in one group).

Trials were ineligible if non RCT, animal studies, population age < 50 years, non-English language publications, posters, or conference abstracts, and if vibration was applied locally, by electrical current, non-standing, with random frequencies, using vibrating insoles, or by ultrasound.

Data extraction and quality assessment

Data was independently extracted by two authors (DJ, KT), using a standardized data extraction form. For all included studies information was gathered on country of origin, design, randomization, population, intervention, adherence, analyses per intention to treat (ITT) or per protocol, and results.

Primary outcomes of interest were fractures and falls, and secondary outcomes were bone parameters including BMD (spine and hip), bone microarchitecture (assessed by high resolution peripheral quantitative computed tomography (HRpQCT) or bone biopsy), bone turnover markers (carboxy-terminal collagen crosslink (CTX) (bone resorption) or amino terminal propeptide of type I collagen (P1NP) (bone formation)), or calcaneal quantitative ultrasound (BUA).

Data was extracted from the intervention and control groups, and if the WBV was an add-on to exercise then the exercise and WBV arm was compared to the exercise arm.

The numbers of fractures and the participants contributing with data were extracted in the groups. Regarding falls, the number of falls, the number of participants who experienced falls, and the number of participants contributing with data and length of follow-up were extracted. To reduce the clinical heterogeneity, only falls data from the intervention periods of the studies were extracted. For BMD, bone turnover markers, microarchitecture parameters, and BUA the absolute mean difference (with standard deviations) from baseline to follow-up were extracted in the intervention and control groups.

If the data were reported different than stated above, the corresponding authors of the included studies were contacted in order to acquire the data.

The risk of bias for each included study was assessed using the Cochrane 'Risk of bias tool' (36). The performance biases were divided in patient reported outcomes (falls) and bone property parameters. The quality of evidence was assessed for each outcome using the five GRADE considerations and summaries of findings were created using the GRADE guidelines (37).

Strategy for data synthesis and analysis

The results across studies were pooled by numbers of events calculating relative risk of fractures and for experiencing one or more falls (fallers) with 95% CI. Fall incident rate ratio per patient year with 95% CI were calculated using the reported rate of falls (falls per person year) or the rate of falls in each group were calculated from the total number of falls and the total length of the intervention duration (person years) for participants contributing with data in each group using STATA (Stata Statistical Software: Release 14, TX: StataCorp LP). The mean differences in BMD, bone turnover markers, microarchitecture parameters, and BUA were pooled calculating the absolute mean difference and 95% CI. The mean differences were calculated subtracting the baseline means from the follow-up or by multiplying percent change with baseline means. The standard deviations (SD) were calculated using the formula ((HCI-LCI/2/TINV(0.05;n-1)*$\sqrt{}$ (n)), where HCI is the highest value of 95% CI, LCI the lowest value of 95% CI, and n the sample size of the group (36), by using p-values for change over time in Review Manager calculator (RevMan) (version 5.3, Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration 2014), or by the formula SD = (($m_i - m_c$) / TINV(p-value; df)) / $\sqrt{}$ ($1/n_i + 1/n_c$), where m_i is the mean difference in the intervention group, m_c is the mean difference in the control group, df is degrees of freedom, n_i is the sample size in the intervention group, and n_c is the sample size in the control group (36). When cluster randomization was used adjustments were applied (36). The number of participants contributing with data in each group was used for the calculations if this was reported, otherwise the number of participants randomized to each group was extracted. Where possible the longest follow-up times were used (with two papers reporting three and six month data, six month data were used) (26, 27). In case of post hoc study extension, the originally planned duration was used (22). Calculations were performed using Excel (Microsoft Excel (2010)), and STATA14. To allow for variability among the participants and interventions, the random effect meta-analysis model in RevMan was used. Heterogeneity was assessed by forest plots and the I-squared statistics. Pre-assigned subgroup analyses for sinusoidal vertical and side-alternating WBV were done where possible.

The review protocol was registered 1st of April 2016 in PROSPERO (ID:CRD42016036320) and reported according to the PRISMA 2009 statement, and the checklist was completed (38).

Results

Study selection and characteristics

A total of 3,207 titles and abstracts were initially identified, and after removal of 959 duplicates, 2,248 titles and abstracts were screened for relevance. The majority of identified papers were excluded because they described animal studies, were not RCTs, or did not meet the definition of the intervention. A total of 107 full text papers were read and matched to the inclusion and exclusion criteria. Selection of the included studies is illustrated in the PRISMA flow diagram (Figure 1). The updated search revealed no new relevant studies.

Study characteristics

A total of 15 papers (14 studies) met the criteria for the qualitative synthesis and are described in Table 1. The studies were published from 2004 to 2015, with an accumulated population of 1,839 (ranging from 42 (20) to 710 (21) participants in the included studies). The mean age of the overall population was 74 years, with 82% living independently and 90% being women. All studies were RCT with one trial using cluster-randomisation (21). The Six studies compared WBV to continued daily activities (20, 21, 26, 40, 41), with one study using two different forms of WBV (39). Three studies compared WBV to exercise or wellness therapy (24, 25, 42), and one study compared WBV to exercise and to continued daily activities (12). Two studies compared WBV to sham (19, 22). One study compared WBV and high or low dose vitamin D supplementation to no training and high or low dose vitamin D supplementation (43). One study compared WBV and alendronate to no training and alendronate (23). Eight trials reported supervised training (19, 20, 25, 26, 39-41, 43), two electronically monitored (21, 22), two using attendance logs (24, 42), and two did not state any form of measurement of adherence (12, 23).

Table 1. Description of the included studies

Author and year (ref)	Design	Setting	Participants No.	Women %	Age (mean, SD, range)	Analysed	Outcomes of interest	Supervision
Beck 2010 (39)	3-arm RCT LWBV vs. HWBV vs. continue daily activities	Australian independently living postmenopausal women	47 (15, 17, 15)	100	71.5±9.5	ITT/PP	aBMD hip and spine, BUA of calcaneus, falls as adverse effects	yes
Beaudart 2011 / Buckinx 2013 (27, 26)	2-arm RCT WBV vs. continue daily activities	Belgium nursing home residents	62 (31, 31)	76	83.2±7.9	ITT	falls	yes
Corrie 2014 (19)	3-arm RCT vWBV vs. svWBV vs. sham	England referred to Geriatric falls clinic	61 (21, 20, 20)	61	80.2±6.5	ITT	turnover markers (CTX, P1NP)	yes
Gomez-Cabello 2013 (40)	2-arm RCT WBV vs. continue daily activities	Spain non-institutionalised elderly	49 (24, 25)	59	WBV 75.2±4.7 CON 74.8±4.9	ITT	aBMD hip and spine, pQCT	yes
Iwamoto 2004 (23)	2-arm RCT WBV + alendronate vs. alendronate	Japan osteoporotic women	50 (25, 25)	100	55-88	not stated	aBMD spine, falls as adverse effects	not stated
Kiel 2015 (22)	2-arm RCT WBV vs. sham	North America independently living elderly	174 (89, 85)	67	82±7	ITT	vBMD hip and spine, turnover markers (CTX,P1NP)	electronic monitoring
Leung 2014 (21)	2-arm cluster RCT WBV vs. continue daily activities	China ≥ 60 yr independently living women	710 (364, 346)	100	74.5±7.1 71.3±7.2	ITT	fractures, falls, aBMD hip and spine	electronic monitoring
Liphardt 2015 (20)	2-arm RCT WBV vs. continue daily activities	Canada osteopenic women	42 (22, 20)	100	58.5±3.3 59.1±4.6	not stated	HRpQCT, aBMD	yes
Santin-Medeiros 2014 (41)	2-arm RCT WBV vs. continue daily activities	Spain women >79 yr	43 (25, 18)	100	82.4±5.7	ITT/PP	aBMD hip	yes

Sitjà-Rabert 2015 (25)	2-arm RCT WBV + exercise vs. exercise	Spain nursing home residents >65 yr	159 (81, 79)	67	82	ITT	falls	yes
Von Stegel 2011 (42)	3-armRCT WBV + exercise vs. exercise vs. wellness therapy	Germany women ≥65 yr, living independently	151 (50, 50, 51)	100	68.5±3.1	ITT	falls, aBMD hip and spine	attendance list
Von Stegel 2011ElvisII (24)	3-arm RCT vWBVvs. svWBV vs.wellness therapy	Germany women ≥65 yr, living independently	108 (36, 36, 36)	100	68.5±3.1	ITT	aBMD femoral neck and spine	attendance logs
Verschueren 2004 (12)	3-armRCT WBV vs. exercise vs. no training	Belgium postmenopausal women non institutionalized	70 (25, 22, 23)	100	58-74	not stated	aBMD hip and spine, turnover markers (CTX)	not stated
Verschueren 2011 (43)	4-arm RCT WBV + HDvit vs.WBV + Dvit vs. no training + HDvit vs. no training + Dvit	Belgium women living in nursing homes	113	100	79.6	ITT	aBMD hip	yes

Abbreviations: aBMD = areal bone mineral density, CON = controls, CTX = carboxy-terminal collagen crosslink, Dvit = conventional dose vitamin D, HDvit = high dose vitamin D, HR-pQCT = high resolution peripheral quantitative computed tomography, HWBV = high magnitude whole body vibration, ITT = intent to treat, LWBV = low magnitude whole body vibration, P1NP = amino terminal propeptide of type I collagen, PP = per protocol, pQCT = peripheral quantitative computed tomography , SD = standard deviation, svWBV = side-alternating whole-body vibration, vBMD = volumetric bone mineral density, vWBV = vertical whole-body vibration, WBV = whole body vibration exercise, and yr = years of age

The studies varied in the intervention protocols with differences in vibration design, duration, and follow-up (Table 2). Eleven studies used high magnitude WBV (≥1 *g* in peak acceleration) (HWBV) (12, 19, 20, 23-26, 40-43) with two of these studies comparing vertical with side-alternating vibration and wellness therapy/sham vibration (19, 24). Two studies used low magnitude WBV (<1 *g* in peak acceleration) (LWBV) (21-22), and one study compared low magnitude WBV to high magnitude side alternating WBV (39). In the studies using high magnitude WBV five used side-alternating vibration (19, 20, 23, 24, 39) and nine studies used vertical vibration (12, 19, 24, 25, 39-43). Frequencies ranged from 12.5 - 40 Hertz, peak to peak displacement ranged from 0.7-4.2 mm, and peak acceleration from 0.3 - 8 *g*. The exercises were most often vibration spouts lasting from 15 seconds to 20 minutes, from every day to once a week, and the duration of the intervention were from 6 weeks to 24 months. In two studies the participants used flat soled shoes/gymnastic shoes (12, 24), two studies described the intervention shoeless (19, 26), while the other ten studies did not report a protocol for footwear (Table 2).

Table 2. Intervention parameters in the included studies

Author and year (ref)	Intervention (frequency, peak to peak displacement/ amplitude, peak acceleration)	Vibration type/ device	Protocol exercise	Training time (total vibration per session, training frequency)	Duration	Footwear
Beck 2010 (39)	LWBV 30 Hz, not stated, 0.3 *g*	vWBV/ Juvent 1000DMT	standing full upright no bending	15 min, 2 days/week	8 months	not stated
	HWBV 12.5 Hz, 0-14 mm amplitude, 1 *g*	svWBV/ Galileo 2000	knees slightly bent	6 min, 2 days/week		
Beaudart 2013/ Buckinx 2014 (26, 27)	30 Hz 2 mm amplitude, not stated	vWBV/ Vibrosphere	standing on two feet knees flexed	75 s, 3 days/week	6 months	shoeless
Corrie 2014 (19)	vWBV 28.4 Hz, 1.3 mm peak-to-peak, 1.5 *g*	vWBV/ Power plate	standing with bent knees	6 min, 3 days/week	12 weeks	shoeless
	svWBV 29.8 Hz, 2.9 mm peak-to-peak, 3.6 *g*	sv/ Galileo 2000				
Gomez-Cabello 2013 (40)	40 Hz, 2 mm amplitude, not stated	vWBV/ Pro5Power plate	standing with knees slightly bent holding the handrail	7.5 min, 3 days/week	11 weeks	not stated

Iwamoto 2004 (23)	20 Hz, 0.7-4.2 mm peak to peak, not stated	svWBV/ Galileo	standing with bent knees	4 min, 1 days/week	12 months	not stated
Kiel 2015 (22)	37 Hz, 0.09 mm amplitude, 0.3 *g*	vWBV/ not stated	upright relaxed stand	10 min, 7 days/week	24 months	not stated
Leung 2014 (21)	35 Hz, peak-to-peak < 0.1 mm, 0.3 *g*	vWBV/ not stated	upright no without bending knees	20 min, 5 days/week	18 months	not stated
Liphardt 2015 (20)	20 Hz, 3-4 mm amplitude, not stated	svWBV/ Vibraflex Galileo	stable position 30 degree knee flexion angel	10 min, 2-3 days/week	12 months	not stated
Santin-Medeiros 2015 (41)	20 Hz, 2 mm amplitude, not stated	vWBV/ Fitvibe Excel Pro	18 different exercises, squats	6-6.5 min, 2 days/week	8 months	not stated
Sitjà-Rabert 2015 (25)	30-35 Hz, 2-4 mm amplitude, not stated	vWBV/ Powerplate	30 min static/dynamic exercises	3-6 min, 3 days/week	6 weeks	not stated
Von Stegel 2011 Elvis (42)	25-35 Hz, 1.7 mm amplitude, not stated	vWBV/ Vibrafit	45 min dancing, balance and gymnastics and 15 min dynamic leg-strengthening with WBV and two at home sessions (20 min) with no vibration	6 min, 2 days/week	18 months	not stated
Von Stegel 2011ElvisII (24)	vvWBV, 35 Hz, 1.7 mm peak to peak, 8 *g* svWBV 12.5 Hz, 12 mm peak-to-peak, 8 *g*	vWBV/ Vibrafit svWBV/ Qionic	standing position, seven one or two-legged dynamic leg strengthening exercises	10 min, 3 days/week	18 months	flat-soled shoes
Verschueren 2004 (12)	35-40 Hz, 1.7-2.5 mm amplitude,2.28-5.09 *g*	vWBV/ Power plate	static and dynamic exercises on the vibration platform	20 min, 3 days/week	6 months	gymnastic shoes
Verschueren 2011 (43)	30-40 Hz, not stated, 1.6-2.2 *g*.	vWBV/ Power plate	static and dynamic exercises on the vibration platform	12 min, 3 days/week	6 months	not stated

Abbreviations: *g* = 9.81 m/s^2, HWBV = high magnitude vibration, Hz = Hertz, LWBV = low magnitude vibration, min = minutes, mm = millimetre, , s = seconds, svWBV = side alternating whole body vibration, and vWBV = vertical whole body vibration.

Outcomes

One study reported fractures as the primary outcome. A total of six studies reported fall data. Three authors were contacted to obtain data on fall rate (23, 25) and fall risk (42) and this way data were obtained from one trial (25).

Data on bone parameters were reported in percent change, or pre- and post-intervention measurements in eight studies. The corresponding authors were contacted (12, 19-23, 39, 41, 43), and data were obtained this way from three studies (19, 21, 22).

In two studies data were extracted from previous reviews (33, 34), which reported to have primary data available from the authors (12, 23, 41), and in the rest of the studies the outcomes were calculated as described in the method section.

Risk of biases within studies

The majority of studies were categorized as having a low risk of bias in the randomization with unclear risk of bias in the allocation due to insufficient reporting in half of the studies. The performance bias was categorized as high risk when the participants reported falls and were not blinded to the intervention. One study used wellness therapy in the control group and did not inform the participants of the hypotheses, and was thus considered unclear in the risk of performance bias with respect to falls reporting (42). Non-blinding of participants were categorized as unclear risk of bias when the outcome were bone parameters. The risk of bias in selective reporting was categorized as low risk if the trial reported all stated outcomes in the papers and was conducted before 2005. After 2005 trials had to be registered online at a registry or having published a study protocol reporting the pre-specified outcomes. Figure 2 shows a summary of the risk of bias assessment.

Fractures

One study reported fractures as a primary outcome (Risk Ratio (RR) 0.48 (95% CI 0.14-1.56), with an intra-cluster correlation coefficient of 0.000 (Figure 3).

Falls

Four studies reported falls as primary outcome (21, 25, 26, 42). Three studies reported fallers and the number of falls in total in each group during the intervention (21, 25, 26) and one study reported the mean number of falls per participants (42). One study reported no events in the control arm in the six weeks intervention and adjusted rate ratio could not be calculated. Pooling the studies with falls reported as outcomes showed a fall rate ratio of 0.67 (95% CI 0.50-0.89, p=0.006, I^2=19%) (Figure 4a) in the intervention groups compared to non-intervention and a relative risk of experiencing falls of 0.76 (95% CI 0.48-1.20, p=0.24, I^2=24%) (Figure 4b).

Two trials reported falls as adverse effects (23, 39). A post hoc sensitivity analysis was conducted to assess if the inclusion of these trials would alter the result. In this analysis a fall rate/person years rate ratio of 0.65 (95% CI 0.50-0.85, p=0.002, I^2=8%) was found and a relative risk of experiencing falls of 0.67 (95% CI 0.46-0.98, p=0.04, I^2=13%) (Supplement data Figure 1 a-b).

Bone Mineral Density

Seven studies reported data on lumbar spine BMD (12, 21, 23, 24, 39, 40, 42). The results showed no overall effect with a mean difference of 0.00 (95% CI -0.00-0.01, p=0.11, I^2=22%) (Figure 5a). Six studies reported data on total hip BMD (12, 21, 40-43) showing similar results with a mean difference of 0.00 (95% CI -0.00-0.01, p=0.27, I^2=50%) (Figuar 5b). Subgroup analyses with vertical and side-alternation vibration explaned 44.5% of the heterogeneity in the lumbar spine BMD, and side-alternation vibration showed a mean difference of 0.01 (95% CI 0.00-0.02, p=0.04, I^2=0%) with 117 participants. All studies reporting BMD in total hip used vertical vibration.

One study reported change in total proximal femoral trabecular BMD and change in integral lumbar spine vertebral BMD (22). The results from the originally planned duration of 24 months showed no effect on integral lumbar spine vertebral BMD with a mean difference of 0.00 (95% CI -0.00-0.00) and total femoral trabecular BMD mean difference of 0.00 (95% CI -0.00-0.01) (Supplement data Figure 2 a-b). Two studies reported volumetric BMD (vBMD) of radius and tibia using HR-pQCT (20) or quantitative computed tomography (pQCT) scans (37). The results for the ultradistal site using HR-pQCT and a 4% site in tibia and radius using pQCT were combined in forestplots showing no statistically significant effects with a vBMD tibia mean difference of -0.68 (95% CI -2.29-0.93, p=0.41, I^2=0) and a vBMD radius mean difference of 1.87 (95% CI -0.62-4.36, p=0.30, I^2=8) (Figure 5c-d).

Bone microarchitecture

One study reported measurements of cortical porosity (Ct.Po) and trabecular BMD (tbBMD) (20) using HR-pQCT. We refrained from performing a meta-analysis due to the limited data (see Supplement data Figure 3). In tibia, WBV compared to control showed an increase in mean difference in Ct.Po of 0.20 % (95% CI -0.25-0.65) and decrease in tbBMD mean difference -0.3 mg HA/cm^3 (95% CI -0.58-0.02). In radius, WBV compared to no intervention showed an increase mean difference in Ct.Po of 0.10 % (95% CI -0.15-0.35) and decrease in tbBMD mean difference -0.90 mg HA/cm^3 (95% CI -0.90-2.10) (Supplement data Figure 3).

Bone turnover markers

One study reported data on the bone resorption marker CTX (12) and two studies on both CTX and the bone formation marker P1NP (19, 22). One of the studies reported log transformed CTX and P1NP (19) and no untransformed data could be obtained from the authors. The result for the meta-analysis on CTX was a mean difference of 0.01 ng/mL (95% CI -0.06-0.08, p=0.73, I^2=0) and with data available from only one trial the result for P1NP was a mean difference of 4.92 ng/mL (95% CI -3.06-12.90) (Figure 6a-b).

Calcaneal BUA

A single study reported calcaneal BUA mean change in comparing two vibration groups with a control group (39), we refrained from performing a meta-analysis due to the limited data (see Supplement data Figure 4). The low magnitude vertical vibration group had a mean difference of 1.99 dB/MHz (95% CI-0.84- 4.82) and the high magnitude side-altering vibration group a mean change of 4.69 dB/MHz (95% CI 1.61-7.77) compared to the controls (Supplement data Figure 4).

Quality assesment

Quality of evidence was assessed for each outcome (Table 3). For the outcome of fractures the evidence was downgraded for imprecision due to the 95% confidence interval around the pooled estimate of effect includes both the possibility of no effect and appreciable benefit. The evidence for falls rate was downgraded for study limitations due to non-blinding of the participants. The risk of falls was downgraded for imprecision and study limitations due to non-blinding of the participants. Bone parameters were all downgraded for indirectness since they are surrogate markers for bone strength. Regarding bone parameters the outcomes were downgraded for imprecision if the 95% confidence interval around the pooled estimate of effect includes both the possibility of no effect and appreciable benefit and for inconsistency if the I^2 statistics showed substantial heterogeneity. Publication bias could not be assessed by a funnel plot with Egger's test since all of the meta-analyses contained less than 10 studies (36).

Table 3. Summary of findings table presents the findings and the quality of each outcome using the GRADE considerations

WBV compared to usual care for fracture risk

Bibliography:

Outcomes	№ of participants (studies) Follow-up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with usual care	Risk difference with WBV

WBV compared to usual care for fracture risk

Bibliography:

Outcomes	**№ of participants (studies) Follow-up**	**Quality of the evidence (GRADE)**	**Relative effect (95% CI)**	**Anticipated absolute effects**	
				Risk with usual care	**Risk difference with WBV**
fractures	710 (1 RCT)	⊕⊕⊕◯ MODERATE [a]	**RR 0.48** (0.14-1.56)	2 per 100	**1 fewer per 100** (2 fewer to 1 more)
fall rate/person years	746 (3 RCTs)	⊕⊕⊕◯ MODERATE [b]	**Rate ratio 0.67** (0.50-0.89)	34 per 100	**11 fewer per 100** (17 fewer to 4 fewer)
The risk of experiencing falls (fallers)	805 (3 RCTs)	⊕⊕◯◯ LOW [c]	**RR 0.76** (0.48-1.20)	23 per 100	**6 fewer per 100** (12 fewer to 5 more)
Total bone mineral density lumbar spine (BMD spine)	911 (7 RCTs)	⊕⊕⊕◯ MODERATE [d]	-		mean **0** (0 to 0.01 higher)
Bone mineral density total hip (BMD hip)	870 (6 RCTs)	⊕⊕◯◯ LOW [e]	-		mean **0** (0 to 0.01 higher)
Volumetric bone mineral density tibia	80 (2 RCTs)	⊕⊕◯◯ LOW [f]	-		mean **0.68 lower** (2.29 lower to 0.93 higher)
Volumetric bone mineral density radius	80 (2 RCTs)	⊕◯◯◯ VERY LOW [g]	-		mean **1.87 higher** (0.62 lower to 4.36 higher)

WBV compared to usual care for fracture risk

Bibliography:

Outcomes	**№ of participants (studies) Follow-up**	**Quality of the evidence (GRADE)**	**Relative effect (95% CI)**	**Anticipated absolute effects**	
				Risk with usual care	**Risk difference with WBV**
Serum biomarker of bone resorption (CTX)	138 (2 RCTs)	⊕⊕◯◯ LOW[f]	-		mean **0.01 higher** (-0.06 lower to 0.08 higher)
Serum biomarker of bone formation (P1NP)	118 (1 RCT)	⊕⊕◯◯ LOW [f]	-		mean **4.92 higher** (3.06 lower to 12.9 higher)

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

a. serious imprecision, due to the 95% confidence interval around the estimate of effect includes both the possibility of no effect and appreciable benefit.

b. serious study limitations- lack of blinding of the participants reporting falls.

c. serious study limitations- lack of blinding of the participants reporting fall, and serious imprecision, due to the 95% confidence interval around the pooled estimate of effect includes both the possibility of no effect and appreciable benefit.

d. indirectness (surrogate marker for bone strength).

e. indirectness, and statistical heterogeneity

f. indirectness, and imprecision due to the 95% confidence interval around the estimate of effect includes both the possibility of no effect and appreciable benefit.

g. indirectness, and imprecision due to the 95% confidence interval around the estimate of effect includes both the possibility of no effect and appreciable benefit and statistical heterogeneity.

Discussion

This systematic review and meta-analysis provides evidence that whole-body vibration exercise reduces fall rate in adults above 50 years of age. We found a tendency in reduction of the proportion of fallers, no overall effect on BMD whereas only sparse data were available regarding bone microarchitecture parameters, bone turnover markers, and BUA. One study reported fractures showing non-significant fracture reduction.

Strengths and limitations

This study had some limitations. By not including non-English language literature and not extracting data from grey literature or adverse effects the risk of selection bias exists. Looking at the studies reporting falls as adverse effects in the included studies, the WBV reduces the falls rate and risk in agreement with our findings.

Only one study had fractures as primary outcome and had a low fracture rate (21). The studies contributing with falls data were unblinded which could be important when reporting falls. However, all studies included in the primary falls analysis did record falls prospectively limiting the risk of recall bias (21, 25, 26, 42). The populations in the studies consisted of 82% community dwelling adults with 90% being female, making the results generalizable only to people with similar characteristics.

Strengths of this review include that the evidence is obtained from randomized controlled trials, followed the PRISMA guidelines of reporting, and was registered at PROSPERO to improve transparency. A thorough literature search was conducted with assistance from a research librarian and we furthermore performed a hand search of the reference lists of included papers and earlier reviews references (28, 29, 32-35). The risk of selection bias was reduced by having two independent reviewers select the papers and extract the data. In the systematic review all outcomes were assessed regarding quality using the GRADE guidelines where fracture is classified as a critical outcome (37). We classified falls as an important outcome, and bone parameters being of limited importance as surrogate makers for fracture risk (37). We only pooled homogeneous outcomes in the meta-analysis leading to low statistical heterogeneity in the falls analysis with moderate statistical heterogeneity regarding BMD of the hip and spine. Pre-assigned subgroup analysis for vertical vs. side-alternating vibration could explain 44.5% of the heterogeneity in the lumbar spine analysis, whereas regarding total hip BMD all studies used vertical vibration and no subgroup analysis was performed. Meta-regression analysis was not performed due to the insufficient number of studies in the analysis (36).

Comparisons with other studies and reviews

Prior reviews of exercise have shown that exercise programs designed to prevent falls in older adults also seem to prevent injuries caused by falls, including fractures (44, 45). The majority of these exercise programs included balance training, functional training, and strengthening exercises. Earlier reviews have shown that WBV have balance improving capabilities and the ability to improve muscle strength of the lower extremities (27-31), and WBV might thus prevent fractures by its fall reducing capacity or by lowering the impact of a fall.

Our meta-analysis shows that rate of falls can be reduced, and suggests a reduction in the proportion of fallers. The number needed to treat to prevent one fall was 11 (Table 3). Sustaining a fall increases the risk of injury, and reducing the number of times an individual falls, even if not the number of fallers may have clinical and economic relevance to the individual and to society. Falls are very prevalent among the aging population with one in every three 65+ year olds experiencing a fall every year (6). Due to an ageing population a focus on interventions capable of reducing falls seems of utmost importance (10). Prior systematic reviews have shown that other exercise programmes can reduce fall rate through muscle strength and balance training, and it has been found that exercising for a period of more than three hours per week is associated with a larger decrease in fall rate (46). WBV exercise consists of shorter workouts and with the ability to stand as the only requirement for physical function. To our knowledge this is the first meta-analysis conducted on WBV and falls but earlier findings of a positive effect on surrogate markers for falls (balance and muscle strength) (27-31) can be viewed as an improvement in important risk factors for falls in agreement with our findings.

Our results on BMD are consistent with other systematic reviews, showing no overall effect on BMD (31-34). Earlier reviews suggested a positive effect on BMD in adolescents (32) and in a subgroup analysis with improvements after low-magnitude WBV on lumbar spine BMD (33) and high magnitude WBV on total hip BMD (32). We found a similar but small effect of side alternating vibration on lumbar spine BMD. In contrast to others, this systematic review also comprehensively assessed other bone parameters i.e. bone microarchitecture, turnover markers, and BUA. We found one study assessing cortical porosity and trabecular BMD of tibia and radius (20) with no overall effect, which is in line with results found in a younger age group (47). We found no effect on bone resorption markers in line with studies in younger participants (48, 49). One study in this review had a positive effect in bone formation markers, but with logarithmic transformed data it could not be pooled with non-transformed data (19) (Supplement data Figure 5). One study looked at BUA of the calcaneus showing a positive effect (39) in conflict with earlier findings from younger participants (47). Animal data suggest an effect of WBV on bone strength (15-18), but the same effect in humans is not evident. Reasons for this include diversities in training protocols, duration, adherence, damping of the vibration by the use of shoes, and different standing positions on the vibration plates.

In summary, the the evidence from this systematic review indicate that WBV may reduce fall rate with moderate certainty, and the risk of falls with low certainty. Future trials could enhance the certainty by systematically reporting falls when monitoring adverse effects, and if possible by blinding participants. The quality of evidence for the effect on bone parameters is moderate to low, partly since they aresurrogate markers of fracture risk and future research should focus on the critical outcome fractures with larger trial sizes and adequate follow-up.

Conclusion

In conclusion, our data shows a reduced rate of falls by WBV. Only one study reported fractures showing a non-significant reduction. We found no effect on BMD, and the data on microarchitecture and bone turnover markers were sparse. WBV exercise could be implemented in current falls prevention guidelines. It might potentially reduce fractures by reducing falls but the impact on fractures needs further larger adequately powered studies.

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Conflict of interest

All authors have completed the ICMJE uniform disclosure form at and declare no conflict of interests. DJ has received research grants from the Odense University Hospital, The Region of Southern Denmark Ph.D. foundation, the Faculty of Health Sciences, University of Southern Denmark, and the Danish Osteoporosis Foundation. The funding parties have no influence on the study design, study conduct, results, or dissemination.

Author contributions

All authors helped in the conception and design of the work and interpretation of data. Three authors reviewed the papers (DJ, KT, and JR) and two authors extracted the data (DJ, KT). DJ, TM, and JR did the first draft and all authors revised it critically for important intellectual content. All authors approved the final version for publication. DJ is guarantor.

Data sharing statement

No additional data are available.

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Figures

Figure 1. PRISMA Flow Diagram presenting the literature searches and the included studies

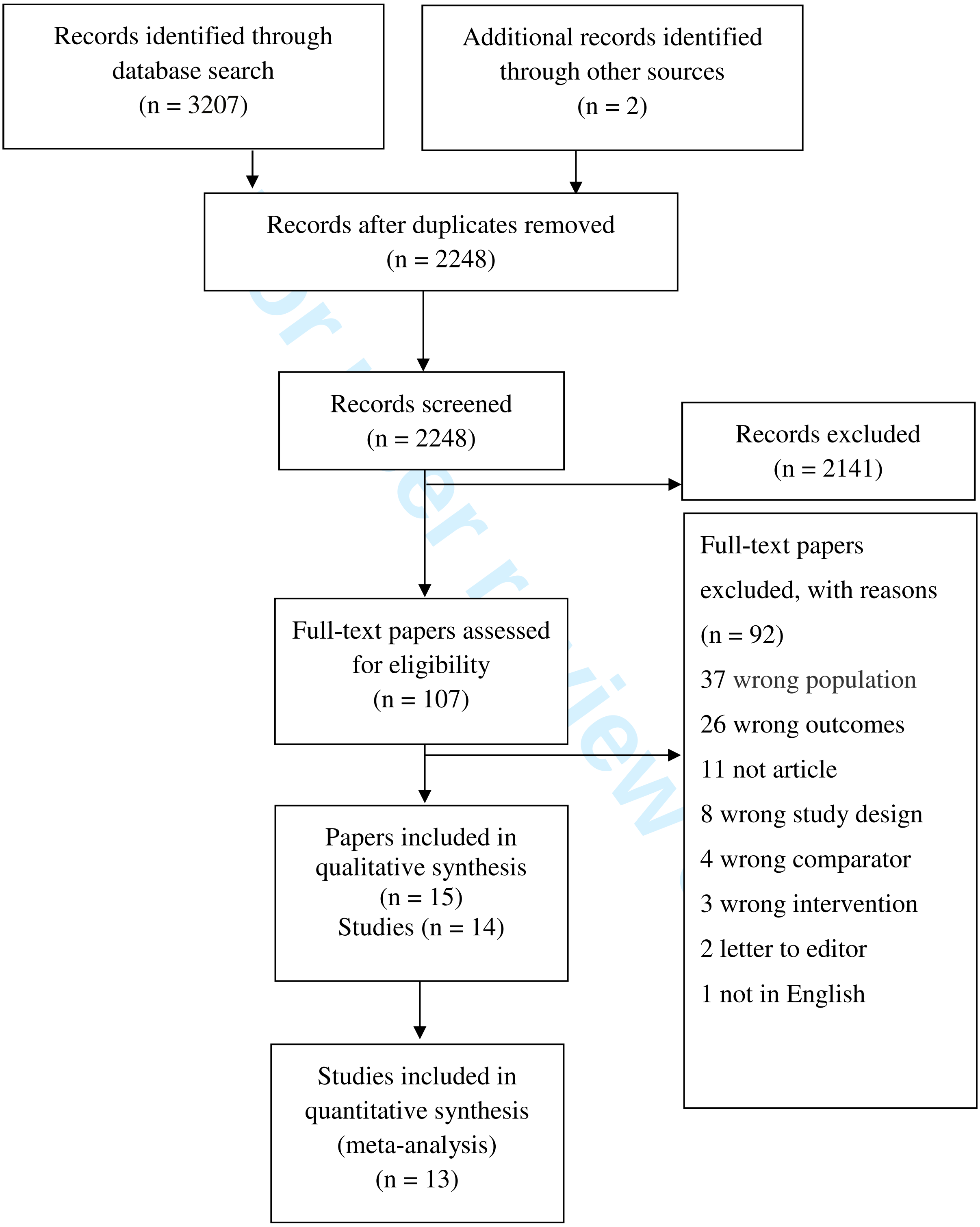


Figure 2.

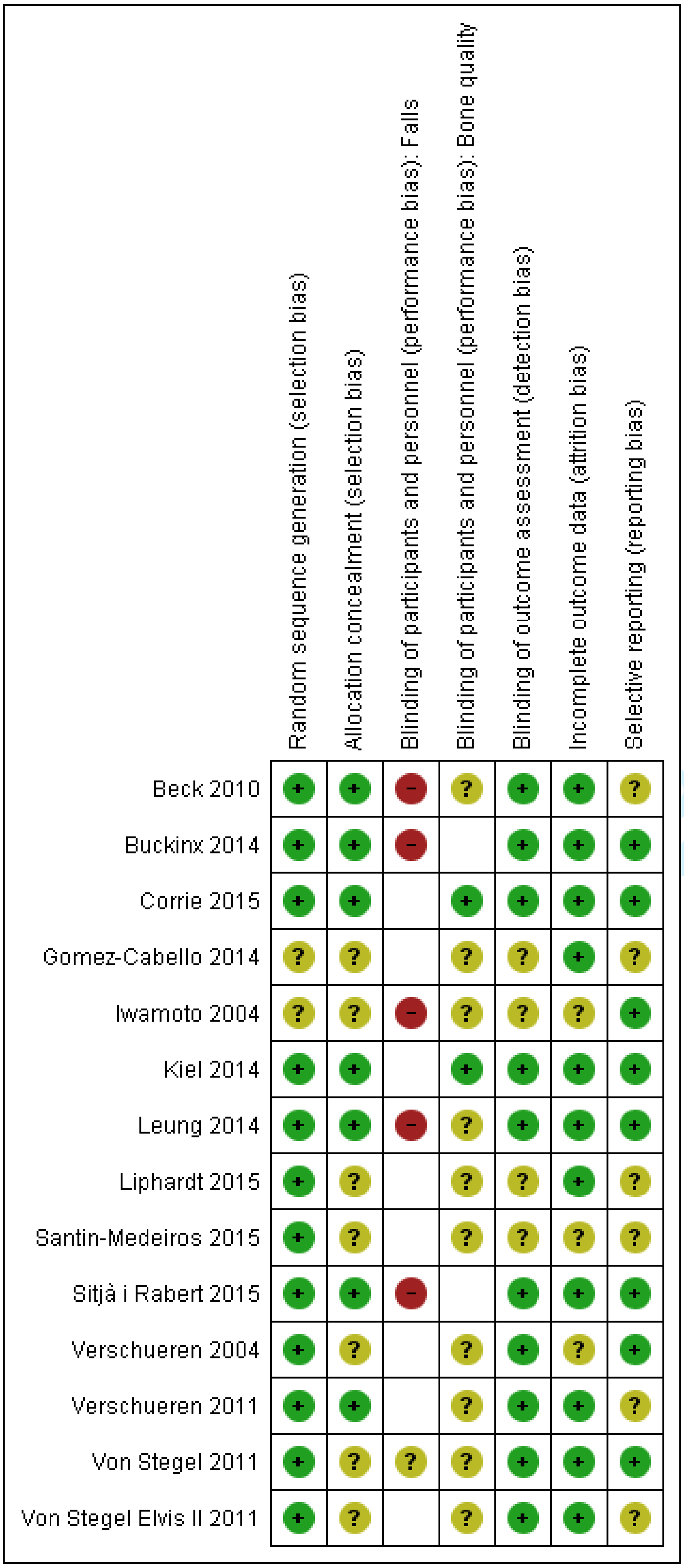

Random sequence generation (selection bias)
Allocation concealment (selection bias)
Blinding of participants and personnel (performance bias): Falls
Blinding of participants and personnel (performance bias): Bone quality
Blinding of outcome assessment (detection bias)
Incomplete outcome data (attrition bias)
Selective reporting (reporting bias)
Beck 2010
Buckinx 2014
Corrie 2015
Gomez-Cabello 2014
Iwamoto 2004
Kiel 2014
Leung 2014
Liphardt 2015
Santin-Medeiros 2015
Sitjà i Rabert 2015
Verschueren 2004
Verschueren 2011
Von Stegel 2011
Von Stegel Elvis II 2011

Figure 3. Effect of whole-body vibration (WBV) on the relative risk of experiencing a fracture.

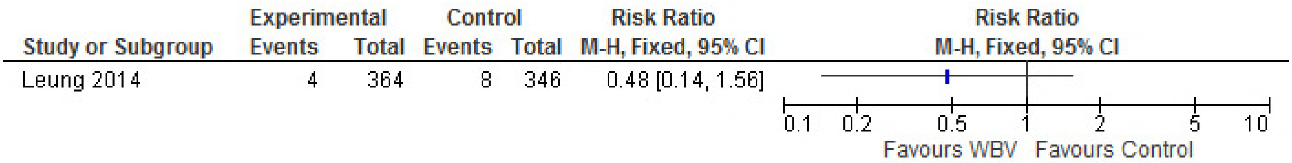


Figure 4. Forest plot of the effect of whole-body vibration (WBV) on falls.

Figure 4-a.

Study or Subgroup	log[Rate Ratio]	SE	Whole body vibration Total	Control Total	Weight	Rate Ratio IV, Random, 95% CI
Buckinx 2014	-0.0225	0.3333	31	31	17.3%	0.98 [0.51, 1.88]
Leung 2014	-0.5756	0.1679	295	289	51.9%	0.56 [0.40, 0.78]
Sitjà i Rabert 2015	0	0	0	0		Not estimable
Von Stegel 2011	-0.3159	0.2375	50	50	30.9%	0.73 [0.46, 1.16]
Total (95% CI)			**376**	**370**	**100.0%**	**0.67 [0.50, 0.89]**

Heterogeneity: Tau² = 0.01; Chi² = 2.47, df = 2 (P = 0.29); I² = 19%
Test for overall effect: Z = 2.73 (P = 0.006)

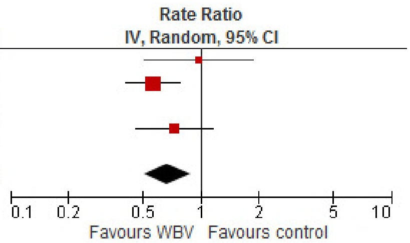


Figure 4-b.

Study or Subgroup	Favours WBV Events	Favours WBV Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Buckinx 2014	9	31	9	31	26.0%	1.00 [0.46, 2.18]
Leung 2014	55	295	83	289	71.8%	0.65 [0.48, 0.88]
Sitjà i Rabert 2015	2	81	0	78	2.3%	4.82 [0.23, 98.77]
Total (95% CI)		**407**		**398**	**100.0%**	**0.76 [0.48, 1.20]**
Total events	66		92			

Heterogeneity: Tau² = 0.05; Chi² = 2.62, df = 2 (P = 0.27); I² = 24%
Test for overall effect: Z = 1.18 (P = 0.24)

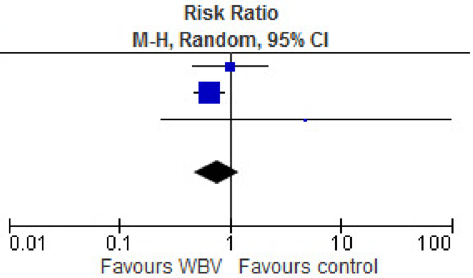


Figure 5. The effect of whole-body vibration exercise (WBV) in forest plots on bone mineral density

Figure 5-a.

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
2.1.1 vertical vibration								
Beck 2010	0	0.0604	13	-0.01	0.0165	7	1.9%	0.01 [-0.03, 0.05]
Gomez-Cabello 2014	0.01	0.0546	24	0.0001	0.0006	25	4.7%	0.01 [-0.01, 0.03]
Leung 2014	0.0006	0.0363	250	-0.005	0.0421	282	27.3%	0.01 [-0.00, 0.01]
Verschueren 2004	-0.003	0.019	25	0.004	0.02	24	14.9%	-0.01 [-0.02, 0.00]
Von Stegel 2011	0.014	0.022	46	0.019	0.031	47	15.0%	-0.00 [-0.02, 0.01]
Von Stegel Elvis II 2011	0.005	0.017	34	-0.005	0.018	17	16.3%	0.01 [-0.00, 0.02]
Subtotal (95% CI)			**392**			**402**	**80.1%**	**0.00 [-0.00, 0.01]**
Heterogeneity: Tau² = 0.00; Chi² = 8.18, df = 5 (P = 0.15); I² = 39%								
Test for overall effect: Z = 0.77 (P = 0.44)								
2.1.2 side-alternating vibration								
Beck 2010	-0.004	0.044	15	-0.01	0.0165	7	3.6%	0.01 [-0.02, 0.03]
Iwamoto 2004	0.051	0.045	25	0.042	0.046	25	3.6%	0.01 [-0.02, 0.03]
Von Stegel Elvis II 2011	0.007	0.023	29	-0.005	0.018	16	12.7%	0.01 [-0.00, 0.02]
Subtotal (95% CI)			**69**			**48**	**19.9%**	**0.01 [0.00, 0.02]**
Heterogeneity: Tau² = 0.00; Chi² = 0.19, df = 2 (P = 0.91); I² = 0%								
Test for overall effect: Z = 2.06 (P = 0.04)								
Total (95% CI)			**461**			**450**	**100.0%**	**0.00 [-0.00, 0.01]**
Heterogeneity: Tau² = 0.00; Chi² = 10.26, df = 8 (P = 0.25); I² = 22%								
Test for overall effect: Z = 1.61 (P = 0.11)								
Test for subgroup differences: Chi² = 1.80, df = 1 (P = 0.18), I² = 44.5%								

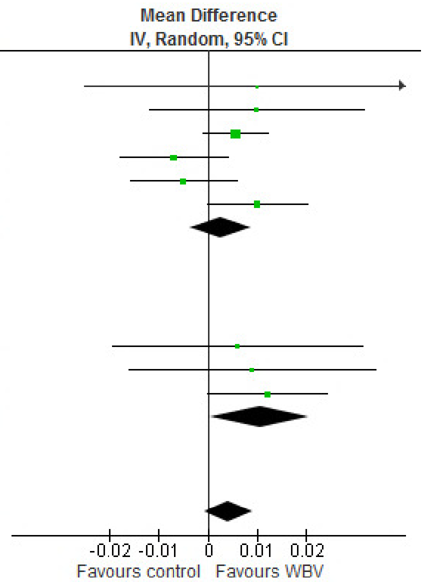


Figure 5-b.

Study or Subgroup	Whole body vibration Mean	Whole body vibration SD	Whole body vibration Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
Gomez-Cabello 2014	-0.02	0.551	24	0.0013	0.551	25	0.0%	-0.02 [-0.33, 0.29]
Santin-Medeiros 2015	-0.022	0.046	19	-0.034	0.133	18	0.5%	0.01 [-0.05, 0.08]
Verschueren 2004	0.008	0.016	25	-0.006	0.013	23	18.7%	0.01 [0.01, 0.02]
Verschueren 2011	0.006	0.017	54	0.007	0.019	57	22.9%	-0.00 [-0.01, 0.01]
Leung 2014	-0.013	0.0257	250	-0.014	0.0347	282	27.9%	0.00 [-0.00, 0.01]
Von Stegel 2011	0.001	0.0017	46	0.001	0.016	47	29.9%	0.00 [-0.00, 0.00]
Total (95% CI)			**418**			**452**	**100.0%**	**0.00 [-0.00, 0.01]**
Heterogeneity: Tau² = 0.00; Chi² = 9.93, df = 5 (P = 0.08); I² = 50%								
Test for overall effect: Z = 1.11 (P = 0.27)								

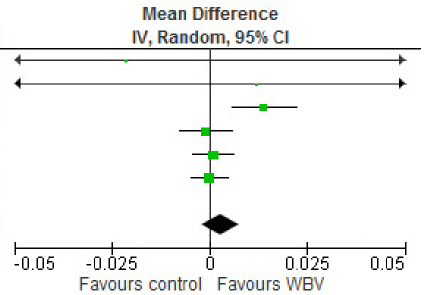


Figure 5-c.

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
Gomez-Cabello 2014	-1.01	13.1422	24	-5.09	67.6322	25	0.4%	4.08 [-22.95, 31.11]
Liphardt 2015	-2.7	2.7727	17	-2	1.7729	14	99.6%	-0.70 [-2.31, 0.91]
Total (95% CI)			**41**			**39**	**100.0%**	**-0.68 [-2.29, 0.93]**
Heterogeneity: Tau² = 0.00; Chi² = 0.12, df = 1 (P = 0.73); I² = 0%								
Test for overall effect: Z = 0.83 (P = 0.41)								

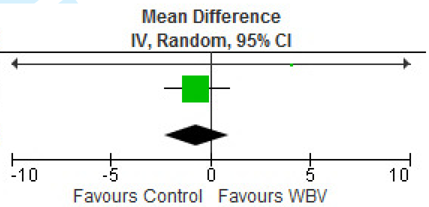


Figure 5-d.

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
Gomez-Cabello 2014	-5.11	22.4823	24	-2.08	9.3495	25	6.3%	-3.03 [-12.74, 6.68]
Liphardt 2015	1.5	3.0016	17	-0.7	1.2483	14	93.7%	2.20 [0.63, 3.77]
Total (95% CI)			**41**			**39**	**100.0%**	**1.87 [-0.62, 4.36]**
Heterogeneity: Tau² = 1.08; Chi² = 1.09, df = 1 (P = 0.30); I² = 8%								
Test for overall effect: Z = 1.47 (P = 0.14)								

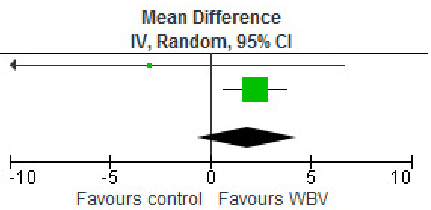


Figure 6. Presents the effect of whole body vibration exercise on bone turnover markers

Figure 6-a.

	WBV			Control				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Kiel 2014	0.01596	0.2058	56	0.00495	0.1755	62	99.9%	0.01 [-0.06, 0.08]
Verschueren 2004	-0.084	0.4224	25	-0.98	4.9281	25	0.1%	0.90 [-1.04, 2.83]
Total (95% CI)			**81**			**87**	**100.0%**	**0.01 [-0.06, 0.08]**
Heterogeneity: Tau² = 0.00; Chi² = 0.80, df = 1 (P = 0.37); I² = 0%								
Test for overall effect: Z = 0.34 (P = 0.73)								

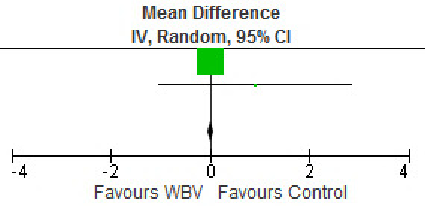
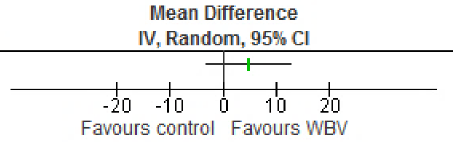


Figure 6-b.

	WBV			Control				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Kiel 2014	3.901	23.5	56	-1.02	20.4	62		4.92 [-3.06, 12.90]



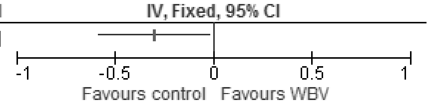
Supplement data Figure 1. presents supplement data on a) fall rate/ person years including adverse effect data on the effect of who

Supplement data Figure 2. presents supplement data of whole-body vibration exercises (WBV) effect on bone architecture parameters with mean difference and 95% CI

Supplement data Figure 3. presents supplement data analysis for microarchitecture parameters of whole-body vibration exercises (WBV) effect on microarchitecture parameters with mean difference and 95% confidence intervals a.) analysis is with total trabecular BMD in tibia (mg HA/cm^3), b) cortical porosity in % in tibia, c) total trabecular BMD for radius (mg HA/cm^3) and d) cortical porosity in % for radius.

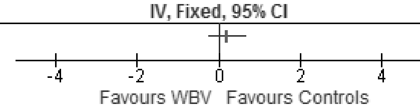
Supplement data figure 3-a.

	Experimental			Control				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Liphardt 2015	-0.2	0.5325	17	0.1	0.2387	14		-0.30 [-0.58, -0.02]



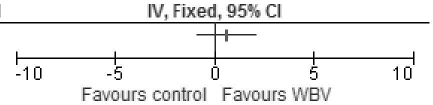
Supplement data figure 3-b.

	Experimental			Control				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Liphardt 2015	-0.3	0.4961	17	-0.5	0.7324	14		0.20 [-0.25, 0.65]



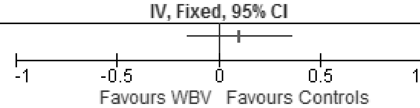
Supplement data figure 3-c.

	Experimental			Control				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Liphardt 2015	-0.1	0.4479	17	-0.7	2.8265	14		0.60 [-0.90, 2.10]



Supplement data figure 3-d.

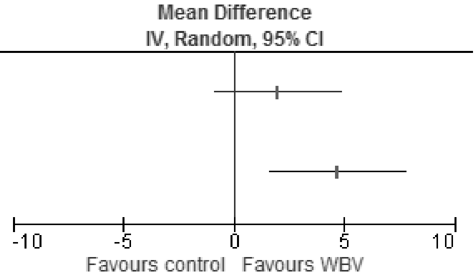
	Experimental			Control				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Liphardt 2015	-0.1	0.2414	17	-0.2	0.4322	14		0.10 [-0.15, 0.35]



Supplement data Figure 4. presents supplement data of whole-body vibration exercises (WBV) effect on Broadband ultrasound attenuation (BUA) of calcaneus with mean difference and 95% CI. First study line is results from vertical vibration and second line is side alternating vibration, the control group is divided between the two.

Supplement data figure 4.

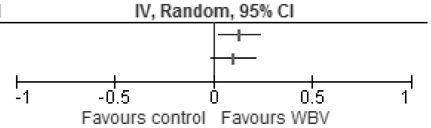
	Experimental			Control			Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Random, 95% CI
2.11.1 VV							
Beck 2010	-0.6	2.7086	13	-2.59	3.2564	7	1.99 [-0.84, 4.82]
2.11.2 SV							
Beck 2010	2.1	3.7921	15	-2.59	3.2564	7	4.69 [1.61, 7.77]



Supplement data Figure 5. presents reported effect on logaritmically transformed data of whole-body vibration exercises (WBV) effect on a) amino terminal propeptide of type I collagen (P1NP) (marker of bone formation) with mean difference and 95% CI, and b) carboxy-terminal collagen crosslink (CTX) (marker of bone resorption) with weighted mean difference with 95% CI. First study line is results from side alternating vibration and second line is vertical vibration, the control group is divided between the two.

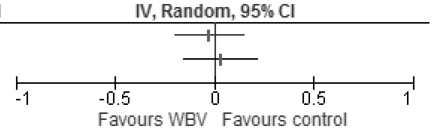
Supplement data Figure 5-a.

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Corrie 2015	0.079	0.107	11	-0.054	0.108	6		0.13 [0.03, 0.24]
Corrie 2015	0.049	0.106	12	-0.054	0.108	5		0.10 [-0.01, 0.22]



Supplement data Figure 5-b.

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Corrie 2015	0.09	0.17	12	0.115	0.176	6		-0.03 [-0.20, 0.15]
Corrie 2015	0.144	0.178	11	0.115	0.176	5		0.03 [-0.16, 0.22]



PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3-4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4-5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	7
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	4-6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	appendix
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5-6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5-6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5-7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	5-6
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	6-7
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	6-7

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	5-6 Table 3
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	6-7
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Table 1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Figure 2 Table 3
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Figure 3-6 Supplement Figure 1-5
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Figure 3-6
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Table 3
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Supplement figure 1
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	18-19 Table 3
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	18-20
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	19-20
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	20

PRISMA 2009 Checklist

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

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The Effect Of Whole Body Vibration Exercise In Preventing Falls And Fractures: A Systematic Review And Meta-analysis

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Complete List of Authors:	Jepsen, Ditte; Odense Universitetshospital, Department of Geriatric Medicine; Syddansk Universitet Det Sundhedsvidenskabelige Fakultet, Institute of Clinical Research Thomsen , Katja ; Odense Universitetshospital, Department of geriatric medicine; Syddansk Universitet Det Sundhedsvidenskabelige Fakultet, Institute of Clinical Research Hansen, Stinus; Odense Universitetshospital, Department of Endocrinology; Syddansk Universitet Det Sundhedsvidenskabelige Fakultet, Institute of Clinical Research Jørgensen, Niklas; Syddansk Universitet Det Sundhedsvidenskabelige Fakultet, OPEN- Odense Patient data Explorative Network; Rigshospitalet, Department of Clinical Biochemistry Masud, Tahir ; Nottingham University Hospitals NHS Trust, Department of Geriatric Medicine; Syddansk Universitet Det Sundhedsvidenskabelige Fakultet, Institute of Clinical Research Ryg, Jesper; Odense University Hospital, Department of Geriatric Medicine; Syddansk Universitet Det Sundhedsvidenskabelige Fakultet, Institute of Clinical Research
Primary Subject Heading:	Geriatric medicine
Secondary Subject Heading:	Sports and exercise medicine
Keywords:	Whole-body vibration, WBV, Exercise, Fractures, Accidental falls, Meta-analysis

The Effect Of Whole Body Vibration Exercise In Preventing Falls And Fractures: A Systematic Review And Meta-analysis

Ditte Beck Jepsen, MD, PhD student[1,2], ditte.beck.jepsen2@rsyd.dk

Katja Thomsen, MD, PhD, ass. Professor[2,3], Katja.Thomsen@rsyd.dk

Stinus Hansen MD, PhD[2,4], Stinus.Jorn.Hansen@rsyd.dk

Niklas Rye Jørgensen MD, Professor[5,6], Niklas.Rye.Joergensen@regionh.dk

Tahir Masud MD, Professor[1,2,7], Tahir.Masud@nuh.nhs.uk

Jesper Ryg, MD, PhD, ass. Professor[1,2], Jesper.Ryg@rsyd.dk

1: Department of Geriatric Medicine, Odense University Hospital, Denmark

2: Institute of Clinical Research, University of Southern Denmark, Denmark

3: Department of Geriatric Medicine, Odense University Hospital, Svendborg, Denmark

4: Department of Endocrinology, Odense University Hospital, Denmark

5: Department of Clinical Biochemistry, Rigshospitalet, Denmark

6: OPEN- Odense Patient data Explorative Network, Odense University Hospital/ University of Southern Denmark

7: Department of Geriatric Medicine, Nottingham University Hospitals Trust NHS, United Kingdom

Corresponding author

Ditte Beck Jepsen

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Word count abstract: 295

Figures: 6

Tables: 3

Appendix: Search string

Supplemental figures: 6

Abstract

Objective - To investigate the effect of Whole Body Vibration exercise (WBV) on fracture risk in adults ≥ 50 years of age.

Design - A systematic review and meta-analysis calculating relative risk ratios, fall rate ratio, and absolute weighted mean difference using random effects models. Heterogeneity was estimated using I^2 statistics and Cochrane Collaboration's risk of bias tool and the GRADE approach were used to evaluate quality of evidence and summarize conclusions.

Data sources - the databases PubMed, EMBASE, and the Cochrane Central Register from inception to April 2016, and reference lists of retrieved publications.

Eligibility criteria for selecting studies - randomized controlled trials examining the effect of WBV on fracture risk in adults ≥ 50 years of age. The primary outcomes were fractures, fall rates, and the proportion of participants who fell. Secondary outcomes were bone mineral density (BMD), bone microarchitecture, bone turnover markers, and calcaneal broadband attenuation (BUA).

Results - 15 papers (14 trials) met the inclusion criteria. Only one study had fracture data reporting a non-significant fracture reduction (RR=0.47, 95% CI 0.14-1.57, p=0.22) (Moderate quality of evidence). Four studies (n=746) showed that WBV reduced the rate of falls with a rate ratio of 0.67 (95% CI 0.50-0.89, p=0.0006; I^2=19%) (moderate quality of evidence). Furthermore, data from three studies (n=805) found a trend towards falls reduction (RR=0.76, 95% CI 0.48-1.20, p=0.24; I^2=24%) (low quality of evidence). Finally moderate to low quality of evidence showed no overall effect on BMD and only sparse data were available regarding microarchitecture parameters, bone turnover markers, and BUA.

Conclusions - WBV reduces fall rate, but seems to have no overall effect on BMD or microarchitecture. The impact of WBV on fractures requires further larger adequately powered studies. This meta-analysis suggests that WBV may prevent fractures by reducing falls.

Systematic review registration - PROSPERO ID CRD42016036320.

Key words:
Whole-body vibration, WBV, Exercise, Fractures, Accidental falls, Bone strength, BMD, Meta-analysis

Strengths and limitations of this study

- This is the first systematic review comprehensively conducting a meta-analysis on the effect of Whole Body Vibration exercise (WBV) on the overall risk of fractures, including falls
- An extensive systematic literature search identified all available randomised controlled trials using WBV in adults aged 50 on falls, fractures, and bone parameters
- A risk of selection bias exists due to no inclusion of non-English language literature, grey literature, or adverse effects

Introduction

Fragility fractures are associated with much morbidity, mortality, and cost to society (1, 2). In Europe, the direct medical cost of these fractures has been estimated at 31.7 billion Euros per year, expected to rise to 76.7 billion Euros by 2050 (3). Propensity to fall and osteoporosis are the major determinants of fragility fractures (1, 4, 5).

One third of the population over 65 years of age falls at least once a year (6). Increasing age, frailty, comorbidity, reduced muscle strength, and impaired balance contribute to the risk of falls (4, 6). In Europe 22 million women and 5.5 million men were estimated to have osteoporosis in 2010 (1). WHO criteria for diagnosing osteoporosis is based on measurement of bone mineral density (BMD), but there are also other important aspects of bone fragility including microarchitecture and bone turnover (7, 8). The combination of age-related bone loss and an increased risk of falls, cause a higher incidence of fragility fractures in people aged 50 years or more (1, 9). With an aging population the increased cost caused by fragility fractures poses a significant challenge to healthcare systems (1, 3). Reducing fracture risk with the dual approach of lowering fall risk and enhancing bone strength is therefore desirable (10).

Whole body vibration exercise (WBV) has been proposed as an exercise modality anabolic to bone, capable of enhancing balance, and improving muscle strength (11-14). Animal studies have showed that mechanical signals introduced via vibration stimulate bone formation and suppress bone resorption (15-17). The accelerations from vibration platforms are transmitted to the person standing on the plate from the feet to the adjacent muscles and bones. When the plate moves the adjacent muscles provide contractions as a reflex to the stimulus (18). Whole body vibration has been proposed to counteract aging's suppression on osteoblast activity thereby preventing bone loss (15). WBV with high magnitude (high frequency and/or amplitude) has shown to increase muscular activation and this technique has been suggested as an alternative to weight bearing exercise (18). WBV training protocols varies from a few minutes vibration up to 20 minutes depending on the peak acceleration.

The vibration plates can be assessed at home, in the local community or at rehabilitation units with different forms of monitoring and supervision. The WBV is used as an intervention aimed at preventing bone loss, enhancing muscle strength and balance.

Several studies have investigated the role of WBV on BMD, muscle strength, and balance (11, 12, 14, 19-24). However, the results have been inconsistent perhaps due to differences in types of vibration studied; intervention designs, populations assessed, and study quality. Fewer studies have focused on the effect of WBV on falls and bone strength parameters other than BMD (19, 20, 25-27).

Previous systematic reviews on the effect of WBV on balance and muscle strength in older adults have reported improvement in lower extremity muscle strength or in certain balance measures (28-32). Systematic reviews focusing on BMD have shown inconsistent results (32-35), with some showing no overall effect (32), others a small increase in BMD of the hip (33) or no effect on the hip but an effect on lumbar spine (35), whilst some found a BMD increase in certain subgroups only (34). To the best of our knowledge no systematic review has comprehensively investigated the role of WBV on fragility fractures and overall risk of fragility fractures, including falls and bone quality.

The objectives of this systematic review were to address if WBV in adults over 50 years of age could affect the incidence of fractures, falls, as well as estimates of bone mass, architecture and turnover.

Methods

Data sources and searches

Literature searches were conducted in the following electronic bibliographic databases: PubMed, EMBASE, and The Cochrane Library (Cochrane Central Register of Controlled Trials (CENTRAL)). The searches were conducted from inception to fourth- of April 2016. Additionally we performed manual searches of the reference lists of retrieved publications and earlier reviews (29, 32-35). An updated search was conducted by end of January 2017, to check for any new relevant studies prior to submission.

The search string was structured with librarian assistance using the PICO method: P (population) = adults ≥50 years of age, I (intervention) = whole-body sinusoidal vibration (i.e. constant vibration frequency) from a platform, C (comparison) = no intervention, sham, normal care, or same exercise in both arms, and O (outcome) = fractures, falls, and bone property parameters.

The searches were conducted without filters or restrictions and the search string is available as appendix 1.

Study selection

One author (DJ) screened title and abstracts. Two authors (DJ, KT) independently evaluated the full-text papers and eligibility. Conflicts were resolved by a third author (JR). The selection was conducted using the software Covidence (Covidence systematic review software, Veritas Health Innovation, Melbourne, Australia) and a standardized eligibility form.

Inclusion criteria: randomized controlled trials (RCT) investigating the effect of WBV on fractures, falls, and bone properties within the population ≥ 50 years of age. WBV had to be whole-body sinusoidal vibration (i.e. constant vibration frequency) from a platform that vibrates vertically or side alternating, with no restriction on frequency, amplitude, or magnitude. The participants had to stand during the WBV. The control groups had to have either no intervention, usual care, sham vibration, activity unlikely to influence bone or fall risk parameters, or exercise or interventions identical in both arms (where WBV was an add on in one group).

Trials were ineligible if non RCT, animal studies, population age < 50 years given by the mean age minus two times the standard deviation, or if the participants were younger than 50 years of age, non-English language publications, posters, or conference abstracts, and if vibration was applied locally, by electrical current, non-standing, with random frequencies, using vibrating insoles, or by ultrasound.

Data extraction and quality assessment

Data was independently extracted by two authors (DJ, KT), using a standardized data extraction form. For all included studies information was gathered on country of origin, design, randomization, population, intervention, adherence, analyses per intention to treat (ITT) or per protocol, and results.

Primary outcomes of interest were fractures and falls, and secondary outcomes were bone parameters including BMD (spine and hip), bone microarchitecture (assessed by high resolution peripheral quantitative computed tomography (HRpQCT) or bone biopsy), bone turnover markers (carboxy-terminal collagen crosslink (CTX) (bone resorption) or amino terminal propeptide of type I collagen (P1NP) (bone formation)), or calcaneal quantitative ultrasound (BUA).

Data was extracted from the intervention and control groups, and if the WBV was an add-on to exercise then the exercise and WBV arm was compared to the exercise arm.

The numbers of fractures and the participants contributing with data were extracted in the groups.

Regarding falls, the number of falls, the number of participants who experienced falls, and the number of participants contributing with data and length of follow-up were extracted. To reduce the clinical heterogeneity, only falls data from the intervention periods of the studies were extracted.

For BMD, bone turnover markers, microarchitecture parameters, and BUA the absolute mean difference (with standard deviations) from baseline to follow-up were extracted in the intervention and control groups.

If the data were reported different than stated above, the corresponding authors of the included studies were contacted in order to acquire the data.

The risk of bias for each included study was assessed using the Cochrane 'Risk of bias tool' (36). The performance biases were divided in patient reported outcomes (falls) and bone property parameters. The quality of evidence was assessed for each outcome using the five GRADE considerations and summaries of findings were created using the GRADE guidelines (37).

Strategy for data synthesis and analysis

The results across studies were pooled by numbers of events calculating relative risk of fractures and for experiencing one or more falls (fallers) with 95% CI. Fall incident rate ratio per patient year with 95% CI were calculated using the reported rate of falls (falls per person year) or the rate of falls in each group were calculated from the total number of falls and the total length of the intervention duration (person years) for participants contributing with data in each group using STATA (Stata Statistical Software: Release 14, TX: StataCorp LP). The mean differences in BMD, bone turnover markers, microarchitecture parameters, and BUA were pooled calculating the absolute mean difference and 95% CI. The mean differences were calculated subtracting the baseline means from the follow-up or by multiplying percent change with baseline means. The standard deviations (SD) were calculated using the formula ((HCI-LCI/2/TINV(0.05;n-1)*√(n)), where HCI is the highest value of 95% CI, LCI the lowest value of 95% CI, and n the sample size of the group, TINV(0.05;n-1)= t value for a 95% confidence interval from a sample size of n, (36), by using p-values for change over time in Review Manager calculator (RevMan) (version 5.3, Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration 2014), or by the formula SD = (($m_i - m_c$) / TINV(p-value; df)) / √ ($1/n_i + 1/n_c$), where m_i is the mean difference in the intervention group, m_c is the mean difference in the control group, df is degrees of freedom, n_i is the sample size in the intervention group, and n_c is the sample size in the control group (36). When cluster randomization was used adjustments were applied (36). The number of participants contributing with data in each group was used for the calculations if this was reported, otherwise the number of participants randomized to each group was extracted. Where possible the longest follow-up times were used (with two papers reporting three and six month data, six month data were used) (26, 27). In case of post hoc study extension, the originally planned duration was used (22). Calculations were performed using Excel (Microsoft Excel (2010)), and STATA14. To allow for variability among the participants and interventions, the random effect meta-analysis model in RevMan was used. Heterogeneity was assessed by forest plots and the I-squared statistics. Pre-assigned subgroup analyses for sinusoidal vertical and side-alternating WBV were done where possible.

The review protocol was registered 1st of April 2016 in PROSPERO (ID:CRD42016036320) and reported according to the PRISMA 2009 statement, and the checklist was completed (38).

Results

Study selection and characteristics

A total of 3,207 titles and abstracts were initially identified, and after removal of 959 duplicates, 2,248 titles and abstracts were screened for relevance. The majority of identified papers were excluded because they described animal studies, were not RCTs, or did not meet the definition of the intervention. A total of 107 full text papers were read and matched to the inclusion and exclusion criteria. Selection of the included studies is illustrated in the PRISMA flow diagram (Figure 1). The updated search revealed no new relevant studies.

Study characteristics

A total of 15 papers (14 studies) met the criteria for the qualitative synthesis and are described in Table 1. The studies were published from 2004 to 2015, with an accumulated population of 1,839 (ranging from 42

(20) to 710 (21) participants in the included studies). The mean age of the overall population was 74 years, with 82% living independently and 90% being women. All studies were RCT with one trial using cluster-randomisation (21). The Six studies compared WBV to continued daily activities (20, 21, 26, 39-41), with one study using two different forms of WBV (39). Three studies compared WBV to exercise or wellness therapy (24, 25, 42), and one study compared WBV to exercise and to continued daily activities (12). Two studies compared WBV to sham (19, 22). One study compared WBV and high or low dose vitamin D supplementation to no training and high or low dose vitamin D supplementation (43). One study compared WBV and alendronate to no training and alendronate (23). Eight trials reported supervised training (19, 20, 25, 26, 39-41, 43), two electronically monitored (21, 22), two using attendance logs (24, 42), and two did not state any form of measurement of adherence (12, 23).

Table 1. Description of the included studies

Author and year (ref)	Design	Setting	Participants No.	Women %	Age (mean, SD, range)	Analysed	Outcomes of interest	Supervision
Beck 2010 (39)	3-arm RCT LWBV vs. HWBV vs. continue daily activities	Australian independently living postmenopausal women	47 (15, 17, 15)	100	71.5±9.5	ITT/PP	aBMD hip and spine, BUA of calcaneus, falls as adverse effects	yes
Beaudart 2011 / Buckinx 2013 (27, 26)	2-arm RCT WBV vs. continue daily activities	Belgium nursing home residents	62 (31, 31)	76	83.2±7.9	ITT	falls	yes
Corrie 2014 (19)	3-arm RCT vWBV vs. svWBV vs. sham	England referred to Geriatric falls clinic	61 (21, 20, 20)	61	80.2±6.5	ITT	turnover markers (CTX, P1NP)	yes
Gomez-Cabello 2013 (40)	2-arm RCT WBV vs. continue daily activities	Spain non-institutionalised elderly	49 (24, 25)	59	WBV 75.2±4.7 CON 74.8±4.9	ITT	aBMD hip and spine, pQCT	yes
Iwamoto 2004 (23)	2-arm RCT WBV + alendronate vs. alendronate	Japan osteoporotic women	50 (25, 25)	100	55-88	not stated	aBMD spine, falls as adverse effects	not stated
Kiel 2015 (22)	2-arm RCT WBV vs. sham	North America independently living elderly	174 (89, 85)	67	82±7	ITT	vBMD hip and spine, turnover markers (CTX,P1NP)	electronic monitoring
Leung 2014 (21)	2-arm cluster RCT WBV vs. continue daily activities	China ≥ 60 yr independently living women	710 (364, 346)	100	74.5±7.1 71.3±7.2	ITT	fractures, falls, aBMD hip and spine	electronic monitoring
Liphardt 2015 (20)	2-arm RCT WBV vs. continue daily activities	Canada osteopenic women	42 (22, 20)	100	58.5±3.3 59.1±4.6	not stated	HRpQCT, aBMD	yes
Santin-Medeiros 2014 (41)	2-arm RCT WBV vs. continue daily activities	Spain women >79 yr	43 (25, 18)	100	82.4±5.7	ITT/PP	aBMD hip	yes

Sitjà-Rabert 2015 (25)	2-arm RCT WBV + exercise vs. exercise	Spain nursing home residents >65 yr	159 (81, 79)	67	82	ITT	falls	yes
Von Stegel 2011 (42)	3-armRCT WBV + exercise vs. exercise vs. wellness therapy	Germany women ≥65 yr, living independently	151 (50, 50, 51)	100	68.5±3.1	ITT	falls, aBMD hip and spine	attendance list
Von Stegel 2011ElvisII (24)	3-arm RCT vWBVvs. svWBV vs.wellness therapy	Germany women ≥65 yr, living independently	108 (36, 36, 36)	100	68.5±3.1	ITT	aBMD femoral neck and spine	attendance logs
Verschueren 2004 (12)	3-armRCT WBV vs. exercise vs. no training	Belgium postmenopausal women non institutionalized	70 (25, 22, 23)	100	58-74	not stated	aBMD hip and spine, turnover markers (CTX)	not stated
Verschueren 2011 (43)	4-arm RCT WBV + HDvit vs.WBV + Dvit vs. no training + HDvit vs. no training + Dvit	Belgium women living in nursing homes	113	100	79.6	ITT	aBMD hip	yes

Abbreviations: aBMD = areal bone mineral density, CON = controls, CTX = carboxy-terminal collagen crosslink, Dvit = conventional dose vitamin D, HDvit = high dose vitamin D, HR-pQCT = high resolution peripheral quantitative computed tomography, HWBV = high magnitude whole body vibration, ITT = intent to treat, LWBV = low magnitude whole body vibration, P1NP = amino terminal propeptide of type I collagen, PP = per protocol, pQCT = peripheral quantitative computed tomography , SD = standard deviation, svWBV = side-alternating whole-body vibration, vBMD = volumetric bone mineral density, vWBV = vertical whole-body vibration, WBV = whole body vibration exercise, and yr = years of age

The studies varied in the intervention protocols with differences in vibration design, duration, and follow-up (Table 2). Eleven studies used high magnitude WBV (≥1 *g* in peak acceleration) (HWBV) (12, 19, 20, 23-26, 40-43) with two of these studies comparing vertical with side-alternating vibration and wellness therapy/sham vibration (19, 24). Two studies used low magnitude WBV (<1 *g* in peak acceleration) (LWBV) (21-22), and one study compared low magnitude WBV to high magnitude side alternating WBV (39). In the studies using high magnitude WBV five used side-alternating vibration (19, 20, 23, 24, 39) and nine studies used vertical vibration (12, 19, 24, 25, 39-43). Frequencies ranged from 12.5 - 40 Hertz, peak to peak displacement ranged from 0.7-4.2 mm, and peak acceleration from 0.3 - 8 *g*. The exercises were most often vibration spouts lasting from 15 seconds to 20 minutes, from every day to once a week, and the duration of the intervention were from 6 weeks to 24 months. In two studies the participants used flat soled shoes/gymnastic shoes (12, 24), two studies described the intervention shoeless (19, 26), while the other ten studies did not report a protocol for footwear (Table 2).

Table 2. Intervention parameters in the included studies

Author and year (ref)	Intervention (frequency, peak to peak displacement/ amplitude, peak acceleration)	Vibration type/ device	Protocol exercise	Training time (total vibration per session, training frequency)	Duration	Footwear
Beck 2010 (39)	LWBV 30 Hz, not stated, 0.3 *g*	vWBV/ Juvent 1000DMT	standing full upright no bending	15 min, 2 days/week	8 months	not stated
	HWBV 12.5 Hz, 0-14 mm amplitude, 1 *g*	svWBV/ Galileo 2000	knees slightly bent	6 min, 2 days/week		
Beaudart 2013/ Buckinx 2014 (26, 27)	30 Hz 2 mm amplitude, not stated	vWBV/ Vibrosphere	standing on two feet knees flexed	75 s, 3 days/week	6 months	shoeless
Corrie 2014 (19)	vWBV 28.4 Hz, 1.3 mm peak-to-peak, 1.5 *g*	vWBV/ Power plate	standing with bent knees	6 min, 3 days/week	12 weeks	shoeless
	svWBV 29.8 Hz, 2.9 mm peak-to-peak, 3.6 *g*	sv/ Galileo 2000				
Gomez-Cabello 2013 (40)	40 Hz, 2 mm amplitude, not stated	vWBV/ Pro5Power plate	standing with knees slightly bent holding the handrail	7.5 min, 3 days/week	11 weeks	not stated

Iwamoto 2004 (23)	20 Hz, 0.7-4.2 mm peak to peak, not stated	svWBV/ Galileo	standing with bent knees	4 min, 1 days/week	12 months	not stated
Kiel 2015 (22)	37 Hz, 0.09 mm amplitude, 0.3 *g*	vWBV/ not stated	upright relaxed stand	10 min, 7 days/week	24 months	not stated
Leung 2014 (21)	35 Hz, peak-to-peak < 0.1 mm, 0.3 *g*	vWBV/ not stated	upright no without bending knees	20 min, 5 days/week	18 months	not stated
Liphardt 2015 (20)	20 Hz, 3-4 mm amplitude, not stated	svWBV/ Vibraflex Galileo	stable position 30 degree knee flexion angel	10 min, 2-3 days/week	12 months	not stated
Santin-Medeiros 2015 (41)	20 Hz, 2 mm amplitude, not stated	vWBV/ Fitvibe Excel Pro	18 different exercises, squats	6-6.5 min, 2 days/week	8 months	not stated
Sitjà-Rabert 2015 (25)	30-35 Hz, 2-4 mm amplitude, not stated	vWBV/ Powerplate	30 min static/dynamic exercises	3-6 min, 3 days/week	6 weeks	not stated
Von Stegel 2011 Elvis (42)	25-35 Hz, 1.7 mm amplitude, not stated	vWBV/ Vibrafit	45 min dancing, balance and gymnastics and 15 min dynamic leg-strengthening with WBV and two at home sessions (20 min) with no vibration	6 min, 2 days/week	18 months	not stated
Von Stegel 2011ElvisII (24)	vvWBV, 35 Hz, 1.7 mm peak to peak, 8 *g* svWBV 12.5 Hz, 12 mm peak-to-peak, 8 *g*	vWBV/ Vibrafit svWBV/ Qionic	standing position, seven one or two-legged dynamic leg strengthening exercises	10 min, 3 days/week	18 months	flat-soled shoes
Verschueren 2004 (12)	35-40 Hz, 1.7-2.5 mm amplitude,2.28-5.09 *g*	vWBV/ Power plate	static and dynamic exercises on the vibration platform	20 min, 3 days/week	6 months	gymnastic shoes
Verschueren 2011 (43)	30-40 Hz, not stated, 1.6-2.2 *g*.	vWBV/ Power plate	static and dynamic exercises on the vibration platform	12 min, 3 days/week	6 months	not stated

Abbreviations: *g* = 9.81 m/s², HWBV = high magnitude vibration, Hz = Hertz, LWBV = low magnitude vibration, min = minutes, mm = millimetre, , s = seconds, svWBV = side alternating whole body vibration, and vWBV = vertical whole body vibration.

Outcomes

One study reported fractures as the primary outcome. A total of six studies reported fall data. Three authors were contacted to obtain data on fall rate (23, 25) and fall risk (42) and this way data were obtained from one trial (25).

Data on bone parameters were reported in percent change, or pre- and post-intervention measurements in eight studies. The corresponding authors were contacted (12, 19-23, 39, 41, 43), and data were obtained this way from three studies (19, 21, 22).

In two studies data were extracted from previous reviews (33, 34), which reported to have primary data available from the authors (12, 23, 41), and in the rest of the studies the outcomes were calculated as described in the method section.

Risk of biases within studies

The majority of studies were categorized as having a low risk of bias in the randomization with unclear risk of bias in the allocation due to insufficient reporting in half of the studies. The performance bias was categorized as high risk when the participants reported falls and were not blinded to the intervention. One study used wellness therapy in the control group and did not inform the participants of the hypotheses, and was thus considered unclear in the risk of performance bias with respect to falls reporting (42). Non-blinding of participants were categorized as unclear risk of bias when the outcome were bone parameters. The risk of bias in selective reporting was categorized as low risk if the trial reported all stated outcomes in the papers and was conducted before 2005. After 2005 trials had to be registered online at a registry or having published a study protocol reporting the pre-specified outcomes. Figure 2 shows a summary of the risk of bias assessment.

Fractures

One study reported fractures as a primary outcome (Risk Ratio (RR) 0.48 (95% CI 0.14-1.56), with an intra-cluster correlation coefficient of 0.000 (Figure 3).

Falls

Four studies reported falls as primary outcome (21, 25, 26, 42). Three studies reported fallers and the number of falls in total in each group during the intervention (21, 25, 26) and one study reported the mean number of falls per participants (42). One study reported no events in the control arm in the six weeks intervention and adjusted rate ratio could not be calculated. Pooling the studies with falls reported as outcomes showed a fall rate ratio of 0.67 (95% CI 0.50-0.89, p=0.006, I^2=19%) (Figure 4-a) in the intervention groups compared to non-intervention and a relative risk of experiencing falls of 0.76 (95% CI 0.48-1.20, p=0.24, I^2=24%) (Figure 4-b).

Two trials reported falls as adverse effects (23, 39). A post hoc sensitivity analysis was conducted to assess if the inclusion of these trials would alter the result. In this analysis a fall rate/person years rate ratio of 0.65 (95% CI 0.50-0.85, p=0.002, I^2=8%) was found and a relative risk of experiencing falls of 0.67 (95% CI 0.46-0.98, p=0.04, I^2=13%) (Supplement data Fig 1 a-b).

Post hoc subgroup analyses were conducted to assess the association between the duration and the magnitude of the vibration and falls, duration over six months fall rate ratio of 0.61 (95% CI 0.47-0.80, p=0.0004, I^2=0%, 2 studies), duration over six months and relative risk of experiencing falls of 0.61 (95% CI 0.47-0.80, p=0.0004, I^2=0%, 2 studies), low magnitude vibration fall rate ratio of 0.56 (95% CI 0.40-0.78, p=0.0006, 1 study), high magnitude vibration fall rate ratio of 0.80 (95% CI 0.55-1.18, p=0.26, I^2=0%, 2 studies) (supplement data Fig 2 a-c).

Bone Mineral Density

Seven studies reported data on lumbar spine BMD (12, 21, 23, 24, 39, 40, 42). The results showed no overall effect with a mean difference of 0.00 (95% CI -0.00-0.01, p=0.11, I^2=22%) (Figure 5-a). Six studies reported data on total hip BMD (12, 21, 40-43) showing similar results with a mean difference of 0.00 (95% CI -0.00-0.01, p=0.27, I^2=50%) (Figure 5-b). Subgroup analyses with vertical and side-alternation vibration explained 44.5% of the heterogeneity in the lumbar spine BMD, and side-alternation vibration showed a mean difference of 0.01 (95% CI 0.00-0.02, p=0.04, I^2=0%) with 117 participants. All studies reporting BMD in total hip used vertical vibration.

One study reported change in total proximal femoral trabecular BMD and change in integral lumbar spine vertebral BMD (22). The results from the originally planned duration of 24 months showed no effect on integral lumbar spine vertebral BMD with a mean difference of 0.00 (95% CI -0.00-0.00) and total femoral trabecular BMD mean difference of 0.00 (95% CI -0.00-0.01) (Supplement data Fig 3 a-b). Two studies reported volumetric BMD (vBMD) of radius and tibia using HR-pQCT (20) or quantitative computed tomography (pQCT) scans (37). The results for the ultradistal site using HR-pQCT and a 4% site in tibia and radius using pQCT were combined in forestplots showing no statistically significant effects with a vBMD tibia mean difference of -0.68 (95% CI -2.29-0.93, p=0.41, I^2=0) and a vBMD radius mean difference of 1.87 (95% CI -0.62-4.36, p=0.30, I^2=8) (Figure 5 c-d).

Bone microarchitecture

One study reported measurements of cortical porosity (Ct.Po) and trabecular BMD (tbBMD) (20) using HR-pQCT. We refrained from performing a meta-analysis due to the limited data (Supplement data Fig 4). In tibia, WBV compared to control showed an increase in mean difference in Ct.Po of 0.20 % (95% CI -0.25-0.65) and decrease in tbBMD mean difference -0.3 mg HA/cm^3 (95% CI -0.58-0.02). In radius, WBV compared to no intervention showed an increase mean difference in Ct.Po of 0.10 % (95% CI -0.15-0.35) and decrease in tbBMD mean difference -0.90 mg HA/cm^3 (95% CI -0.90-2.10) (Supplement data Fig 4).

Bone turnover markers

One study reported data on the bone resorption marker CTX (12) and two studies on both CTX and the bone formation marker P1NP (19, 22). One of the studies reported log transformed CTX and P1NP (19) and no untransformed data could be obtained from the authors. The result for the meta-analysis on CTX was a mean difference of 0.01 ng/mL (95% CI -0.06-0.08, p=0.73, I^2=0) and with data available from only one trial the result for P1NP was a mean difference of 4.92 ng/mL (95% CI -3.06-12.90) (Figure 6 a-b).

Calcaneal BUA

A single study reported calcaneal BUA mean change in comparing two vibration groups with a control group (39), we refrained from performing a meta-analysis due to the limited data (Supplement data Fig 5). The low magnitude vertical vibration group had a mean difference of 1.99 dB/MHz (95% CI-0.84- 4.82) and the high magnitude side-altering vibration group a mean change of 4.69 dB/MHz (95% CI 1.61-7.77) compared to the controls (Supplement data Fig 5).

Quality assesment

Quality of evidence was assessed for each outcome (Table 3). For the outcome of fractures the evidence was downgraded for imprecision due to the 95% confidence interval around the pooled estimate of effect includes both the possibility of no effect and appreciable benefit. The evidence for falls rate was downgraded for study limitations due to non-blinding of the participants. The risk of falls was downgraded for imprecision and study limitations due to non-blinding of the participants. Bone parameters were all downgraded for indirectness since they are surrogate markers for bone strength. Regarding bone parameters the outcomes were downgraded for imprecision if the 95% confidence interval around the pooled estimate of effect includes both the possibility of no effect and appreciable benefit and for inconsistency if the I^2 statistics showed substantial heterogeneity. Publication bias could not be assessed by a funnel plot with Egger's test since all of the meta-analyses contained less than 10 studies (36).

Table 3. Summary of findings table presents the findings and the quality of each outcome using the GRADE considerations

WBV compared to usual care for fracture risk
Bibliography:

Outcomes	№ of participants (studies) Follow-up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with usual care	Risk difference with WBV
fractures	710 (1 RCT)	⊕⊕⊕◯ MODERATE [a]	**RR 0.48** (0.14-1.56)	2 per 100	**1 fewer per 100** (2 fewer to 1 more)
fall rate/person years	746 (3 RCTs)	⊕⊕⊕◯ MODERATE [b]	**Rate ratio 0.67** (0.50-0.89)	34 per 100	**11 fewer per 100** (17 fewer to 4 fewer)
The risk of experiencing falls (fallers)	805 (3 RCTs)	⊕⊕◯◯ LOW [c]	**RR 0.76** (0.48-1.20)	23 per 100	**6 fewer per 100** (12 fewer to 5 more)
Total bone mineral density lumbar spine (BMD spine)	911 (7 RCTs)	⊕⊕⊕◯ MODERATE [d]	-		mean **0** (0 to 0.01 higher)
Bone mineral density total hip (BMD hip)	870 (6 RCTs)	⊕⊕◯◯ LOW [e]	-		mean **0** (0 to 0.01 higher)
Volumetric bone mineral density tibia	80 (2 RCTs)	⊕⊕◯◯ LOW [f]	-		mean **0.68 lower** (2.29 lower to 0.93 higher)
Volumetric bone mineral density radius	80 (2 RCTs)	⊕◯◯◯ VERY LOW [g]	-		mean **1.87 higher** (0.62 lower to 4.36 higher)
Serum biomarker of bone resorption (CTX)	138 (2 RCTs)	⊕⊕◯◯ LOW[f]	-		mean **0.01 higher** (-0.06 lower to 0.08 higher)

WBV compared to usual care for fracture risk

Bibliography:

Outcomes	№ of participants (studies) Follow-up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with usual care	Risk difference with WBV
Serum biomarker of bone formation (P1NP)	118 (1 RCT)	⊕⊕◯◯ LOW [f]	-		mean **4.92 higher** (3.06 lower to 12.9 higher)

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

a. serious imprecision, due to the 95% confidence interval around the estimate of effect includes both the possibility of no effect and appreciable benefit.

b. serious study limitations- lack of blinding of the participants reporting falls.

c. serious study limitations- lack of blinding of the participants reporting fall, and serious imprecision, due to the 95% confidence interval around the pooled estimate of effect includes both the possibility of no effect and appreciable benefit.

d. indirectness (surrogate marker for bone strength).

e. indirectness, and statistical heterogeneity

f. indirectness, and imprecision due to the 95% confidence interval around the estimate of effect includes both the possibility of no effect and appreciable benefit.

g. indirectness, and imprecision due to the 95% confidence interval around the estimate of effect includes both the possibility of no effect and appreciable benefit and statistical heterogeneity.

Discussion

This systematic review and meta-analysis provides evidence that whole-body vibration exercise reduces fall rate in adults above 50 years of age. We found a tendency in reduction of the proportion of fallers, no overall effect on BMD whereas only sparse data were available regarding bone microarchitecture parameters, bone turnover markers, and BUA. One study reported fractures showing non-significant fracture reduction.

Strengths and limitations

This study had some limitations. By not including non-English language literature and not extracting data from grey literature or adverse effects the risk of selection bias exists. Looking at the studies reporting falls as adverse effects in the included studies, the WBV reduces the falls rate and risk in agreement with our findings.

Only one study had fractures as primary outcome and had a low fracture rate (21). The studies contributing with falls data were unblinded which could be important when reporting falls. However, all studies included in the primary falls analysis did record falls prospectively limiting the risk of recall bias (21, 25, 26, 42). The populations in the studies consisted of 82% community dwelling adults with 90% being female, making the results generalizable only to people with similar characteristics.

Strengths of this review include that the evidence is obtained from randomized controlled trials, followed the PRISMA guidelines of reporting, and was registered at PROSPERO to improve transparency. A thorough literature search was conducted with assistance from a research librarian and we furthermore performed a hand search of the reference lists of included papers and earlier reviews references (28, 29, 32-35). The risk of selection bias was reduced by having two independent reviewers select the papers and extract the data. In the systematic review all outcomes were assessed regarding quality using the GRADE guidelines where fracture is classified as a critical outcome (37). We classified falls as an important outcome, and bone parameters being of limited importance as surrogate makers for fracture risk (37). We only pooled homogeneous outcomes in the meta-analysis leading to low statistical heterogeneity in the falls analysis with moderate statistical heterogeneity regarding BMD of the hip and spine. Pre-assigned subgroup analysis for vertical vs. side-alternating vibration could explain 44.5% of the heterogeneity in the lumbar spine analysis, whereas regarding total hip BMD all studies used vertical vibration and no subgroup analysis was performed. Meta-regression analysis was not performed due to the insufficient number of studies in the analysis (36).

Comparisons with other studies and reviews

Prior reviews of exercise have shown that exercise programs designed to prevent falls in older adults also seem to prevent injuries caused by falls, including fractures (44, 45). The majority of these exercise programs included balance training, functional training, and strengthening exercises. Earlier reviews have shown that WBV have balance improving capabilities and the ability to improve muscle strength of the lower extremities (27-31), and WBV might thus prevent fractures by its fall reducing capacity or by lowering the impact of a fall.

Our meta-analysis shows that rate of falls can be reduced, and suggests a reduction in the proportion of fallers. The number needed to treat to prevent one fall was 11 (Table 3). Sustaining a fall increases the risk of injury, and reducing the number of times an individual falls, even if not the number of fallers may have clinical and economic relevance to the individual and to society. Falls are very prevalent among the aging population with one in every three 65+ year olds experiencing a fall every year (6). Due to an ageing population a focus on interventions capable of reducing falls seems of utmost importance (10). Prior systematic reviews have shown that other exercise programmes can reduce fall rate through muscle strength and balance training, and it has been found that exercising for a period of more than three hours per week is associated with a larger decrease in fall rate (46). WBV exercise consists of shorter workouts and with the ability to stand as the only requirement for physical function. With the available data the analysis shows a fall reduction in the vibration groups with low heterogeneity and with the observational power of the post hoc subgroup analyses we found an association between studies with duration longer than 6 months and a larger reduction in falls.

To our knowledge this is the first meta-analysis conducted on WBV and falls but earlier findings of a positive effect on surrogate markers for falls (balance and muscle strength) (27-31) can be viewed as an improvement in important risk factors for falls in agreement with our findings.

Our results on BMD are consistent with other systematic reviews, showing no overall effect on BMD (31-34). Earlier reviews suggested a positive effect on BMD in adolescents (32) and in a subgroup analysis with improvements after low-magnitude WBV on lumbar spine BMD (33) and high magnitude WBV on total hip BMD (32). We found a similar but small effect of side alternating vibration on lumbar spine BMD. In contrast to others, this systematic review also comprehensively assessed other bone parameters i.e. bone microarchitecture, turnover markers, and BUA. We found one study assessing cortical porosity and trabecular BMD of tibia and radius (20) with no overall effect, which is in line with results found in a younger age group (47). We found no effect on bone resorption markers in line with studies in younger participants (48, 49). One study in this review had a positive effect in bone formation markers, but with logarithmic transformed data it could not be pooled with non-transformed data (19) (Supplement data Fig 6). One study looked at BUA of the calcaneus showing a positive effect (39) in conflict with earlier findings from younger participants (47). Animal data suggest an effect of WBV on bone strength (15-18), but the same effect in humans is not evident. Reasons for this include diversities in training protocols, duration, adherence, damping of the vibration by the use of shoes, and different standing positions on the vibration plates.

In summary, the the evidence from this systematic review indicate that WBV may reduce fall rate with moderate certainty, and the risk of falls with low certainty. Future trials could enhance the certainty by systematically reporting falls when monitoring adverse effects, and if possible by blinding participants. The quality of evidence for the effect on bone parameters is moderate to low, partly since they aresurrogate markers of fracture risk and future research should focus on the critical outcome fractures with larger trial sizes and adequate follow-up.

Conclusion

In conclusion, our data shows a reduced rate of falls by WBV. Only one study reported fractures showing a non-significant reduction. We found no effect on BMD, and the data on microarchitecture and bone turnover markers were sparse. WBV exercise could be implemented in current falls prevention guidelines. It might potentially reduce fractures by reducing falls but the impact on fractures needs further larger adequately powered studies.

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Conflict of interest

All authors have completed the ICMJE uniform disclosure form at and declare no conflict of interests. DJ has received research grants from the Odense University Hospital, The Region of Southern Denmark Ph.D. foundation, the Faculty of Health Sciences, University of Southern Denmark, and the Danish Osteoporosis Foundation. The funding parties have no influence on the study design, study conduct, results, or dissemination.

Author contributions

All authors helped in the conception and design of the work and interpretation of data. Three authors reviewed the papers (DJ, KT, and JR) and two authors extracted the data (DJ, KT). DJ, TM, and JR did the first draft and all authors revised it critically for important intellectual content. All authors approved the final version for publication. DJ is guarantor.

Data sharing statement

No additional data are available.

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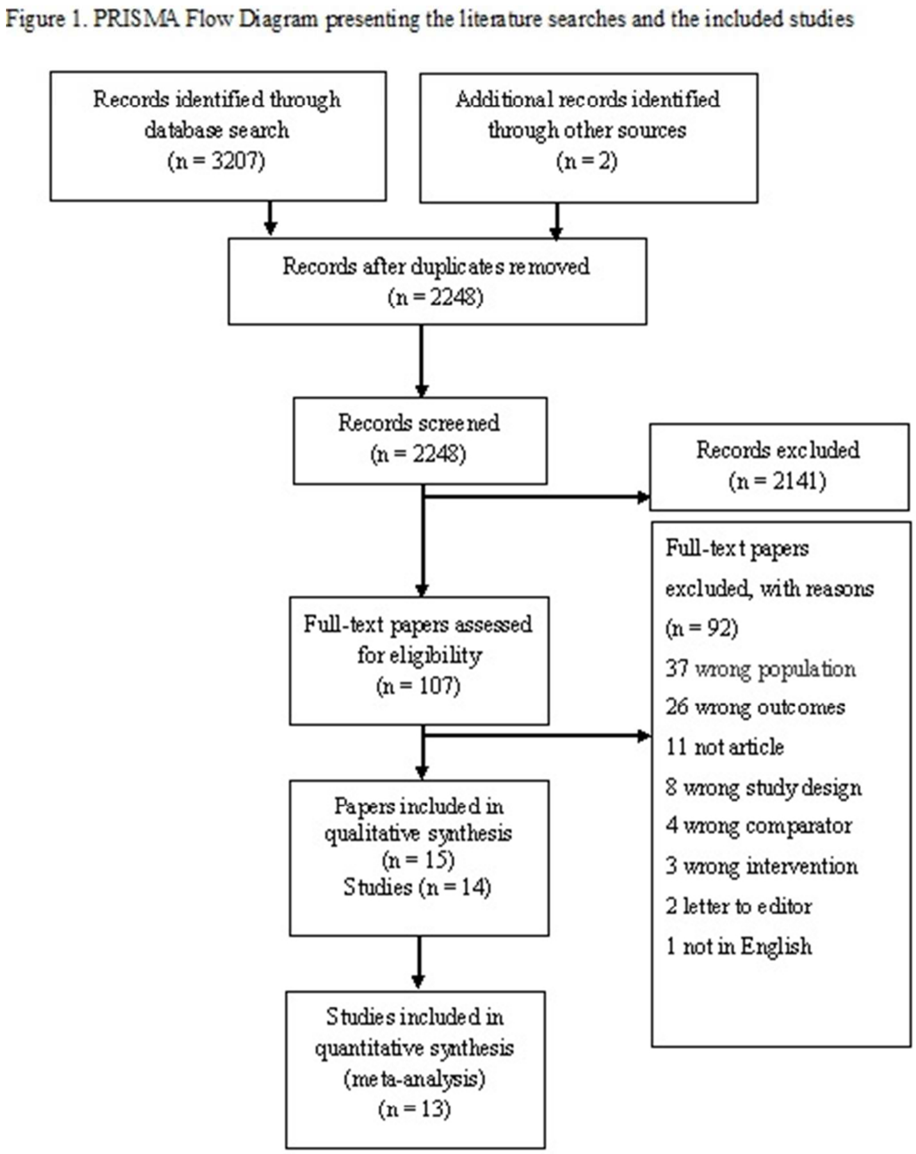

Figure 1. PRISMA Flow Diagram presenting the literature searches and the included studies.

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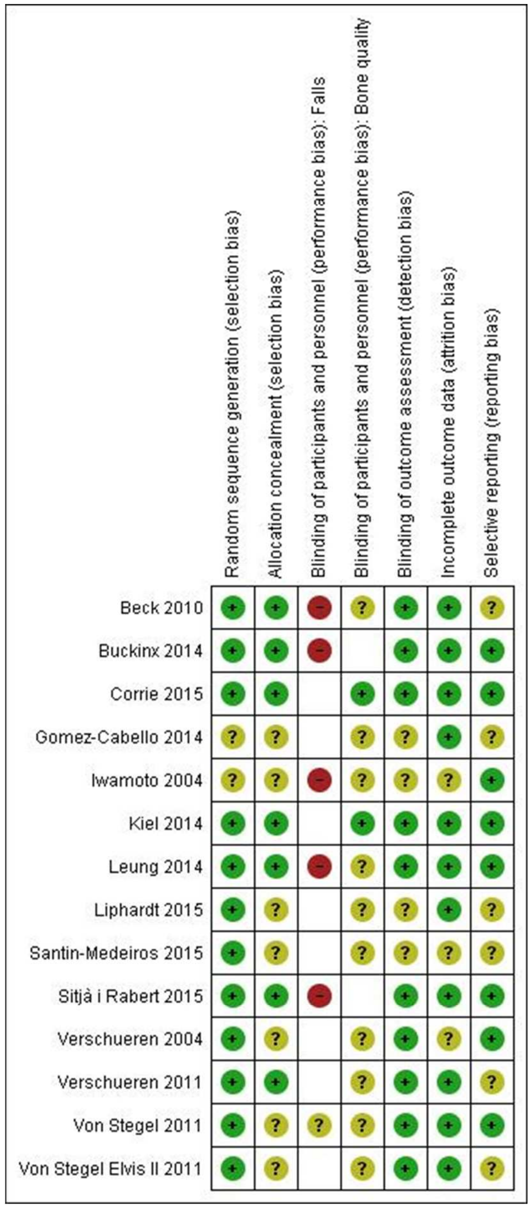

Figure 2. The risk of bias assessment.

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Figure 3. Effect of whole-body vibration (WBV) on the relative risk of experiencing a fracture

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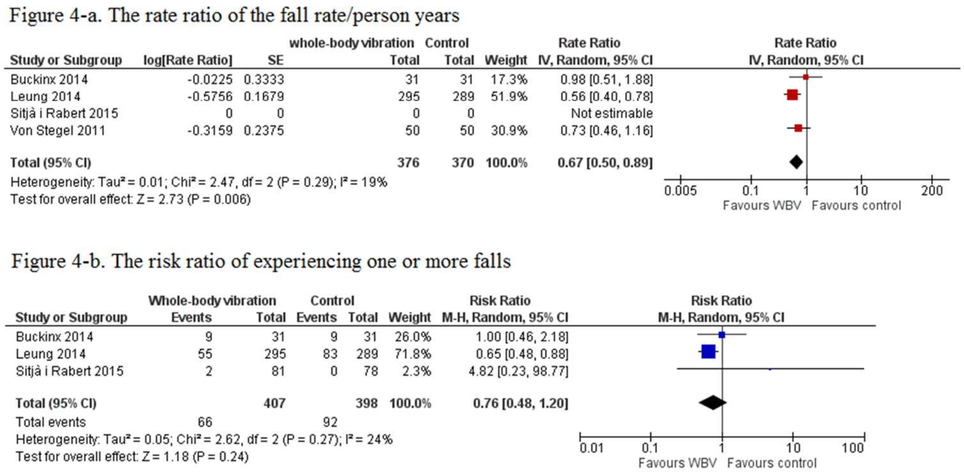

Figure 4-a. The rate ratio of the fall rate/person years

Study or Subgroup	log[Rate Ratio]	SE	whole-body vibration Total	Control Total	Weight	Rate Ratio IV, Random, 95% CI
Buckinx 2014	-0.0225	0.3333	31	31	17.3%	0.98 [0.51, 1.88]
Leung 2014	-0.5756	0.1679	295	289	51.9%	0.56 [0.40, 0.78]
Sitjà i Rabert 2015	0	0	0	0		Not estimable
Von Stegel 2011	-0.3159	0.2375	50	50	30.9%	0.73 [0.46, 1.16]
Total (95% CI)			**376**	**370**	**100.0%**	**0.67 [0.50, 0.89]**

Heterogeneity: Tau² = 0.01; Chi² = 2.47, df = 2 (P = 0.29); I² = 19%
Test for overall effect: Z = 2.73 (P = 0.006)

Figure 4-b. The risk ratio of experiencing one or more falls

Study or Subgroup	Whole-body vibration Events	Whole-body vibration Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Buckinx 2014	9	31	9	31	26.0%	1.00 [0.46, 2.18]
Leung 2014	55	295	83	289	71.8%	0.65 [0.48, 0.88]
Sitjà i Rabert 2015	2	81	0	78	2.3%	4.82 [0.23, 98.77]
Total (95% CI)		**407**		**398**	**100.0%**	**0.76 [0.48, 1.20]**
Total events	66		92			

Heterogeneity: Tau² = 0.05; Chi² = 2.62, df = 2 (P = 0.27); I² = 24%
Test for overall effect: Z = 1.18 (P = 0.24)

Figure 4. Forest plot of the effect of whole-body vibration (WBV).‼ ┼ Figure 4-a. The rate ratio of the fall rate/person years between the WBV and control group. Figure 4-b. The risk ratio of experiencing one or more falls. Area of each square is proportional to study weight in meta-analysis and horizontal lines represent exact 95% confidence intervals. Diamonds represent pooled effect estimates from random effects meta-analysis‼ ┼ .

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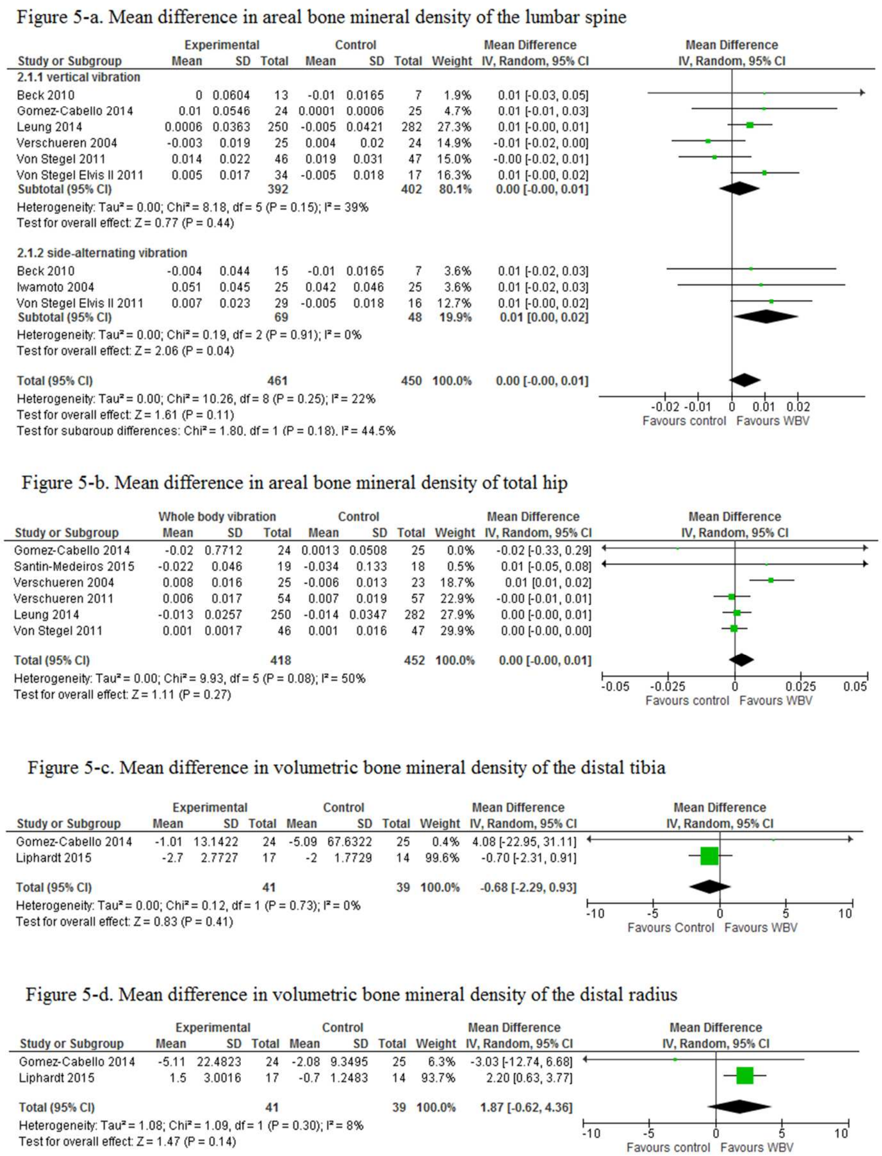

Figure 5. The effect of whole-body vibration exercise (WBV) in forest plots on a) areal bone mineral density (BMD) of the lumbar spine with weighted mean difference and 95% confidence intervals (CI), divided in subgroups with vertical vibration and side-alternating vibration, b) areal BMD in total hip with weighted mean difference and 95% CI, c) volumetric BMD of the distal tibia with weighted mean difference with 95% CI, and d) WBVs effect on volumetric BMD of the distal radius with weighted mean difference and 95% CI. Area of each square is proportional to study weight in meta-analysis and horizontal lines represent exact 95% confidence intervals. Diamonds represent pooled effect estimates from random effects meta-analysis.

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Figure 6-a. Mean difference in bone resorption marker CTX

	WBV			Control				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Kiel 2014	0.01596	0.2058	56	0.00495	0.1755	62	99.9%	0.01 [-0.06, 0.08]
Verschueren 2004	-0.084	0.4224	25	-0.98	4.9281	25	0.1%	0.90 [-1.04, 2.83]
Total (95% CI)			**81**			**87**	**100.0%**	**0.01 [-0.06, 0.08]**

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.80$, $df = 1$ ($P = 0.37$); $I^2 = 0\%$
Test for overall effect: $Z = 0.34$ ($P = 0.73$)

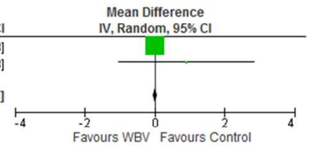


Figure 6-b. Mean difference in bone formation marker P1NP

	WBV			Control				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Kiel 2014	3.901	23.5	56	-1.02	20.4	62		4.92 [-3.06, 12.90]

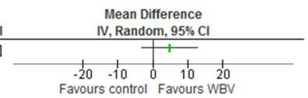


Figure 6. Presents the effect of whole body vibration exercise on bone resorption markers in forest plot with carboxy-terminal collagen crosslink (CTX) and the reported effect on bone formation marker amino terminal propeptide of type I collagen (P1NP). Area of each square is proportional to study weight in meta-analysis and horizontal lines represent exact 95% confidence intervals. Diamonds represent pooled effect estimates from random effects meta-analysis.

201x104mm (300 x 300 DPI)

Appendix

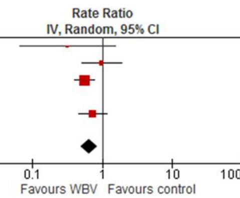
Appendix 1. The search string

(vibration OR vibrations OR vibratory) AND (Fractures OR fracture OR DXA OR Dual-energy X-ray absorptiometry OR dual energy x-ray absorptiometry OR dual energy x ray absorptiometry OR dual-energy X ray absorptiometry OR BMD OR bone mineral density OR bone density OR bone mass OR bone quality OR bone qualities OR bone formation OR bone turnover OR accidental fall OR accidental falls OR falls OR fall OR falling OR bone biomarker OR bone biomarkers OR CTX OR P1NP OR carboxy-terminal collagen crosslink OR carboxy terminal crosslink OR amino-terminal propeptide of type I collagen OR amino terminal propeptide of type I collagen OR Calcaneal quantitative ultrasound OR QUS OR Bone Biopsy OR bone biopsies OR HRQCT OR High resolution peripheral quantitative computed tomography OR HRpQCT OR High resolution quantitative computed tomography)

Supplement data Figure 1-a. Fall rate ratio/person years including adverse effect data

Study or Subgroup	log[Rate Ratio]	SE	Whole body vibration Total	Control Total	Weight	Rate Ratio IV, Random, 95% CI
Beck 2010	-1.1474	0.8022	28	14	2.8%	0.32 [0.07, 1.53]
Buckinx 2014	-0.0225	0.3333	31	31	15.7%	0.98 [0.51, 1.88]
Leung 2014	-0.5756	0.1679	295	289	52.4%	0.56 [0.40, 0.78]
Sitjà i Rabert 2015	0	0	0	0		Not estimable
Von Stegel 2011	-0.3159	0.2375	50	50	29.1%	0.73 [0.46, 1.16]
Total (95% CI)			**404**	**384**	**100.0%**	**0.65 [0.50, 0.85]**

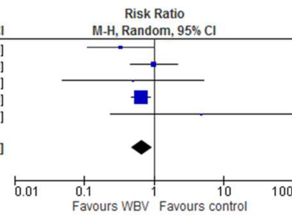
Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 3.27$, df = 3 (P = 0.35); $I^2 = 8\%$
Test for overall effect: Z = 3.16 (P = 0.002)



Supplement data Figure 1-b Risk ratio of experiencing falls including advers effect data

Study or Subgroup	Favours WBV Events	Favours WBV Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Beck 2010	4	28	6	14	9.0%	0.33 [0.11, 0.99]
Buckinx 2014	9	31	9	31	16.8%	1.00 [0.46, 2.18]
Iwamoto 2004	1	25	2	25	2.1%	0.50 [0.05, 5.17]
Leung 2014	55	295	83	289	70.8%	0.65 [0.48, 0.88]
Sitjà i Rabert 2015	2	81	0	78	1.2%	4.82 [0.23, 98.77]
Total (95% CI)		**460**		**437**	**100.0%**	**0.67 [0.48, 0.94]**
Total events	71		100			

Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 4.34$, df = 4 (P = 0.36); $I^2 = 8\%$
Test for overall effect: Z = 2.32 (P = 0.02)



Supplement data Figure 1. presents supplement data on a) fall rate/ person years including adverse effect data on the effect of whole-body vibration (WBV) on rate ratio of the fall rate/person years between the whole-body vibration and control group and b) risk ratio of experiencing one or more falls including adverse effect data. Area of each square is proportional to study weight in meta-analysis and horizontal lines represent exact 95% confidence intervals. Diamonds represent pooled effect estimates from random effects meta-analysis.

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Figure 2-a. Post hoc subgroup analysis fall rate divided by duration

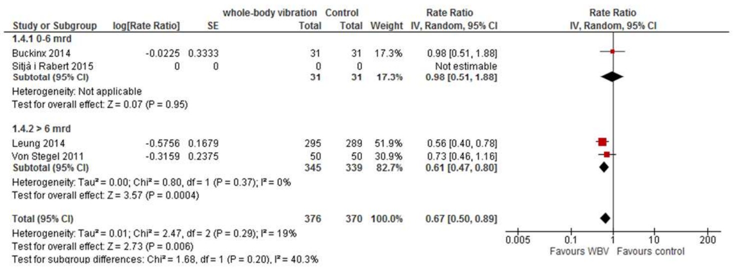


Figure 2-b. Post hoc subgroup fallers vs non fallers divided by duration

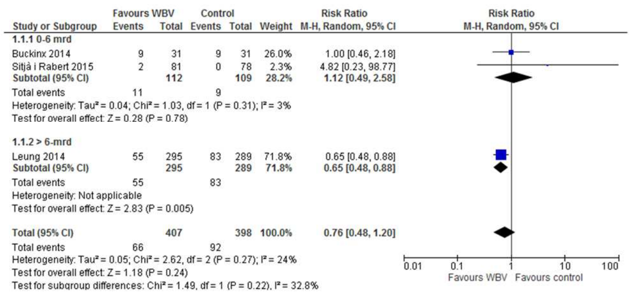
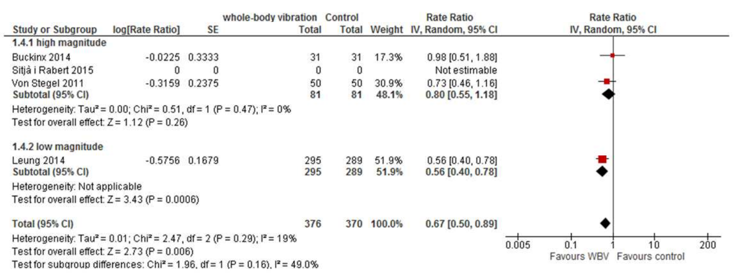


Figure 2-c. post hoc subgroup analysis fall rate ratio divided in High vs low magnitude vibration

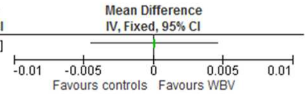


Supplement data Figure 2. presents post hoc subgroup analysis on a) fall rate/ person years divided in interventions of longer duration than six months, b) risk ratio of experiencing one or more falls divided in interventions of longer than six months, c) fall rate/ person years divided in high and low magnitude vibration. Area of each square is proportional to study weight in meta-analysis and horizontal lines represent exact 95% confidence intervals. Diamonds represent pooled effect estimates from random effects meta-analysis.

201x314mm (300 x 300 DPI)

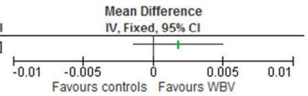
Supplement data Figure 3-a. vertebral integral BMD

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Kiel 2014	0.0037	0.0124	47	0.0036	0.0105	52		0.00 [-0.00, 0.00]



Supplement data Figure 3-b. femoral trabecular BMD

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Kiel 2014	0.002905	0.00996	50	0.001106	0.00632	58		0.00 [-0.00, 0.01]

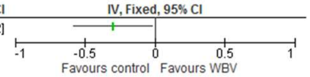


Supplement data Figure 3. Presents supplement data of whole-body vibration exercises (WBV) effect on bone architecture parameters with mean difference and 95% CI. a) mean difference change in vertebral integral bone mineral density and b) mean difference change in total femoral trabecular bone mineral density.

201x104mm (300 x 300 DPI)

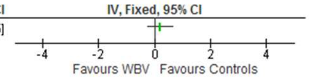
Supplement data figure 4-a. total trabecular BMD in tibia

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
Liphardt 2015	-0.2	0.5325	17	0.1	0.2387	14		-0.30 [-0.58, -0.02]



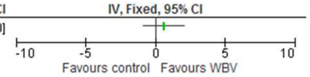
Supplement data figure 4-b. cortical porosity in % in tibia

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
Liphardt 2015	-0.3	0.4961	17	-0.5	0.7324	14		0.20 [-0.25, 0.65]



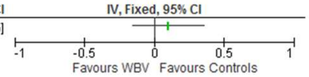
Supplement data figure 4-c. total trabecular BMD in radius

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
Liphardt 2015	-0.1	0.4479	17	-0.7	2.8265	14		0.60 [-0.90, 2.10]



Supplement data figure 4-d. cortical porosity in % in radius

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
Liphardt 2015	-0.1	0.2414	17	-0.2	0.4322	14		0.10 [-0.15, 0.35]

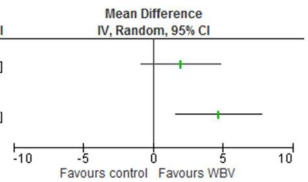


Supplement data Figure 4. presents supplement data analysis for microarchitecture parameters of whole-body vibration exercises (WBV) effect on microarchitecture parameters with mean difference and 95% confidence intervals a.) analyses is with total trabecular BMD in tibia (mg HA/cm^3), b) cortical porosity in % in tibia, c) total trabecular BMD for radius (mg HA/cm^3) and d) cortical porosity in % for radius.

201x193mm (300 x 300 DPI)

Supplement data figure 5. Broadband ultrasound attenuation of calcaneus

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Mean Difference IV, Random, 95% CI
2.11.1 VV							
Beck 2010	-0.6	2.7086	13	-2.59	3.2564	7	1.99 [-0.84, 4.82]
2.11.2 SV							
Beck 2010	2.1	3.7921	15	-2.59	3.2564	7	4.69 [1.61, 7.77]

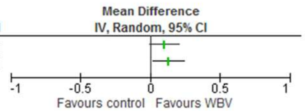


Supplement data Figure 5. presents supplement data of whole-body vibration exercises (WBV) effect on Broadband ultrasound attenuation (BUA) of calcaneus with mean difference and 95% CI. First study line is results from vertical vibration and second line is side alternating vibration, the control group is divided between the two.

201x85mm (300 x 300 DPI)

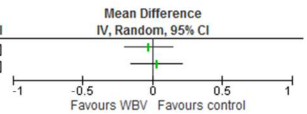
Supplement data Figure 6-a P1NP

	Experimental			Control				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Corrie 2015	0.049	0.106	12	-0.054	0.108	6		0.10 [-0.00, 0.21]
Corrie 2015	0.079	0.107	11	-0.054	0.108	5		0.13 [0.02, 0.25]



Supplement data Figure 6-b. CTX

	Experimental			Control				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Corrie 2015	0.09	0.17	12	0.115	0.176	6		-0.03 [-0.20, 0.15]
Corrie 2015	0.144	0.178	11	0.115	0.176	5		0.03 [-0.16, 0.22]



Supplement data Figure 6. presents reported effect on logaritmically transformed data of whole-body vibration exercises (WBV) effect on a) amino terminal propeptide of type I collagen (P1NP) (marker of bone formation) with mean difference and 95% CI, and b) carboxy-terminal collagen crosslink (CTX) (marker of bone resorption) with weighted mean difference with 95% CI. First study line is results from vertical vibration and second line is side alternating vibration, the control group is divided between the two.

201x122mm (300 x 300 DPI)

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3-4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4-5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	6
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	4-6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4-5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	appendix
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5-6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5-6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5-6
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	5-6
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	5-6
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	5-6

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	5-6 Table 3
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	5-6
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Table 1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Figure 2 Table 3
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Figure 3-6 Supplement Figure 1-5
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Figure 3-6
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Table 3
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Supplement figure 1
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	18-19 Table 3
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	18-20
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	19-20
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	20

PRISMA 2009 Checklist

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

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Trends and correlates of the public's perception of the healthcare system in the European Union from 2009 to 2013

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Trends and correlates of the public's perception of the healthcare system in the European Union from 2009 to 2013

AlJohara M. AlSaud [a], Henock B. Taddese [a], Filippos T. Filippidis [a]

[a] Department of Primary Care and Public Health, School of Public Health, Imperial College London, United Kingdom

Corresponding author:

Filippos T Filippidis

Address: School of Public Health, Imperial College London, 310 Reynolds Building, St. Dunstan's Road, London W6 8RP, United Kingdom

Tel: +44 (0)20 7594 7142

Email: f.filippidis@imperial.ac.uk

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ABSTRACT

Objective: The aim of the study is to assess trends in public perceptions of health systems in 27 European Union (EU) member states following the financial crisis (2009 – 2013), in order to discuss observed changes in the context of the financial crisis.

Design: Repeated cross-sectional studies.

Setting: 27 EU countries.

Participants: EU citizens aged 15 years and older.

Methods: The study mainly uses the Eurobarometer Social Climate Surveys, conducted annually between 2009 and 2013, thereby analysing 116,706 observations. A multilevel logistic regression was carried out to analyse trends over time and the factors associated with citizens' perceptions of their healthcare systems.

Results: Europeans generally exhibit positive perceptions of their national healthcare systems, 64.0% (95% CI 63.6-64.4%). However, we observed a significant drop in positive perceptions in the years following the crisis, especially within countries most affected by the crisis. Concerning fiscal characteristics, wealthier countries and those dedicating higher proportion of their national income to health were more likely to maintain positive perceptions. At the individual level, perceptions of healthcare systems were significantly associated with respondents' self-perceptions of their social status, financial capacity and overall satisfaction in life.

Conclusions: Our finding confirms previous observations that citizens' perceptions of their healthcare systems may reflect their overall prospects within the broader socio-economic systems they live in; which have in-turn been affected by the financial crisis and the policy measures instituted in response.

Strengths and limitations of this study

- This study uses a large sample size and includes data from 27 EU countries.
- The cross-sectional nature of the study limits the potential to make causal associations between the crisis and changes in the perceptions.
- The Eurobarometer survey used a single question to assess citizens' perceptions, rather than using composite indices to be able to capture the multidimensional nature of 'public perception', more comprehensively.

Introduction

The global financial crisis that started in 2008 has precipitated major economic and financial impacts, and prompted austerity policy responses across Europe; majorly austerity and public sector retrenchment policies.[1 2] Most of the healthcare reforms following the financial crisis involved cuts to public services and a related increase in citizens' out-of-pocket expenditure, which in turn affected people's access to care.[1 3] The broader socio-economic effects of the crisis such as rising unemployment, income reduction, increased out of pocket spending (through coinsurance and shared payments) and retrenchment of welfare support were more pronounced in the most affected countries, which had also instituted stringent austerity measures (e.g. Greece, Spain, Ireland and Portugal).[1 4] Whilst a full account of the effects of the crisis in terms of mortality and morbidity rates may take several years, early health effects have already been documented in these countries in the form of rising mental disorders, high suicide rates and deteriorating access to services.[1 4 5] In contrast, some countries followed a different path in their responses to the crisis by implementing a fiscal stimulus package and investing in social protection (Germany) or protecting their health budgets (Belgium, Denmark, the UK).[1]

In light of the above, there is growing interest in studying the consequences of the crisis on health systems, as well as the different trajectories of healthcare systems across countries which may correlate to the differences in the type of policy responses adopted to mitigate the effects of the crisis. In this regard, mortality and morbidity data as well as healthcare access and quality data constitute the primary measures of interest for gauging effects on health systems. Beyond these measures, public perception metrics have also become integral to cross-country and across-time comparisons of health systems; which are in turn a reflection of the shift towards people centered health systems and the corresponding emphasis on responsiveness of health systems.[6 7] Technically, public perception surveys are known to represent a mixture of citizens' personal experiences with the healthcare system on the one hand, and their broader views of the system on the other.[8] Unlike satisfaction surveys, where patients are typically surveyed after an episode of service utilization to evaluate their experiences in receiving care, the results of public perception surveys are known to be influenced by wide ranging factors: respondents' views on the general state-of-affairs in the country[8]; the national political debate around the nature, effectiveness and constitution of the health system; culture of support for the welfare state in the country; and portrayals of the health system in the media.[6 9] Still, findings of public perception surveys are used to compare and explain distinct changes over time in healthcare systems in different countries[6 7]; to validate and argue for the impacts of particular health policy reforms[10]; to counter expert opinions on the ranking of national health systems[8]; and to ascertain people's perspectives on aspects of health policy such as levels of government financing of health care[11].

The aim of our study is to assess trends in public perceptions of health systems in 27 European Union (EU) member states between 2009 and 2013, in order to discuss observed changes in the context of the financial crisis and the European governments' responses to it.

Methods

Data Sources

To evaluate EU citizens' perceptions of their healthcare systems, this study used data from the Eurobarometer Social Climate survey between 2009 and 2013 as well as other public data sources. The Eurobarometer is a series of public opinion surveys that consists of approximately 1,000 face-to-face interviews per country with individuals aged 15 years and older.[12]

A multi-stage random (probability) sampling design was applied in all member-states.[13] To ensure the samples are representative of the population, each sample was weighted according to a national weighting procedure for sex, age, and region. Since country samples are approximately the same size (n=1000), population size weighting factors were used to ensure that each country is represented in proportion to its population size.[14] The sample sizes for the countries included in each survey wave are presented in Supplementary Table 1. The specific Eurobarometer waves that were analysed were 71.2 (2009), 73.5 (2010), 75.4 (2011), 77.4 (2012), and 79.4 (2013). Their sample size for each wave were 26,756, 26,691, 26,840, 26,622, and 26,680 respectively.

Measures

The variable representing citizens' perception of the healthcare system is based on the question, 'How would you judge the current situation in each of the following: healthcare provision in (OUR COUNTRY)?'. Responses were dichotomized into 'positive perceptions' ('Very good' and 'Rather good') and 'negative perceptions' ('Very bad' and 'Rather bad'). 'Don't know' responses were treated as missing responses and were excluded from the analysis.

The individual-level factors were treated as categorical variables in the model. Age was divided into seven groups (15-24, 25-34, 35-44, 45-54, 55-64, 65-74, 75 years and older), with the oldest age group (75 years and older) set as the reference group. Gender was reported as male and female. Area of residence was divided into three groups ('Rural area or village', 'Small or middle sized town', and 'Large town') based on self-report. Respondents' marital status was divided into three categories ('Single', 'Married or Living with a partner', and 'Separated, Divorced, or Widowed').

The Eurobarometer survey lacked a specific question regarding income, whereby the following question was used as proxy for measuring financial status: 'During the last twelve months, would you say you had difficulties to pay your bills at the end of the month?'. Possible answers were categorised into two ('Almost never' vs. 'From time to time' and 'Most of the time'). Self-perception of respondents' position in society was assessed with a question asking what level they would place themselves in. The survey offered 10 levels (1 being the lowest level). For simplicity three categories were created for the purposes of analysis (Low= levels 1-4, Middle= levels 5-6, High= levels 7-10). Individuals were also asked about their age of completion of full-time education (≤15, 16-19, 20-22, ≥23 years old).

The Eurobarometer Social Climate survey also asked respondents about their overall satisfaction with the life they lead. Recent studies have not analyzed this factor in depth, however Cleary and McNeil[15] suggest a correlation between an individual's satisfaction with healthcare and their overall life satisfaction. Therefore, the variable was included in the model. The possible answers respondents could choose from were 'Very satisfied', 'Fairly satisfied', 'Not very satisfied', and 'Not at all satisfied'. The four categories were included in the model, with 'Not at all satisfied' set as the reference group.

Given that various studies have demonstrated an association between citizens' perceptions of the healthcare system and national level macro-economic and social indicators, we collected these data from the World Bank and the World Health Organization to include in the analysis.[16 17] GDP per capita, total expenditure on health as % of GDP, and government expenditure on health as % of total expenditure on health were included in the model and were treated as continuous variables (Supplementary tables 2 & 3). The GDP variable was recoded so that results are presented for $1000 changes in GDP per capita. Government expenditure on health as % of total expenditure on health was also recoded so that results are presented for a 10% increase.

Statistical Analysis

A multilevel logistic regression (member state being the higher level of analysis) was carried out in STATA v.13.0 in order to analyze trends over time and the factors associated with citizens' perceptions of their healthcare system. The dependent variable in the analysis was citizens' perceptions of the healthcare system. The independent variables included in the model were year of the survey, gender, age, marital status, area of residence (rural, small town or large town), employment status, place/level in society, difficulty paying bills, education, life satisfaction, GDP per capita, total expenditure on health as % of GDP, and government expenditure on health as % of total expenditure on health. The year variable included in the model was treated as a categorical variable. The dataset initially included 133,589 observations, however due to a lack of sufficient data regarding national-level variables, Lithuania was excluded from the analysis (accounting for 5,135 missing observations). The remainder of the missing observations related to 'Don't know' responses in the survey, which were also excluded from the analysis. Survey weights provided in the original Eurobarometer datasets were used in descriptive analyses, as needed, in order to account for the complexity of the study design.

A sensitivity analysis was performed excluding life satisfaction from the model, since the direction of causality could be debatable. Finally, in order to examine trends in individual countries and explore differences in citizens' perceptions across the various countries, logistic regressions were conducted including the 'year' variable and individual-level variables for each EU member state separately.

Results

A complete description of survey respondents' socio-demographic characteristics for the corresponding years can be found in Supplementary Table 1. European citizens tend to have a positive perception of their healthcare system, which can be seen in the descriptive statistics presented in Table 1. In 2009, 64.9% of respondents, across the EU, stated that healthcare provision in their country was either 'Very good' or 'Rather good'. This proportion was about the same in 2013, and there appears to be little variation from year to year. The unadjusted relationships between positive perceptions of healthcare provision and socio-demographic characteristics are shown in Table 1, in which the proportion of positive perceptions exceeded 50% in almost all the groups, except for those who stated they were not satisfied with their lives overall. Regarding the national-level variables, there appears to be an increasing trend in the proportion of positive perceptions when moving from the lowest quartile to the highest quartile for GDP per capita, total expenditure on health as % of GDP, and government expenditure on health as % of total expenditure on health.

The number of observations included in the multi-level logistic regression analysis after accounting for missing data was 116,706. Looking at the regression results presented in Table 2, there appears to be significant decrease in positive perceptions. Respondents in 2013 had 15% lower odds (95% CI 10-20%) of having a positive perception of healthcare provision in comparison to respondents in 2009 (p-value <0.001).

With regards to individual-level variables, the unadjusted and adjusted results appear to be compatible. Respondents who had difficulty paying their bills 'sometimes or most of the time' had approximately 20% lower odds (95% CI 16-21%) of reporting that healthcare provision in their country was good when compared to those who 'almost never' had difficulty paying their bills (Table 2). Moreover, self-perceptions of position in society (society level) appear to be positively and significantly related to good perceptions of the healthcare system. Those who considered themselves to belong to higher ranks in society had 27% higher odds (95% CI 21-32%) of having good perception than those who placed themselves in a low societal level. Regarding life satisfaction, individuals who were 'very satisfied' with the life they lead had five times the odds of having a good perception of healthcare provision, relative to individuals who were 'not at all satisfied'.

GDP per capita and total expenditure on health as a percent of GDP were positively and significantly associated to good perceptions of healthcare systems. The odds of reporting good perceptions of the healthcare system increased by 8% (95% CI 7-9%) for every $1,000 increase in GDP per capita. A positive association was also evident between total expenditure on health and healthcare perceptions, in which a 1% increase in total expenditure on health as a percent of GDP increased the odds that citizens would have a good perception of their healthcare system by 17% (95% CI 11-24%).

Country Specific Results

The proportion of individuals who reported positive perceptions of their country's healthcare system varied between countries. The unadjusted proportions for each of the countries between 2009 and 2013 can be found in Supplementary Table 4. Overall, data from Belgium, the Netherlands, Luxembourg, and Austria revealed the highest proportions of positive perceptions. At the other end of the spectrum were Greece, Bulgaria, and Romania which had the lowest proportion of respondents reporting positive perceptions (below 30%). Figure 1 illustrates the change in perceptions across countries over the years, specifically comparing the percent of respondents with good perceptions of the healthcare system in 2009 and 2013. In examining the results, it is evident that Greece and Spain experienced the greatest drop in positive perceptions between 2009 and 2013.

The results of the regression analyses for both Greece and Spain show that respondents in 2013 had 61% (95% CI 50-70%) and 65% (95% CI 56-72%) lower odds of reporting positive perceptions than respondents in 2009. In total, in seven member states the odds of positive perceptions were significantly lower in 2013 compared to 2009; odds of positive perceptions were higher in 2013 than in 2009 in twelve member states (Figure 2).

In the sensitivity analysis, excluding ‘life satisfaction’ from the model appeared to have the greatest impact on the association between education and perceptions, as well as employment status and perceptions. Individuals who completed full-time education at the age of twenty-three years or older had 12% (95% CI 6-18%) higher odds of reporting good perceptions of healthcare provision in their country compared to individuals who were fifteen years and below when they exited full time education or those who had no full-time education. Furthermore, the direction of the association between employment status and perceptions was reversed in the sensitivity analysis. The key findings from the regression analysis however were fairly similar to those in the sensitivity analysis.

Discussion

Main Findings

We found that there was a reduction in positive perceptions of healthcare systems over the years following the financial crisis in Europe. Our analysis also showed that higher national income per capita and higher spending on health were associated with better perceptions throughout the financial crisis. In addition, we observed starkly different trends among member states over the years following the financial crisis, with those hit the hardest by the financial crisis reporting the greatest declines in positive perceptions.

Our finding that the biggest drop in perceptions has occurred in Spain and Greece is in line with evidence from other studies regarding negative health effects documented so far in these countries.[1 4 5] Conversely, countries such as Germany and Denmark, which have either opted to invest in further social protection or decided to protect public spending on health appear to have seen an improvement in the public's perception of the healthcare systems, although we did not formally test whether national policies were associated with changes in perceptions. These changes in perceptions may not be entirely informed by people's first-hand experiences of the changes precipitated by the policy choices on the healthcare systems, but may be reflective of the general mood precipitated nationally by these policies, essentially highlighting the role of factors 'external' to the health systems. These external factors include the nature of the political debates around the crisis and proposed policy measures, media representation of the changes, and shifts in the general outlook regarding the overall state-of-affairs in the countries.[6 9] Indeed, perceptions of public expenditure retrenchment can have a major influence on public perception. Wendt et al.[18] found public expenditure on health to be a significant determinant of perceptions, irrespective of whether there was a corresponding increase in other sources of finance, such as the private sector. In addition, total health expenditure has been found to be associated with perceptions of safety in healthcare, which arguably impacts overall perceptions of the health system.[19]

The socio-demographic variables also revealed the importance of factors external to the health system in influencing people's perception. Positive perceptions were more frequent among people with no financial difficulties and those who regarded themselves as having high status in society. Bleich et al.[9] report similar findings and we share their explanation that this is possibly the result of people drawing on their general outlooks and their prospects in life as they participate in these surveys. To add further credence to this argument, the strongest association in our study was found between perceptions of health systems and people's self-reported levels of satisfaction with life in general. This association between overall outlook on life in general and perceptions of the state of the health care system has long been recognized. [15] Across the EU, individuals who were older and had lower social status were also found to be more satisfied with the health system, findings which have been reported previously with regards to both patient satisfaction and overall perception of the health system. [20-22] These associations may be explained by different notions of what qualifies as a good healthcare system among different population groups. [20] For example, younger and highly educated individuals may expect more out of their healthcare system leading to lower satisfaction if those expectations are not met.

The decline in positive perceptions of healthcare services identified in our regression analysis is not reflected in the unadjusted estimates, which seem to be fairly stable over time across the EU. Consistent with previous research, [9] we found that perceptions of healthcare systems were positively associated with GDP per capita. Almost all member states experienced an increase in GDP between 2009 and 2013, which may explain the discrepancy between unadjusted and adjusted results.

Strengths and Limitations

We analysed a multiyear dataset covering 27 EU member states to assess trends in public perceptions of national health systems in the aftermath of the financial crisis of 2008. The study used a large sample size coming from a far larger number of countries than similar studies in the past, which had enrolled utmost 21 countries. This has enabled us to study a wide range of countries, which had contrasting experiences and policy responses to the crisis. The cross-sectional nature of the study limits the potential to make causal associations between the crisis and changes in the perceptions; still, the samples were nationally representative, thereby making comparisons meaningful.

Furthermore, the study is guided by critical understanding of the nature of public perception studies, which stipulate that public perception is at least partly explained by factors external to the health system. Studies have determined that people's direct experiences with the healthcare system merely inform up to 13% of their perceptions of national health systems.[6 9] This has specifically guided the selection of factors chosen to test for associations with people's perceptions of their national health systems as well as in the interpretation of the findings. The Eurobarometer survey used a single question to assess citizens' perceptions, rather than using composite indices to be able to capture the multidimensional nature of 'public perception', more comprehensively.[23] Interpreting single item measures may be quite difficult, given that the dimensions of healthcare provision cannot be fully captured in one question.[23] In this study for instance, respondents may have a different understanding of what qualifies as 'very good' healthcare provision. It is also important to note that we could not compare our findings with trends in views about other services that may have also changed during the study period; hence, we were unable to distinguish trends in views about the healthcare system from overall trends about society.

Another limitation of the study was the exclusion of Lithuania from the analysis, due to a lack of sufficient data regarding its national-level indicators. Additionally, 10.1% of all observations had missing values for some of the variables and could not be included in the regression analysis. Chi-square tests were conducted, which revealed significant differences with respect to socio-demographic characteristics between those who were included and those who were excluded from the analysis, which introduces into the study a potential bias due to missing data. This may have affected the associations observed between healthcare perceptions and the individual-level variables analyzed in the study.

Policy Implications and Conclusions

Public perceptions of health systems are considered critical for assessment and comparison of national health systems. Our findings suggest that people's perceptions of their countries' health systems are intertwined with their assessment of their overall wellbeing and prospects more generally. This strongly indicates that perception of health systems cannot be viewed in separation to the overall social and economic outlooks of countries. Countries aiming to improve the public's confidence in their health systems need to frame and propagate policy measures as part of a holistic effort aimed at improving social protection and welfare. Finally, we join previous papers[6 9] in calling for studies exploring the ways in which the factors 'external' to health systems shape the public's perception of health systems.

Data sharing statement

The datasets are publicly available at the GESIS Data Archive at www.gesis.org.

Authors' contribution

FTF conceived the study and AMA conducted the data analysis. AMA, FTF and HBT contributed to data interpretation and manuscript preparation.

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Table 1. Descriptive statistics of positive perceptions of healthcare provision among EU citizens between 2009 and 2013

Variable	% of respondents with positive perceptions of healthcare provision	95% Confidence Interval
Year		
2009	64.9	64.0-65.8
2010	64.9	64.0-65.8
2011	62.9	62.0-63.8
2012	63.3	62.4-64.2
2013	64.0	63.1-64.9
Gender		
Male	65.3	64.7-65.8
Female	62.8	62.3-63.3
Age		
75 years and older	70.1	68.8-71.4
65-74 years	64.5	63.4-65.6
55-64 years	61.9	60.9-62.8
45-54 years	62.2	61.2-63.4
35-44 years	61.6	60.7-62.6
25-34 years	62.6	61.6-63.6
15-24 years	68.9	67.8-70.0
Marital Status		
Single	68.1	67.2-68.9
Married or Living with a partner	62.9	62.3-63.4
Separated/ Divorced/Widowed	62.3	61.4-63.3
Area of Residence		
Rural area or village	63.8	63.1-64.4
Small/Middle town	65.3	64.6-65.9
Large town	62.1	61.4-62.9
Employment Status		
Unemployed	57.3	55.9-58.7
Not working	64.8	64.2-65.4
Employed	64.5	63.9-65.0
Society Level		
Low	53.6	52.7-54.4
Middle	65.1	64.5-65.7
High	71.2	70.4-71.9
Difficulty Paying Bills		
Almost Never	70.8	70.3-71.3
Sometimes or Most of the time	53.4	52.7-54.0
Education		
15 years and below or No full time education	61.6	60.7-62.5
16-19 years	62.6	62.0-63.2

20-22 years	68.4	67.3-69.4
23 years and older	68.4	67.4-69.3
Life Satisfaction		
Not at all satisfied	26.5	24.9-28.1
Not very satisfied	39.1	38.1-40.1
Fairly satisfied	67.4	66.9-67.9
Very satisfied	82.5	81.8-83.2
GDP per capita (PPP current intl. $)		
Lower quartile	30.0	29.3-30.7
2nd quartile	60.3	59.5-61.1
3rd quartile	71.6	71.0-72.3
Upper quartile	80.4	79.6-81.2
Total expenditure on health as % of GDP		
Lower quartile	32.8	32.0-33.6
2nd quartile	58.8	57.8-59.7
3rd quartile	69.1	68.3-69.8
Upper quartile	77.5	76.9-78.1
Government expenditure on health as % of total expenditure on health		
Lower quartile	34.4	33.8-35.1
2nd quartile	57.2	56.4-58.0
3rd quartile	67.3	66.6-68.0
Upper quartile	76.0	75.2-76.7
Overall	**64.0**	**63.6-64.4**

Notes: Weighted percentages were included in the table; all values were rounded to the first decimal place.

Table 2. Results of multi-level logistic regression illustrating adjusted trends and associations of positive perceptions of healthcare provision among EU citizens between 2009 and 2013

Variable	Odds Ratio	P-value	95% Confidence Interval
Year			
2009*			
2010	0.98	0.510	0.94-1.03
2011	0.79	<0.001	0.75-0.84
2012	0.85	<0.001	0.80-0.90
2013	0.85	<0.001	0.80-0.90
Gender			
Male*			
Female	0.89	<0.001	0.87-0.92
Age			
75 years and older*			
65-74 years	0.82	<0.001	0.77-0.88
55-64 years	0.75	<0.001	0.70-0.80
45-54 years	0.75	<0.001	0.70-0.80
35-44 years	0.77	<0.001	0.71-0.82
25-34 years	0.80	<0.001	0.74-0.86
15-24 years	0.90	0.010	0.83-0.98
Marital Status			
Single*			
Married or Living with a partner	0.93	0.001	0.89-0.97
Separated/ Divorced/Widowed	0.97	0.266	0.92-1.02
Area of Residence			
Rural area or village*			
Small/Middle town	1.03	0.069	1.00-1.07
Large town	1.01	0.552	0.97-1.05
Employment Status			
Unemployed*			
Not working	0.98	0.551	0.93-1.04
Employed	0.91	0.001	0.87-0.96
Society Level			
Low*			
Middle	1.12	<0.001	1.08-1.16
High	1.27	<0.001	1.21-1.32
Difficulty Paying Bills			
Almost never*			
Sometimes or Most of the time	0.81	<0.001	0.79-0.84
Education			
15 years and below or no full time education*			
16-19 years	0.97	0.098	0.93-1.01
20-22 years	1.02	0.494	0.97-1.08
23 years and older	1.03	0.219	0.98-1.09

Life Satisfaction			
Not at all satisfied*			
Not very satisfied	1.63	<0.001	1.52-1.75
Fairly satisfied	3.56	<0.001	3.33-3.82
Very satisfied	5.65	<0.001	5.23-6.10
GDP per capita	1.08	<0.001	1.07-1.09
Total expenditure on health as % of GDP	1.17	<0.001	1.11-1.24
Government expenditure on health as % of total expenditure on health	1.02	0.684	0.91-1.15

* Reference category
Notes: Odds Ratios (OR) and 95% CI rounded to two decimal places; OR for GDP per capita refers to a $1000 increase; OR for total expenditure on health as % of GDP refers to a 1% increase; OR for government expenditure on health as % of total expenditure on health refers to a 10% increase.

Figure 1. Proportion of respondents with positive perceptions of healthcare provision in 27 EU member-states in 2009 and 2013

Figure 2. Adjusted trends (OR and 95% CI) of positive perceptions of healthcare provision for each of the 27 EU member-states comparing perceptions in 2013 to 2009

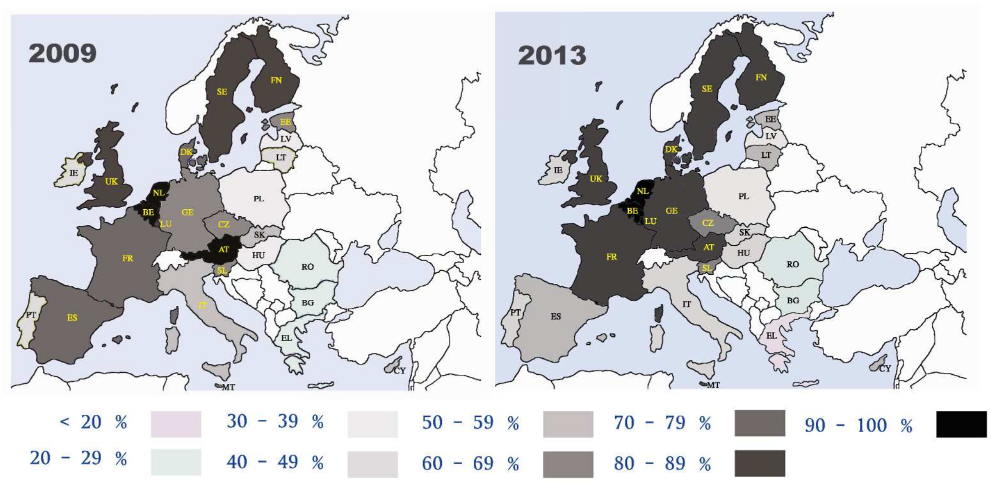

Figure 1. Proportion of respondents with positive perceptions of healthcare provision in 27 EU member-states in 2009 and 2013

279x139mm (300 x 300 DPI)

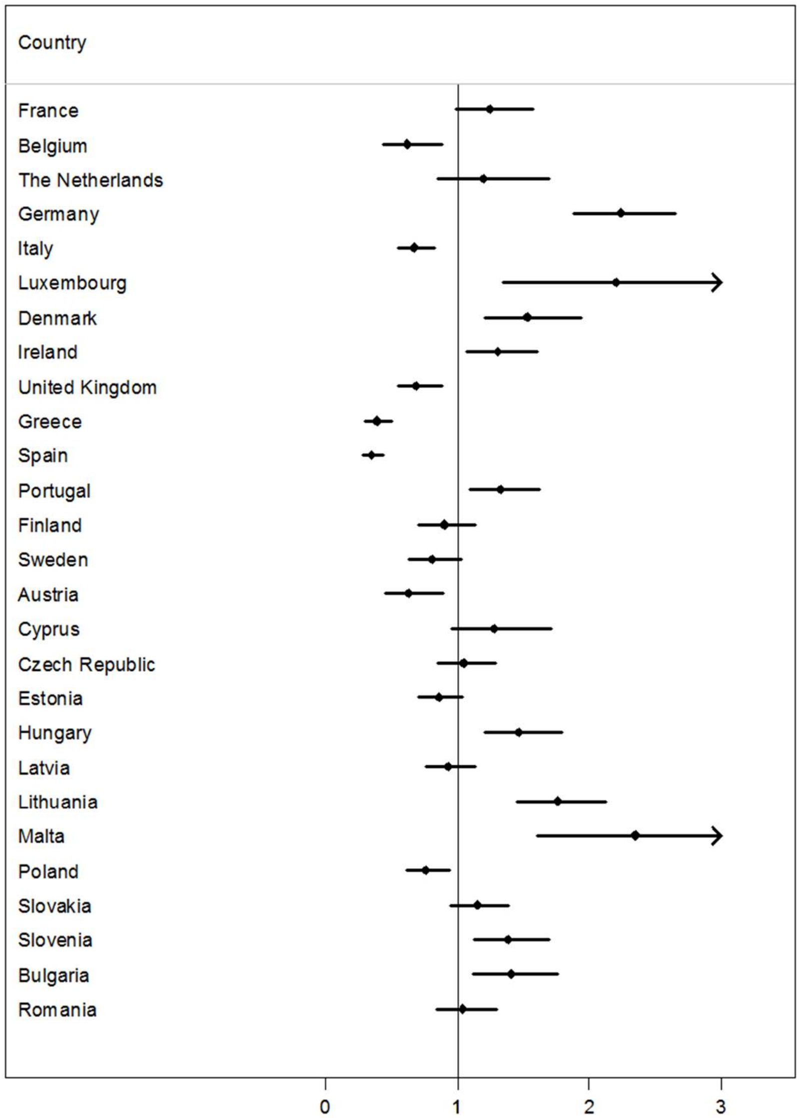

Figure 2. Adjusted trends (OR and 95% CI) of positive perceptions of healthcare provision for each of the 27 EU member-states comparing perceptions in 2013 to 2009

70x94mm (300 x 300 DPI)

Supplementary Table 1. Respondents' socio-demographic characteristics for each survey wave

Characteristic	2009	2010	2011	2012	2013
Gender					
Male (%)	48.3 (47.3-49.2)	48.3 (47.4-49.3)	48.3 (47.4-49.3)	48.3 (47.4-49.3)	48.3 (47.4-49.3)
Female (%)	51.7 (50.8-52.7)	51.7 (50.7-52.6)	51.7 (50.7-52.6)	51.7 (50.7-52.6)	51.7 (50.7-52.6)
Age in years (mean)	46.1 (45.8-46.5)	46.4 (46.0-46.8)	46.7 (46.3-47.0)	46.7 (46.4-47.1)	46.8 (46.5-47.2)
Marital Status					
Single (%)	21.8 (21.0-22.6)	22.3 (21.5-23.1)	21.6 (20.8-22.4)	22.1 (21.3-22.9)	20.4 (19.6-21.2)
Married or living with a partner (%)	63.1 (62.2-64.0)	63.0 (62.1-63.9)	63.8 (62.9-64.7)	62.7 (61.8-63.7)	64.7 (63.8-65.6)
Separated/Divorced/Widowed (%)	15.1 (14.4-15.7)	14.8 (14.1-15.4)	14.6 (14.0-15.2)	15.2 (14.6-15.8)	15.0 (14.4-15.6)
Area of Residence					
Living in rural area or village (%)	34.5 (33.6-35.4)	34.7 (33.8-35.6)	33.6 (32.8-34.5)	32.2 (31.3-33.1)	32.2 (31.3-33.0)
Living in a small/middle town (%)	40.1 (39.2-41.1)	39.3 (38.4-40.3)	41.0 (40.1-42.0)	43.1 (42.1-44.0)	42.8 (41.9-43.7)
Living in a large town (%)	25.4 (24.6-26.2)	26.0 (25.2-26.8)	25.3 (24.6-26.2)	24.8 (24.0-25.6)	25.0 (24.3-25.9)
Employment Status					
Unemployed (%)	8.4 (7.9-9.0)	8.2 (7.7-8.7)	7.5 (7.0-7.9)	9.6 (9.1-10.2)	9.8 (9.3-10.4)
Not working (%)	41.6 (40.7-42.6)	43.5 (42.6-44.5)	43.5 (42.5-44.4)	41.4 (40.5-42.3)	41.3 (40.4-42.2)
Employed (%)	49.9 (49.0-50.9)	48.3 (47.4-49.2)	49.1 (48.1-50.0)	49.0 (48.0-49.9)	48.9 (47.9-49.8)
Society Level					
Low (%)	23.8 (23.0-24.6)	22.2 (21.4-23.0)	20.8 (20.0-21.5)	23.1 (22.3-23.9)	23.8 (23.0-24.6)
Middle (%)	52.3 (51.4-53.3)	51.3 (50.3-52.2)	52.1 (51.2-53.1)	52.4 (51.4-53.4)	51.8 (50.8-52.7)
High (%)	23.9 (23.1-24.7)	26.5 (25.7-27.4)	27.1 (26.3-27.9)	24.5 (23.7-25.3)	24.4 (23.6-25.3)
Financial Situation					
Difficulty paying bills 'almost never' (%)	60.7 (60.0-61.6)	61.2 (60.3-62.1)	62.3 (61.4-63.2)	59.8 (58.8-60.7)	60.8 (60.0-61.7)
Difficulty paying bills 'sometimes or most of the time' (%)	39.3 (38.4-40.2)	38.9 (37.9-39.7)	37.7 (36.8-38.6)	40.2 (39.3-41.2)	39.2 (38.3-40.1)
Education					

Completed education at 15 years and below or no full time education (%)	24.2 (23.3-25.0)	23.8 (22.9-24.6)	24.6 (23.8-25.4)	22.7 (21.9-23.5)	20.4 (19.7-21.2)
Completed education at 16-19 years of age (%)	47.1 (46.2-48.0)	47.3 (46.3-48.2)	46.4 (45.5-47.4)	47.0 (46.1-48.0)	48.2 (47.3-49.1)
Completed education at 20-22 years of age (%)	14.0 (13.4-14.7)	13.9 (13.3-14.6)	13.5 (12.9-14.2)	14.2 (13.6-14.9)	14.9 (14.2-15.6)
Completed education at 23 years or older (%)	14.7 (14.1-15.4)	15.1 (14.4-15.7)	15.4 (14.8-16.1)	16.1 (15.4-16.8)	16.5 (15.8-17.2)
Life Satisfaction					
Not at all satisfied with the life they lead (%)	4.3 (3.9-4.6)	5.1 (4.8-5.5)	4.4 (4.1-4.7)	5.2 (4.8-5.6)	5.7 (5.3-6.1)
Not very satisfied with the life they lead (%)	15.8 (15.2-16.5)	15.4 (14.8-16.1)	14.0 (13.4-14.7)	18.4 (17.7-19.1)	17.1 (16.4-17.8)
Fairly satisfied with the life they lead (%)	57.8 (56.9-58.7)	57.8 (56.9-58.8)	56.8 (55.9-57.7)	56.8 (55.8-57.7)	55.4 (54.5-56.3)
Very satisfied with the life they lead (%)	22.1 (21.3-22.9)	21.6 (20.8-22.4)	24.8 (24.0-25.6)	19.6 (18.9-20.4)	21.8 (21.0-22.6)

Notes: Weighted percentages were included in the table; all values were rounded to first decimal place; numbers may not add up exactly to 100% due to rounding errors; values in parentheses indicate 95% Confidence Intervals (CI).

Supplementary Table 2. GDP per capita of 27 EU member states between 2009 and 2013

Country	2009	2010	2011	2012	2013
France	34797.5	35891.3	37325.3	37473.6	39209.6
Belgium	37629.4	39257.8	40858.7	41927.6	43059.8
Netherlands	44386.5	44773.9	46388.3	46448.9	47954.5
Germany	37112.9	39639.5	42142.5	43600.1	44184.8
Italy	34159.2	34740.1	35901.3	35931.1	35761.6
Luxembourg	80306.1	84589.8	91073.3	90788.3	95928.6
Denmark	39612.1	41835.8	43314.1	43873.9	45270.1
Ireland	41866.5	43249.6	45673.5	46063.3	47599.7
United Kingdom	36361.9	35879.8	36590.2	37569.3	39111.2
Greece	30652.2	28981.4	26626.5	25980.1	26753.1
Spain	32796.7	32372.9	32530.1	32235.6	32842.4
Portugal	26208.9	26943	26932.4	27125.2	27929.9
Finland	37534.5	38322.9	40251.4	40437.6	40831.7
Sweden	39657.2	41756	43709.2	44433.7	45067.4
Austria	40620.4	41892.8	44022.4	45858.2	47416.3
Cyprus	34087.7	33957.9	32983	31920.4	30587.4
Czech Republic	27008.8	27069.6	28604.2	28727.9	30043.6
Estonia	20206.2	21113.1	23954.9	25921	27169.3
Hungary	20860.6	21576.7	22603.2	22701.5	24037.2
Latvia	17032.9	17409.9	19450.9	21122.3	22559
Lithuania	18277.9	20085.1	22541.6	24475.1	26511.1
Malta	25828.6	26690	28177.5	28355.7	29525.6
Poland	19139.5	20883.1	22520	23598.6	24493.8
Slovakia	23172.3	24515.7	25167.5	26091.3	27414.2
Slovenia	27506.3	27607.7	28513.5	28481.7	29097.6
Bulgaria	14870.8	15084.3	15603	16097.8	16573.5
Romania	15815.2	16579.8	17624.5	18952	19576.6

*Notes: GDP per capita, PPP (current international $)

Supplementary Table 3. Total expenditure on health as a percentage of GDP for 27 EU member states between 2009 and 2013

Country	2009	2010	2011	2012	2013
France	11.6	11.6	11.5	11.6	11.7
Belgium	10.7	10.6	10.6	10.9	11.2
Netherlands	11.9	12.1	12.1	12.7	12.9
Germany	11.8	11.7	11.2	11.3	11.3
Italy	9.4	9.4	9.2	9.2	9.1
Luxembourg	8.1	7.7	7.4	7.2	7.1
Denmark	11.5	11.1	10.9	11	10.6
Ireland	9.9	9.2	8.7	8.9	8.9
United Kingdom	9.7	9.4	9.2	9.3	9.1
Greece	10.2	9.5	9.8	9.3	9.8
Spain	9.6	9.6	9.4	9.3	8.9
Portugal	10.8	10.9	10.4	9.9	9.7
Finland	9.2	9	8.9	9.1	9.4
Sweden	9.9	9.5	9.5	9.6	9.7
Austria	11.2	11.1	10.9	11.1	11
Cyprus	7.4	7.3	7.6	7.4	7.4
Czech Republic	7.8	7.4	7.5	7.5	7.2
Estonia	6.9	6.2	5.8	5.9	5.7
Hungary	7.7	8.1	8	8	8
Latvia	6.8	6.6	6.1	5.9	5.7
Lithuania	N/A	N/A	N/A	N/A	N/A
Malta	8.3	8.3	9.5	8.7	8.7
Poland	7.2	7	6.9	6.8	6.7
Slovakia	9.2	8.5	8	8.1	8.2
Slovenia	9.4	9.1	9.1	9.4	9.2
Bulgaria	7.2	7.6	7.4	7.4	7.6
Romania	5.6	5.9	5.6	5.6	5.3

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Supplementary Table 4. Proportion of respondents with good perceptions of healthcare provision by country

Country	2009	2010	2011	2012	2013
France	78.9 (76.2-81.3)	80.5 (77.9-82.9)	73.7 (70.8-76.3)	81.3 (78.7-83.6)	83.0 (80.5-85.2)
Belgium	94.0 (92.4-95.4)	92.8 (91.1-94.3)	94.7 (93.2-95.9)	95.6 (94.1-96.7)	90.2 (88.1-92.0)
Netherlands	91.3 (89.3-92.9)	89.7 (87.4-91.6)	89.4 (87.2-91.3)	91.6 (89.4-93.3)	92.7 (90.8-94.3)
Germany	62.4 (59.6-65.1)	65.7 (62.9-68.5)	66.2 (63.4-68.9)	81.2 (78.8-83.4)	80.8 (78.5-82.9)
Italy	55.6 (52.4-58.8)	53.6 (50.5-56.7)	56.6 (53.5-59.7)	41.1 (38.0-44.2)	44.6 (41.5-47.7)
Luxembourg	87.7 (84.4-90.3)	93.9 (91.4-95.7)	91.8 (89.1-93.9)	93.7 (90.7-95.8)	94.1 (91.4-96.0)
Denmark	77.5 (74.7-80.1)	76.1 (73.3-78.7)	74.9 (72.0-77.7)	83.8 (81.2-86.1)	83.2 (80.5-85.6)
Ireland	41.4 (38.3-44.6)	43.3 (40.1-46.6)	44.5 (41.3-47.7)	45.4 (42.2-48.7)	45.5 (42.3-48.7)
United Kingdom	87.3 (85.0-89.3)	88.5 (86.3-90.4)	85.0 (82.7-87.1)	86.5 (84.1-88.6)	84.0 (81.6-86.2)
Greece	29.9 (27.1-32.8)	23.4 (20.8-26.2)	22.8 (20.2-25.6)	9.1 (7.5-11.1)	13.0 (11.0-15.3)
Spain	78.9 (76.3-81.4)	79.5 (76.8-81.9)	72.9 (70.0-75.6)	69.2 (66.2-72.0)	56.3 (53.2-59.4)
Portugal	46.5 (43.2-49.7)	39.1 (36.1-42.3)	46.4 (43.3-49.4)	35.8 (32.9-38.9)	47.8 (44.6-50.9)
Finland	82.7 (80.1-85.0)	80.3 (77.6-82.8)	78.4 (75.5-81.0)	81.7 (78.9-84.2)	80.9 (78.0-83.5)
Sweden	84.1 (81.5-86.4)	85.5 (82.9-87.7)	78.2 (75.0-81.0)	87.3 (84.7-89.5)	82.0 (78.9-84.7)
Austria	90.5 (88.3-92.3)	91.8 (89.9-93.4)	94.1 (92.4-95.5)	91.0 (88.9-92.6)	87.6 (85.4-89.6)
Cyprus	56.9 (52.1-61.5)	60.4 (55.9-64.7)	59.5 (55.0-63.7)	53.2 (48.8-57.6)	57.0 (52.6-61.3)
Czech Republic	67.2 (64.0-70.3)	75.3 (72.5-77.9)	64.5 (61.4-67.4)	68.6 (65.6-71.4)	69.4 (66.4-72.1)
Estonia	61.0 (57.7-64.1)	63.5 (60.4-66.5)	59.8 (56.6-62.9)	63.1 (59.9-66.1)	56.4 (53.2-59.7)
Hungary	34.2 (31.2-37.4)	36.8 (33.8-40.0)	33.5 (30.6-36.6)	32.3 (29.4-35.4)	43.8 (40.7-47.0)
Latvia	37.2 (34.0-40.5)	30.8 (27.9-33.8)	31.8 (29.0-34.8)	30.1 (27.3-33.1)	38.5 (35.3-41.9)
Lithuania	40.6 (37.5-43.7)	38.6 (35.6-41.7)	39.6 (36.6-42.7)	40.0 (36.9-43.1)	56.0 (52.9-59.1)
Malta	75.8 (70.9-80.1)	81.2 (77.2-84.6)	82.7 (78.9-85.9)	82.6 (78.7-86.0)	88.8 (85.3-91.6)
Poland	37.4 (34.2-40.7)	33.2 (30.2-36.4)	32.6 (29.5-35.8)	21.4 (18.8-24.4)	30.6 (27.6-33.8)
Slovakia	50.1 (46.7-53.5)	58.5 (55.4-61.5)	39.0 (35.8-42.3)	43.2 (39.9-46.5)	49.0 (45.8-52.3)

Slovenia	62.1 (58.9-65.2)	66.7 (63.7-69.7)	68.9 (65.9-71.8)	71.0 (68.1-73.8)	68.7 (65.7-71.5)
Bulgaria	23.3 (20.6-26.1)	25.9 (23.1-28.8)	28.6 (25.8-31.5)	22.3 (19.7-25.1)	29.2 (26.3-32.2)
Romania	26.4 (23.6-29.4)	17.1 (14.8-19.6)	13.0 (11.1-15.2)	19.1 (16.7-21.8)	26.6 (23.9-29.5)
Overall	**64.9 (64.0-65.8)**	**64.9 (64.0-65.8)**	**62.9 (62.0-63.8)**	**63.3 (62.4-64.2)**	**64.0 (63.1-64.9)**

Notes: Weighted percentages were included in the table (special weights were used for Germany and the UK respectively); All values rounded to one decimal place; values in parentheses indicate 95% confidence intervals.

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Reported on page
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	6, 7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6, 7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	6, 7
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-8
Bias	9	Describe any efforts to address potential sources of bias	8-9
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8-9
		(*b*) Describe any methods used to examine subgroups and interactions	8-9
		(*c*) Explain how missing data were addressed	8
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	8
		(*e*) Describe any sensitivity analyses	9
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	n/a
		(b) Give reasons for non-participation at each stage	n/a
		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Sup. Table 1
		(b) Indicate number of participants with missing data for each variable of interest	Sup. Table 1
Outcome data	15*	Report numbers of outcome events or summary measures	n/a
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear	Tables 2

		which confounders were adjusted for and why they were included	
		(*b*) Report category boundaries when continuous variables were categorized	7-8
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	12
Discussion			
Key results	18	Summarise key results with reference to study objectives	13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14-15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	15-16
Generalisability	21	Discuss the generalisability (external validity) of the study results	15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	1

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Trends and correlates of the public's perception of the healthcare system in the European Union: a multi-level analysis of Eurobarometer survey data from 2009 to 2013

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Trends and correlates of the public's perception of the healthcare system in the European Union: a multi-level analysis of Eurobarometer survey data from 2009 to 2013

AlJohara M. AlSaud [a], Henock B. Taddese [a], Filippos T. Filippidis [a]

[a] Department of Primary Care and Public Health, School of Public Health, Imperial College London, United Kingdom

Corresponding author:

Filippos T Filippidis

Address: School of Public Health, Imperial College London, 310 Reynolds Building, St. Dunstan's Road, London W6 8RP, United Kingdom

Tel: +44 (0)20 7594 7142

Email: f.filippidis@imperial.ac.uk

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ABSTRACT

Objective: The aim of the study is to assess trends in public perceptions of health systems in 27 European Union (EU) member states following the financial crisis (2009 – 2013), in order to discuss observed changes in the context of the financial crisis.

Design: Repeated cross-sectional studies.

Setting: 27 EU countries.

Participants: EU citizens aged 15 years and older.

Methods: The study mainly uses the Eurobarometer Social Climate Surveys, conducted annually between 2009 and 2013, thereby analysing 116,706 observations. A multilevel logistic regression was carried out to analyse trends over time and the factors associated with citizens' perceptions of their healthcare systems.

Results: Europeans generally exhibit positive perceptions of their national healthcare systems, 64.0% (95% CI 63.6-64.4%). However, we observed a significant drop in positive perceptions in the years following the crisis, especially within countries most affected by the crisis. Concerning fiscal characteristics, wealthier countries and those dedicating higher proportion of their national income to health were more likely to maintain positive perceptions. At the individual level, perceptions of healthcare systems were significantly associated with respondents' self-perceptions of their social status, financial capacity and overall satisfaction in life.

Conclusions: Our finding confirms previous observations that citizens' perceptions of their healthcare systems may reflect their overall prospects within the broader socio-economic systems they live in; which have in-turn been affected by the financial crisis and the policy measures instituted in response.

Strengths and limitations of this study

- This study uses a large sample size and includes data from 27 EU countries.
- The cross-sectional nature of the study limits the potential to make causal associations between the crisis and changes in the perceptions.
- The Eurobarometer survey used a single question to assess citizens' perceptions, rather than using composite indices to be able to capture the multidimensional nature of 'public perception', more comprehensively.

Introduction

The global financial crisis that started in 2008 has precipitated major economic and financial impacts, and prompted austerity policy responses across Europe; majorly austerity and public sector retrenchment policies.[1 2] Most of the healthcare reforms following the financial crisis involved cuts to public services and a related increase in citizens' out-of-pocket expenditure, which in turn affected people's access to care.[1 3] The broader socio-economic effects of the crisis such as rising unemployment, income reduction, increased out of pocket spending (through coinsurance and shared payments) and retrenchment of welfare support were more pronounced in the most affected countries, which had also instituted stringent austerity measures (e.g. Greece, Spain, Ireland and Portugal).[1 4] Whilst a full account of the effects of the crisis in terms of mortality and morbidity rates may take several years, early health effects have already been documented in these countries in the form of rising mental disorders, high suicide rates and deteriorating access to services.[1 4 5] In contrast, some countries followed a different path in their responses to the crisis by implementing a fiscal stimulus package and investing in social protection (Germany) or protecting their health budgets (Belgium, Denmark, the UK).[1]

In light of the above, there is growing interest in studying the consequences of the crisis on health systems, as well as the different trajectories of healthcare systems across countries which may correlate to the differences in the type of policy responses adopted to mitigate the effects of the crisis. In this regard, mortality and morbidity data as well as healthcare access and quality data constitute the primary measures of interest for gauging effects on health systems. Beyond these measures, public perception metrics have also become integral to cross-country and across-time comparisons of health systems; which are in turn a reflection of the shift towards people centered health systems and the corresponding emphasis on responsiveness of health systems.[6 7] Technically, public perception surveys are known to represent a mixture of citizens' personal experiences with the healthcare system on the one hand, and their broader views of the system on the other.[8] Unlike satisfaction surveys, where patients are typically surveyed after an episode of service utilization to evaluate their experiences in receiving care, the results of public perception surveys are known to be influenced by wide ranging factors: respondents' views on the general state-of-affairs in the country[8]; the national political debate around the nature, effectiveness and constitution of the health system; culture of support for the welfare state in the country; and portrayals of the health system in the media.[6 9] Still, findings of public perception surveys are used to compare and explain distinct changes over time in healthcare systems in different countries[6 7]; to validate and argue for the impacts of particular health policy reforms[10]; to counter expert opinions on the ranking of national health systems[8]; and to ascertain people's perspectives on aspects of health policy such as levels of government financing of health care[11].

The aim of our study is to assess trends in public perceptions of health systems in 27 European Union (EU) member states between 2009 and 2013, in order to discuss observed changes in the context of the financial crisis and the European governments' responses to it.

Methods

Data Sources

To evaluate EU citizens' perceptions of their healthcare systems, this study used data from the Eurobarometer Social Climate survey between 2009 and 2013 as well as other public data sources. The Eurobarometer is a series of public opinion surveys that consists of approximately 1,000 face-to-face interviews per country with individuals aged 15 years and older.[12]

A multi-stage random (probability) sampling design was applied in all member-states.[13] To ensure the samples are representative of the population, each sample was weighted according to a national weighting procedure for sex, age, and region. Since country samples are approximately the same size (n=1000), population size weighting factors were used to ensure that each country is represented in proportion to its population size.[14] The sample sizes for the countries included in each survey wave are presented in Supplementary Table 1. The specific Eurobarometer waves that were analysed were 71.2 (2009), 73.5 (2010), 75.4 (2011), 77.4 (2012), and 79.4 (2013). Their sample size for each wave were 26,756, 26,691, 26,840, 26,622, and 26,680 respectively.

Measures

The variable representing citizens' perception of the healthcare system is based on the question, 'How would you judge the current situation in each of the following: healthcare provision in (OUR COUNTRY)?'. Responses were dichotomized into 'positive perceptions' ('Very good' and 'Rather good') and 'negative perceptions' ('Very bad' and 'Rather bad'). 'Don't know' responses were treated as missing responses and were excluded from the analysis.

The individual-level factors were treated as categorical variables in the model. Age was divided into seven groups (15-24, 25-34, 35-44, 45-54, 55-64, 65-74, 75 years and older), with the oldest age group (75 years and older) set as the reference group. Gender was reported as male and female. Area of residence was divided into three groups (‘Rural area or village’, ‘Small or middle sized town’, and ‘Large town’) based on self-report. Respondents’ marital status was divided into three categories (‘Single’, ‘Married or Living with a partner’, and ‘Separated, Divorced, or Widowed’).

The Eurobarometer survey lacked a specific question regarding income, whereby the following question was used as proxy for measuring financial status: ‘During the last twelve months, would you say you had difficulties to pay your bills at the end of the month?’. Possible answers were categorised into two (‘Almost never’ vs. ‘From time to time’ and ‘Most of the time’). Self-perception of respondents’ position in society was assessed with a question asking what level they would place themselves in. The survey offered 10 levels (1 being the lowest level). For simplicity three categories were created for the purposes of analysis (Low= levels 1-4, Middle= levels 5-6, High= levels 7-10). Individuals were also asked about their age of completion of full-time education (≤15, 16-19, 20-22, ≥23 years old).

The Eurobarometer Social Climate survey also asked respondents about their overall satisfaction with the life they lead. Recent studies have not analyzed this factor in depth, however Cleary and McNeil[15] suggest a correlation between an individual’s satisfaction with healthcare and their overall life satisfaction. Therefore, the variable was included in the model. The possible answers respondents could choose from were ‘Very satisfied’, ‘Fairly satisfied’, ‘Not very satisfied’, and ‘Not at all satisfied’. The four categories were included in the model, with ‘Not at all satisfied’ set as the reference group.

Given that various studies have demonstrated an association between citizens' perceptions of the healthcare system and national level macro-economic and social indicators, we collected these data from the World Bank and the World Health Organization to include in the analysis.[16 17] GDP per capita, total expenditure on health as % of GDP, and government expenditure on health as % of total expenditure on health were included in the model and were treated as continuous variables (Supplementary tables 2 & 3). The GDP variable was recoded so that results are presented for $1000 changes in GDP per capita. Government expenditure on health as % of total expenditure on health was also recoded so that results are presented for a 10% increase.

Statistical Analysis

A multilevel logistic regression (member state being the higher level of analysis) was carried out in STATA v.13.0 in order to analyze trends over time and the factors associated with citizens' perceptions of their healthcare system. The dependent variable in the analysis was citizens' perceptions of the healthcare system. The independent variables included in the model were year of the survey, gender, age, marital status, area of residence (rural, small town or large town), employment status, place/level in society, difficulty paying bills, education, life satisfaction, GDP per capita, total expenditure on health as % of GDP, and government expenditure on health as % of total expenditure on health. The year variable included in the model was treated as a categorical variable. The dataset initially included 133,589 observations, however due to a lack of sufficient data regarding national-level variables, Lithuania was excluded from the analysis (accounting for 5,135 missing observations). The remainder of the missing observations related to 'Don't know' responses in the survey, which were also excluded from the analysis. Survey weights provided in the original Eurobarometer datasets were used in descriptive analyses, as needed, in order to account for the complexity of the study design.

A sensitivity analysis was performed excluding life satisfaction from the model, since the direction of causality could be debatable. Finally, in order to examine trends in individual countries and explore differences in citizens' perceptions across the various countries, logistic regressions were conducted including the 'year' variable and individual-level variables for each EU member state separately.

Results

A complete description of survey respondents' socio-demographic characteristics for the corresponding years can be found in Supplementary Table 1. European citizens tend to have a positive perception of their healthcare system, which can be seen in the descriptive statistics presented in Table 1. In 2009, 64.9% of respondents, across the EU, stated that healthcare provision in their country was either 'Very good' or 'Rather good'. This proportion was about the same in 2013, and there appears to be little variation from year to year. The unadjusted relationships between positive perceptions of healthcare provision and socio-demographic characteristics are shown in Table 1, in which the proportion of positive perceptions exceeded 50% in almost all the groups, except for those who stated they were not satisfied with their lives overall. Regarding the national-level variables, there appears to be an increasing trend in the proportion of positive perceptions when moving from the lowest quartile to the highest quartile for GDP per capita, total expenditure on health as % of GDP, and government expenditure on health as % of total expenditure on health.

The number of observations included in the multi-level logistic regression analysis after accounting for missing data was 116,706. Looking at the regression results presented in Table 2, there appears to be significant decrease in positive perceptions. Respondents in 2013 had 15% lower odds (95% CI 10-20%) of having a positive perception of healthcare provision in comparison to respondents in 2009 (p-value <0.001).

With regards to individual-level variables, the unadjusted and adjusted results appear to be compatible. Respondents who had difficulty paying their bills 'sometimes or most of the time' had approximately 20% lower odds (95% CI 16-21%) of reporting that healthcare provision in their country was good when compared to those who 'almost never' had difficulty paying their bills (Table 2). Moreover, self-perceptions of position in society (society level) appear to be positively and significantly related to good perceptions of the healthcare system. Those who considered themselves to belong to higher ranks in society had 27% higher odds (95% CI 21-32%) of having good perception than those who placed themselves in a low societal level. Regarding life satisfaction, individuals who were 'very satisfied' with the life they lead had five times the odds of having a good perception of healthcare provision, relative to individuals who were 'not at all satisfied'.

GDP per capita and total expenditure on health as a percent of GDP were positively and significantly associated to good perceptions of healthcare systems. The odds of reporting good perceptions of the healthcare system increased by 8% (95% CI 7-9%) for every $1,000 increase in GDP per capita. A positive association was also evident between total expenditure on health and healthcare perceptions, in which a 1% increase in total expenditure on health as a percent of GDP increased the odds that citizens would have a good perception of their healthcare system by 17% (95% CI 11-24%).

Country Specific Results

The proportion of individuals who reported positive perceptions of their country's healthcare system varied between countries. The unadjusted proportions for each of the countries between 2009 and 2013 can be found in Supplementary Table 4. Overall, data from Belgium, the Netherlands, Luxembourg, and Austria revealed the highest proportions of positive perceptions. At the other end of the spectrum were Greece, Bulgaria, and Romania which had the lowest proportion of respondents reporting positive perceptions (below 30%). Figure 1 illustrates the change in perceptions across countries over the years, specifically comparing the percent of respondents with good perceptions of the healthcare system in 2009 and 2013. In examining the results, it is evident that Greece and Spain experienced the greatest drop in positive perceptions between 2009 and 2013.

The results of the regression analyses for both Greece and Spain show that respondents in 2013 had 61% (95% CI 50-70%) and 65% (95% CI 56-72%) lower odds of reporting positive perceptions than respondents in 2009. In total, in seven member states the odds of positive perceptions were significantly lower in 2013 compared to 2009; odds of positive perceptions were higher in 2013 than in 2009 in twelve member states (Figure 2).

In the sensitivity analysis, excluding 'life satisfaction' from the model appeared to have the greatest impact on the association between education and perceptions, as well as employment status and perceptions. Individuals who completed full-time education at the age of twenty-three years or older had 12% (95% CI 6-18%) higher odds of reporting good perceptions of healthcare provision in their country compared to individuals who were fifteen years and below when they exited full time education or those who had no full-time education. Furthermore, the direction of the association between employment status and perceptions was reversed in the sensitivity analysis. The key findings from the regression analysis however were fairly similar to those in the sensitivity analysis.

Discussion

Main Findings

We found that there was a reduction in positive perceptions of healthcare systems over the years following the financial crisis in Europe. Our analysis also showed that higher national income per capita and higher spending on health were associated with better perceptions throughout the financial crisis. In addition, we observed starkly different trends among member states over the years following the financial crisis, with those hit the hardest by the financial crisis reporting the greatest declines in positive perceptions.

Our finding that the biggest drop in perceptions has occurred in Spain and Greece is in line with evidence from other studies regarding negative health effects documented so far in these countries.[1 4 5] Conversely, countries such as Germany and Denmark, which have either opted to invest in further social protection or decided to protect public spending on health appear to have seen an improvement in the public's perception of the healthcare systems, although we did not formally test whether national policies were associated with changes in perceptions. These changes in perceptions may not be entirely informed by people's first-hand experiences of the changes precipitated by the policy choices on the healthcare systems, but may be reflective of the general mood precipitated nationally by these policies, essentially highlighting the role of factors 'external' to the health systems. These external factors include the nature of the political debates around the crisis and proposed policy measures, media representation of the changes, and shifts in the general outlook regarding the overall state-of-affairs in the countries.[6 9] Indeed, perceptions of public expenditure retrenchment can have a major influence on public perception. Wendt et al.[18] found public expenditure on health to be a significant determinant of perceptions, irrespective of whether there was a corresponding increase in other sources of finance, such as the private sector. In addition, total health expenditure has been found to be associated with perceptions of safety in healthcare, which arguably impacts overall perceptions of the health system.[19]

The socio-demographic variables also revealed the importance of factors external to the health system in influencing people's perception. Positive perceptions were more frequent among people with no financial difficulties and those who regarded themselves as having high status in society. Bleich et al.[9] report similar findings and we share their explanation that this is possibly the result of people drawing on their general outlooks and their prospects in life as they participate in these surveys. To add further credence to this argument, the strongest association in our study was found between perceptions of health systems and people's self-reported levels of satisfaction with life in general. This association between overall outlook on life in general and perceptions of the state of the health care system has long been recognized. [15] Across the EU, individuals who were older and had lower social status were also found to be more satisfied with the health system, findings which have been reported previously with regards to both patient satisfaction and overall perception of the health system. [20-22] These associations may be explained by different notions of what qualifies as a good healthcare system among different population groups. [20] For example, younger and highly educated individuals may expect more out of their healthcare system leading to lower satisfaction if those expectations are not met.

The decline in positive perceptions of healthcare services identified in our regression analysis is not reflected in the unadjusted estimates, which seem to be fairly stable over time across the EU. Consistent with previous research, [9] we found that perceptions of healthcare systems were positively associated with GDP per capita. Almost all member states experienced an increase in GDP between 2009 and 2013, which may explain the discrepancy between unadjusted and adjusted results.

Strengths and Limitations

We analysed a multiyear dataset covering 27 EU member states to assess trends in public perceptions of national health systems in the aftermath of the financial crisis of 2008. The study used a large sample size coming from a far larger number of countries than similar studies in the past, which had enrolled utmost 21 countries. This has enabled us to study a wide range of countries, which had contrasting experiences and policy responses to the crisis. The cross-sectional nature of the study limits the potential to make causal associations between the crisis and changes in the perceptions; still, the samples were nationally representative, thereby making comparisons meaningful.

Furthermore, the study is guided by critical understanding of the nature of public perception studies, which stipulate that public perception is at least partly explained by factors external to the health system. Studies have determined that people's direct experiences with the healthcare system merely inform up to 13% of their perceptions of national health systems.[6 9] This has specifically guided the selection of factors chosen to test for associations with people's perceptions of their national health systems as well as in the interpretation of the findings. The Eurobarometer survey used a single question to assess citizens' perceptions, rather than using composite indices to be able to capture the multidimensional nature of 'public perception', more comprehensively.[23] Interpreting single item measures may be quite difficult, given that the dimensions of healthcare provision cannot be fully captured in one question.[23] In this study for instance, respondents may have a different understanding of what qualifies as 'very good' healthcare provision. It is also important to note that we could not compare our findings with trends in views about other services that may have also changed during the study period; hence, we were unable to distinguish trends in views about the healthcare system from overall trends about society.

Another limitation of the study was the exclusion of Lithuania from the analysis, due to a lack of sufficient data regarding its national-level indicators. Additionally, 10.1% of all observations had missing values for some of the variables and could not be included in the regression analysis. Chi-square tests were conducted, which revealed significant differences with respect to socio-demographic characteristics between those who were included and those who were excluded from the analysis, which introduces into the study a potential bias due to missing data. This may have affected the associations observed between healthcare perceptions and the individual-level variables analyzed in the study.

Policy Implications and Conclusions

Public perceptions of health systems are considered critical for assessment and comparison of national health systems. Our findings suggest that people's perceptions of their countries' health systems are intertwined with their assessment of their overall wellbeing and prospects more generally. This strongly indicates that perception of health systems cannot be viewed in separation to the overall social and economic outlooks of countries. Countries aiming to improve the public's confidence in their health systems need to frame and propagate policy measures as part of a holistic effort aimed at improving social protection and welfare. Finally, we join previous papers[6 9] in calling for studies exploring the ways in which the factors 'external' to health systems shape the public's perception of health systems.

Data sharing statement

The datasets are publicly available at the GESIS Data Archive at www.gesis.org.

Authors' contribution

FTF conceived the study and AMA conducted the data analysis. AMA, FTF and HBT contributed to data interpretation and manuscript preparation.

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Table 1. Descriptive statistics of positive perceptions of healthcare provision among EU citizens between 2009 and 2013

Variable	% of respondents with positive perceptions of healthcare provision	95% Confidence Interval
Year		
2009	64.9	64.0-65.8
2010	64.9	64.0-65.8
2011	62.9	62.0-63.8
2012	63.3	62.4-64.2
2013	64.0	63.1-64.9
Gender		
Male	65.3	64.7-65.8
Female	62.8	62.3-63.3
Age		
75 years and older	70.1	68.8-71.4
65-74 years	64.5	63.4-65.6
55-64 years	61.9	60.9-62.8
45-54 years	62.2	61.2-63.4
35-44 years	61.6	60.7-62.6
25-34 years	62.6	61.6-63.6
15-24 years	68.9	67.8-70.0
Marital Status		
Single	68.1	67.2-68.9
Married or Living with a partner	62.9	62.3-63.4
Separated/ Divorced/Widowed	62.3	61.4-63.3
Area of Residence		
Rural area or village	63.8	63.1-64.4
Small/Middle town	65.3	64.6-65.9
Large town	62.1	61.4-62.9
Employment Status		
Unemployed	57.3	55.9-58.7
Not working	64.8	64.2-65.4
Employed	64.5	63.9-65.0
Society Level		
Low	53.6	52.7-54.4
Middle	65.1	64.5-65.7
High	71.2	70.4-71.9
Difficulty Paying Bills		
Almost Never	70.8	70.3-71.3
Sometimes or Most of the time	53.4	52.7-54.0
Education		
15 years and below or No full time education	61.6	60.7-62.5
16-19 years	62.6	62.0-63.2

20-22 years	68.4	67.3-69.4
23 years and older	68.4	67.4-69.3
Life Satisfaction		
Not at all satisfied	26.5	24.9-28.1
Not very satisfied	39.1	38.1-40.1
Fairly satisfied	67.4	66.9-67.9
Very satisfied	82.5	81.8-83.2
GDP per capita (PPP current intl. $)		
Lower quartile	30.0	29.3-30.7
2nd quartile	60.3	59.5-61.1
3rd quartile	71.6	71.0-72.3
Upper quartile	80.4	79.6-81.2
Total expenditure on health as % of GDP		
Lower quartile	32.8	32.0-33.6
2nd quartile	58.8	57.8-59.7
3rd quartile	69.1	68.3-69.8
Upper quartile	77.5	76.9-78.1
Government expenditure on health as % of total expenditure on health		
Lower quartile	34.4	33.8-35.1
2nd quartile	57.2	56.4-58.0
3rd quartile	67.3	66.6-68.0
Upper quartile	76.0	75.2-76.7
Overall	**64.0**	**63.6-64.4**

Notes: Weighted percentages were included in the table; all values were rounded to the first decimal place.

Table 2. Results of multi-level logistic regression illustrating adjusted trends and associations of positive perceptions of healthcare provision among EU citizens between 2009 and 2013

Variable	Odds Ratio	P-value	95% Confidence Interval
Year			
2009*			
2010	0.98	0.510	0.94-1.03
2011	0.79	<0.001	0.75-0.84
2012	0.85	<0.001	0.80-0.90
2013	0.85	<0.001	0.80-0.90
Gender			
Male*			
Female	0.89	<0.001	0.87-0.92
Age			
75 years and older*			
65-74 years	0.82	<0.001	0.77-0.88
55-64 years	0.75	<0.001	0.70-0.80
45-54 years	0.75	<0.001	0.70-0.80
35-44 years	0.77	<0.001	0.71-0.82
25-34 years	0.80	<0.001	0.74-0.86
15-24 years	0.90	0.010	0.83-0.98
Marital Status			
Single*			
Married or Living with a partner	0.93	0.001	0.89-0.97
Separated/ Divorced/Widowed	0.97	0.266	0.92-1.02
Area of Residence			
Rural area or village*			
Small/Middle town	1.03	0.069	1.00-1.07
Large town	1.01	0.552	0.97-1.05
Employment Status			
Unemployed*			
Not working	0.98	0.551	0.93-1.04
Employed	0.91	0.001	0.87-0.96
Society Level			
Low*			
Middle	1.12	<0.001	1.08-1.16
High	1.27	<0.001	1.21-1.32
Difficulty Paying Bills			
Almost never*			
Sometimes or Most of the time	0.81	<0.001	0.79-0.84
Education			
15 years and below or no full time education*			
16-19 years	0.97	0.098	0.93-1.01
20-22 years	1.02	0.494	0.97-1.08
23 years and older	1.03	0.219	0.98-1.09

Life Satisfaction			
Not at all satisfied*			
Not very satisfied	1.63	<0.001	1.52-1.75
Fairly satisfied	3.56	<0.001	3.33-3.82
Very satisfied	5.65	<0.001	5.23-6.10
GDP per capita	1.08	<0.001	1.07-1.09
Total expenditure on health as % of GDP	1.17	<0.001	1.11-1.24
Government expenditure on health as % of total expenditure on health	1.02	0.684	0.91-1.15

* Reference category
Notes: Odds Ratios (OR) and 95% CI rounded to two decimal places; OR for GDP per capita refers to a $1000 increase; OR for total expenditure on health as % of GDP refers to a 1% increase; OR for government expenditure on health as % of total expenditure on health refers to a 10% increase.

Figure 1. Proportion of respondents with positive perceptions of healthcare provision in 27 EU member-states in 2009 and 2013

Figure 2. Adjusted trends (OR and 95% CI) of positive perceptions of healthcare provision for each of the 27 EU member-states comparing perceptions in 2013 to 2009

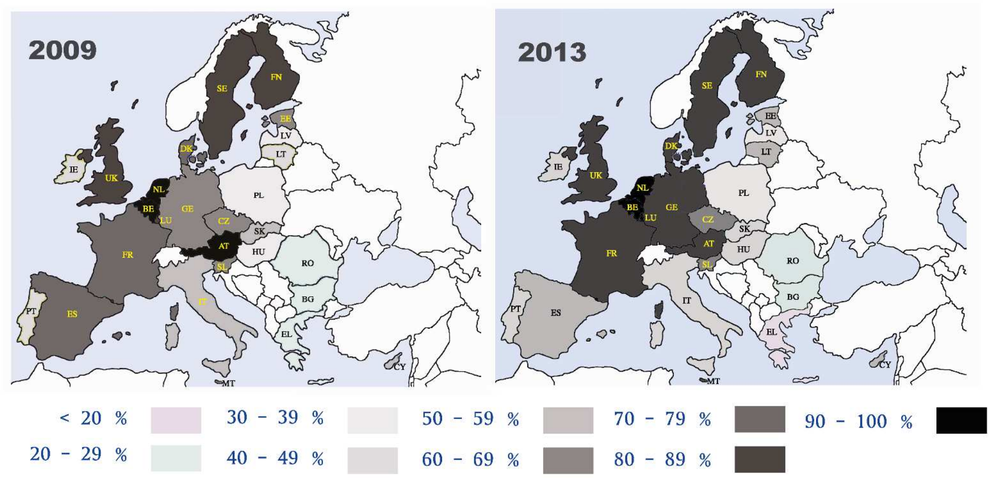

Figure 1. Proportion of respondents with positive perceptions of healthcare provision in 27 EU member-states in 2009 and 2013

279x139mm (300 x 300 DPI)

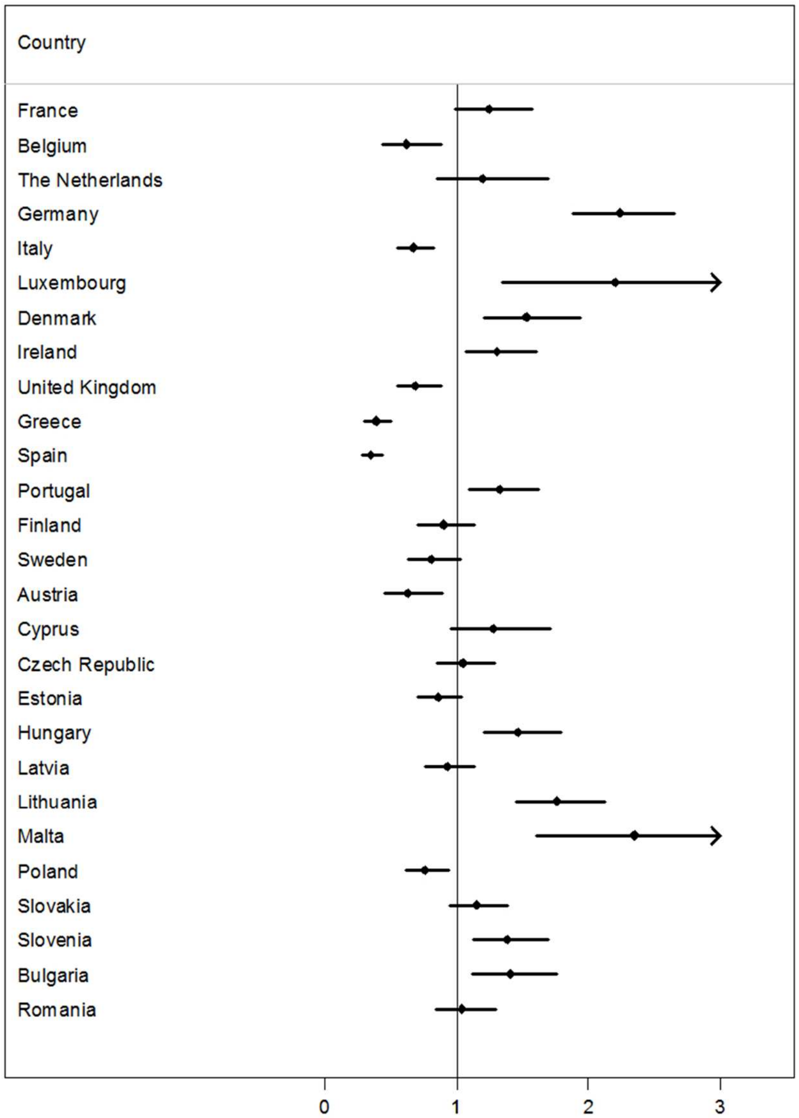

Figure 2. Adjusted trends (OR and 95% CI) of positive perceptions of healthcare provision for each of the 27 EU member-states comparing perceptions in 2013 to 2009

70x94mm (300 x 300 DPI)

Supplementary Table 1. Respondents' socio-demographic characteristics for each survey wave

Characteristic	2009	2010	2011	2012	2013
Gender					
Male (%)	48.3 (47.3-49.2)	48.3 (47.4-49.3)	48.3 (47.4-49.3)	48.3 (47.4-49.3)	48.3 (47.4-49.3)
Female (%)	51.7 (50.8-52.7)	51.7 (50.7-52.6)	51.7 (50.7-52.6)	51.7 (50.7-52.6)	51.7 (50.7-52.6)
Age in years (mean)	46.1 (45.8-46.5)	46.4 (46.0-46.8)	46.7 (46.3-47.0)	46.7 (46.4-47.1)	46.8 (46.5-47.2)
Marital Status					
Single (%)	21.8 (21.0-22.6)	22.3 (21.5-23.1)	21.6 (20.8-22.4)	22.1 (21.3-22.9)	20.4 (19.6-21.2)
Married or living with a partner (%)	63.1 (62.2-64.0)	63.0 (62.1-63.9)	63.8 (62.9-64.7)	62.7 (61.8-63.7)	64.7 (63.8-65.6)
Separated/Divorced/Widowed (%)	15.1 (14.4-15.7)	14.8 (14.1-15.4)	14.6 (14.0-15.2)	15.2 (14.6-15.8)	15.0 (14.4-15.6)
Area of Residence					
Living in rural area or village (%)	34.5 (33.6-35.4)	34.7 (33.8-35.6)	33.6 (32.8-34.5)	32.2 (31.3-33.1)	32.2 (31.3-33.0)
Living in a small/middle town (%)	40.1 (39.2-41.1)	39.3 (38.4-40.3)	41.0 (40.1-42.0)	43.1 (42.1-44.0)	42.8 (41.9-43.7)
Living in a large town (%)	25.4 (24.6-26.2)	26.0 (25.2-26.8)	25.3 (24.6-26.2)	24.8 (24.0-25.6)	25.0 (24.3-25.9)
Employment Status					
Unemployed (%)	8.4 (7.9-9.0)	8.2 (7.7-8.7)	7.5 (7.0-7.9)	9.6 (9.1-10.2)	9.8 (9.3-10.4)
Not working (%)	41.6 (40.7-42.6)	43.5 (42.6-44.5)	43.5 (42.5-44.4)	41.4 (40.5-42.3)	41.3 (40.4-42.2)
Employed (%)	49.9 (49.0-50.9)	48.3 (47.4-49.2)	49.1 (48.1-50.0)	49.0 (48.0-49.9)	48.9 (47.9-49.8)
Society Level					
Low (%)	23.8 (23.0-24.6)	22.2 (21.4-23.0)	20.8 (20.0-21.5)	23.1 (22.3-23.9)	23.8 (23.0-24.6)
Middle (%)	52.3 (51.4-53.3)	51.3 (50.3-52.2)	52.1 (51.2-53.1)	52.4 (51.4-53.4)	51.8 (50.8-52.7)
High (%)	23.9 (23.1-24.7)	26.5 (25.7-27.4)	27.1 (26.3-27.9)	24.5 (23.7-25.3)	24.4 (23.6-25.3)
Financial Situation					
Difficulty paying bills ‘almost never’ (%)	60.7 (60.0-61.6)	61.2 (60.3-62.1)	62.3 (61.4-63.2)	59.8 (58.8-60.7)	60.8 (60.0-61.7)
Difficulty paying bills ‘sometimes or most of the time’ (%)	39.3 (38.4-40.2)	38.9 (37.9-39.7)	37.7 (36.8-38.6)	40.2 (39.3-41.2)	39.2 (38.3-40.1)
Education					

Completed education at 15 years and below or no full time education (%)	24.2 (23.3-25.0)	23.8 (22.9-24.6)	24.6 (23.8-25.4)	22.7 (21.9-23.5)	20.4 (19.7-21.2)
Completed education at 16-19 years of age (%)	47.1 (46.2-48.0)	47.3 (46.3-48.2)	46.4 (45.5-47.4)	47.0 (46.1-48.0)	48.2 (47.3-49.1)
Completed education at 20-22 years of age (%)	14.0 (13.4-14.7)	13.9 (13.3-14.6)	13.5 (12.9-14.2)	14.2 (13.6-14.9)	14.9 (14.2-15.6)
Completed education at 23 years or older (%)	14.7 (14.1-15.4)	15.1 (14.4-15.7)	15.4 (14.8-16.1)	16.1 (15.4-16.8)	16.5 (15.8-17.2)
Life Satisfaction					
Not at all satisfied with the life they lead (%)	4.3 (3.9-4.6)	5.1 (4.8-5.5)	4.4 (4.1-4.7)	5.2 (4.8-5.6)	5.7 (5.3-6.1)
Not very satisfied with the life they lead (%)	15.8 (15.2-16.5)	15.4 (14.8-16.1)	14.0 (13.4-14.7)	18.4 (17.7-19.1)	17.1 (16.4-17.8)
Fairly satisfied with the life they lead (%)	57.8 (56.9-58.7)	57.8 (56.9-58.8)	56.8 (55.9-57.7)	56.8 (55.8-57.7)	55.4 (54.5-56.3)
Very satisfied with the life they lead (%)	22.1 (21.3-22.9)	21.6 (20.8-22.4)	24.8 (24.0-25.6)	19.6 (18.9-20.4)	21.8 (21.0-22.6)

Notes: Weighted percentages were included in the table; all values were rounded to first decimal place; numbers may not add up exactly to 100% due to rounding errors; values in parentheses indicate 95% Confidence Intervals (CI).

Supplementary Table 2. GDP per capita of 27 EU member states between 2009 and 2013

Country	2009	2010	2011	2012	2013
France	34797.5	35891.3	37325.3	37473.6	39209.6
Belgium	37629.4	39257.8	40858.7	41927.6	43059.8
Netherlands	44386.5	44773.9	46388.3	46448.9	47954.5
Germany	37112.9	39639.5	42142.5	43600.1	44184.8
Italy	34159.2	34740.1	35901.3	35931.1	35761.6
Luxembourg	80306.1	84589.8	91073.3	90788.3	95928.6
Denmark	39612.1	41835.8	43314.1	43873.9	45270.1
Ireland	41866.5	43249.6	45673.5	46063.3	47599.7
United Kingdom	36361.9	35879.8	36590.2	37569.3	39111.2
Greece	30652.2	28981.4	26626.5	25980.1	26753.1
Spain	32796.7	32372.9	32530.1	32235.6	32842.4
Portugal	26208.9	26943	26932.4	27125.2	27929.9
Finland	37534.5	38322.9	40251.4	40437.6	40831.7
Sweden	39657.2	41756	43709.2	44433.7	45067.4
Austria	40620.4	41892.8	44022.4	45858.2	47416.3
Cyprus	34087.7	33957.9	32983	31920.4	30587.4
Czech Republic	27008.8	27069.6	28604.2	28727.9	30043.6
Estonia	20206.2	21113.1	23954.9	25921	27169.3
Hungary	20860.6	21576.7	22603.2	22701.5	24037.2
Latvia	17032.9	17409.9	19450.9	21122.3	22559
Lithuania	18277.9	20085.1	22541.6	24475.1	26511.1
Malta	25828.6	26690	28177.5	28355.7	29525.6
Poland	19139.5	20883.1	22520	23598.6	24493.8
Slovakia	23172.3	24515.7	25167.5	26091.3	27414.2
Slovenia	27506.3	27607.7	28513.5	28481.7	29097.6
Bulgaria	14870.8	15084.3	15603	16097.8	16573.5
Romania	15815.2	16579.8	17624.5	18952	19576.6

*Notes: GDP per capita, PPP (current international $)

Supplementary Table 3. Total expenditure on health as a percentage of GDP for 27 EU member states between 2009 and 2013

Country	2009	2010	2011	2012	2013
France	11.6	11.6	11.5	11.6	11.7
Belgium	10.7	10.6	10.6	10.9	11.2
Netherlands	11.9	12.1	12.1	12.7	12.9
Germany	11.8	11.7	11.2	11.3	11.3
Italy	9.4	9.4	9.2	9.2	9.1
Luxembourg	8.1	7.7	7.4	7.2	7.1
Denmark	11.5	11.1	10.9	11	10.6
Ireland	9.9	9.2	8.7	8.9	8.9
United Kingdom	9.7	9.4	9.2	9.3	9.1
Greece	10.2	9.5	9.8	9.3	9.8
Spain	9.6	9.6	9.4	9.3	8.9
Portugal	10.8	10.9	10.4	9.9	9.7
Finland	9.2	9	8.9	9.1	9.4
Sweden	9.9	9.5	9.5	9.6	9.7
Austria	11.2	11.1	10.9	11.1	11
Cyprus	7.4	7.3	7.6	7.4	7.4
Czech Republic	7.8	7.4	7.5	7.5	7.2
Estonia	6.9	6.2	5.8	5.9	5.7
Hungary	7.7	8.1	8	8	8
Latvia	6.8	6.6	6.1	5.9	5.7
Lithuania	N/A	N/A	N/A	N/A	N/A
Malta	8.3	8.3	9.5	8.7	8.7
Poland	7.2	7	6.9	6.8	6.7
Slovakia	9.2	8.5	8	8.1	8.2
Slovenia	9.4	9.1	9.1	9.4	9.2
Bulgaria	7.2	7.6	7.4	7.4	7.6
Romania	5.6	5.9	5.6	5.6	5.3

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Supplementary Table 4. Proportion of respondents with good perceptions of healthcare provision by country

Country	2009	2010	2011	2012	2013
France	78.9 (76.2-81.3)	80.5 (77.9-82.9)	73.7 (70.8-76.3)	81.3 (78.7-83.6)	83.0 (80.5-85.2)
Belgium	94.0 (92.4-95.4)	92.8 (91.1-94.3)	94.7 (93.2-95.9)	95.6 (94.1-96.7)	90.2 (88.1-92.0)
Netherlands	91.3 (89.3-92.9)	89.7 (87.4-91.6)	89.4 (87.2-91.3)	91.6 (89.4-93.3)	92.7 (90.8-94.3)
Germany	62.4 (59.6-65.1)	65.7 (62.9-68.5)	66.2 (63.4-68.9)	81.2 (78.8-83.4)	80.8 (78.5-82.9)
Italy	55.6 (52.4-58.8)	53.6 (50.5-56.7)	56.6 (53.5-59.7)	41.1 (38.0-44.2)	44.6 (41.5-47.7)
Luxembourg	87.7 (84.4-90.3)	93.9 (91.4-95.7)	91.8 (89.1-93.9)	93.7 (90.7-95.8)	94.1 (91.4-96.0)
Denmark	77.5 (74.7-80.1)	76.1 (73.3-78.7)	74.9 (72.0-77.7)	83.8 (81.2-86.1)	83.2 (80.5-85.6)
Ireland	41.4 (38.3-44.6)	43.3 (40.1-46.6)	44.5 (41.3-47.7)	45.4 (42.2-48.7)	45.5 (42.3-48.7)
United Kingdom	87.3 (85.0-89.3)	88.5 (86.3-90.4)	85.0 (82.7-87.1)	86.5 (84.1-88.6)	84.0 (81.6-86.2)
Greece	29.9 (27.1-32.8)	23.4 (20.8-26.2)	22.8 (20.2-25.6)	9.1 (7.5-11.1)	13.0 (11.0-15.3)
Spain	78.9 (76.3-81.4)	79.5 (76.8-81.9)	72.9 (70.0-75.6)	69.2 (66.2-72.0)	56.3 (53.2-59.4)
Portugal	46.5 (43.2-49.7)	39.1 (36.1-42.3)	46.4 (43.3-49.4)	35.8 (32.9-38.9)	47.8 (44.6-50.9)
Finland	82.7 (80.1-85.0)	80.3 (77.6-82.8)	78.4 (75.5-81.0)	81.7 (78.9-84.2)	80.9 (78.0-83.5)
Sweden	84.1 (81.5-86.4)	85.5 (82.9-87.7)	78.2 (75.0-81.0)	87.3 (84.7-89.5)	82.0 (78.9-84.7)
Austria	90.5 (88.3-92.3)	91.8 (89.9-93.4)	94.1 (92.4-95.5)	91.0 (88.9-92.6)	87.6 (85.4-89.6)
Cyprus	56.9 (52.1-61.5)	60.4 (55.9-64.7)	59.5 (55.0-63.7)	53.2 (48.8-57.6)	57.0 (52.6-61.3)
Czech Republic	67.2 (64.0-70.3)	75.3 (72.5-77.9)	64.5 (61.4-67.4)	68.6 (65.6-71.4)	69.4 (66.4-72.1)
Estonia	61.0 (57.7-64.1)	63.5 (60.4-66.5)	59.8 (56.6-62.9)	63.1 (59.9-66.1)	56.4 (53.2-59.7)
Hungary	34.2 (31.2-37.4)	36.8 (33.8-40.0)	33.5 (30.6-36.6)	32.3 (29.4-35.4)	43.8 (40.7-47.0)
Latvia	37.2 (34.0-40.5)	30.8 (27.9-33.8)	31.8 (29.0-34.8)	30.1 (27.3-33.1)	38.5 (35.3-41.9)
Lithuania	40.6 (37.5-43.7)	38.6 (35.6-41.7)	39.6 (36.6-42.7)	40.0 (36.9-43.1)	56.0 (52.9-59.1)
Malta	75.8 (70.9-80.1)	81.2 (77.2-84.6)	82.7 (78.9-85.9)	82.6 (78.7-86.0)	88.8 (85.3-91.6)
Poland	37.4 (34.2-40.7)	33.2 (30.2-36.4)	32.6 (29.5-35.8)	21.4 (18.8-24.4)	30.6 (27.6-33.8)
Slovakia	50.1 (46.7-53.5)	58.5 (55.4-61.5)	39.0 (35.8-42.3)	43.2 (39.9-46.5)	49.0 (45.8-52.3)

Slovenia	62.1 (58.9-65.2)	66.7 (63.7-69.7)	68.9 (65.9-71.8)	71.0 (68.1-73.8)	68.7 (65.7-71.5)
Bulgaria	23.3 (20.6-26.1)	25.9 (23.1-28.8)	28.6 (25.8-31.5)	22.3 (19.7-25.1)	29.2 (26.3-32.2)
Romania	26.4 (23.6-29.4)	17.1 (14.8-19.6)	13.0 (11.1-15.2)	19.1 (16.7-21.8)	26.6 (23.9-29.5)
Overall	**64.9 (64.0-65.8)**	**64.9 (64.0-65.8)**	**62.9 (62.0-63.8)**	**63.3 (62.4-64.2)**	**64.0 (63.1-64.9)**

Notes: Weighted percentages were included in the table (special weights were used for Germany and the UK respectively); All values rounded to one decimal place; values in parentheses indicate 95% confidence intervals.

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Reported on page
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	6, 7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6, 7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	6, 7
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-8
Bias	9	Describe any efforts to address potential sources of bias	8-9
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8-9
		(*b*) Describe any methods used to examine subgroups and interactions	8-9
		(*c*) Explain how missing data were addressed	8
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	8
		(*e*) Describe any sensitivity analyses	9
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	n/a
		(b) Give reasons for non-participation at each stage	n/a
		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Sup. Table 1
		(b) Indicate number of participants with missing data for each variable of interest	Sup. Table 1
Outcome data	15*	Report numbers of outcome events or summary measures	n/a
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear	Tables 2

		which confounders were adjusted for and why they were included	
		(*b*) Report category boundaries when continuous variables were categorized	7-8
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	12
Discussion			
Key results	18	Summarise key results with reference to study objectives	13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14-15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	15-16
Generalisability	21	Discuss the generalisability (external validity) of the study results	15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	1

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.