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SYSTEMATIC REVIEW

# SYSTEMIC EFFECTS OF VIBRATION UNDER CONDITIONS OF LONG-TERM BED REST: A SYSTEMATIC REVIEW

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**Abstract**

**Background:** Prolonged bed rest induces significant dysfunction across multiple physiological systems that can surpass normal aging. Whole-body vibration (WBV) has been proposed as a non-pharmacological countermeasure, yet its systemic impact remains inadequately investigated

**Objective:** This systematic review aimed to explore the effects of WBV under conditions of prolonged immobilization, not only on the musculoskeletal system but also on the endocrine, vascular, and metabolic systems. Particular attention was given to whether WBV alone can elicit systemic responses beyond the site of application.

**Methods:** Following PRISMA guidelines, literature was searched in PubMed, Cochrane, and Greynet until February 2024. Seventeen studies met the inclusion criteria. Methodological quality was assessed using the PEDro scale. Data extraction focused on vibration protocols, physiological outcomes, and the presence or absence of concomitant exercise.

**Results:** WBV demonstrated protective effects on muscle morphology, function, and contractility, as well as bone remodeling and mineral density. Favorable alterations were also reported in endocrine, metabolic, and vascular parameters. However, in most studies, WBV was combined with resistance exercises, limiting conclusions about its independent systemic action. Passive WBV protocols in healthy and critically ill individuals showed localized effects near the application site, but systemic extrapolation remains inconclusive.

**Conclusions:** WBV may confer multi-systemic benefits during prolonged immobilization, particularly when combined with resistance training. Nonetheless, definitive evidence of isolated systemic action is lacking. Future studies should employ rigorous experimental designs isolating WBV to clarify its therapeutic potential as a standalone modality.

**Keywords:** Whole-body vibration, bed rest, immobilization, icu-aw.

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## INTRODUCTION

Prolonged immobilization, whether in clinical or experimental settings, results in rapid and extensive multisystem dysregulation, with effects often exceeding those associated with normal physiological aging.[1] Whole-Body Vibration (WBV) has been proposed as a non-pharmacological intervention to prevent or mitigate these adverse effects, demonstrating beneficial outcomes on musculoskeletal system function, microcirculation, and metabolism.[2,3,4] Despite numerous individual studies, no systematic review to date has exclusively addressed the systemic effects of WBV under prolonged bed rest conditions and the specific modalities of its application. The necessity for such a focused review becomes particularly apparent in contexts involving highly vulnerable populations, where therapeutic responses and safety requirements significantly differ.

## OBJECTIVE

The aim of this review is to evaluate the effects of WBV on various body systems adversely impacted by prolonged immobilization, in both healthy and pathological populations, as well as to document the methodologies employed in corresponding experimental or clinical protocols.

## METHODOLOGY

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[5], while the methodological quality of included studies was assessed using the Physiotherapy Evidence Database (PEDro) scale.[6]

### Search Strategy

The search was conducted in electronic databases PubMed, Cochrane, and Greynet. Greynet was utilized to identify unpublished literature (grey literature). The latest search was completed at the end of February 2024. The search keywords used were: ("bed rest" OR "ICU" OR "ICU-AW" OR "intensive care unit-acquired weakness" OR "hospitalized" OR "immobilization" OR "post intensive care syndrome" OR "PICS") AND ("vibration"). The search yielded 826 studies from PubMed, 411 from Cochrane, and 0 from Greynet. Additionally, the reference lists of identified studies were examined (reference list screening), with no additional eligible articles emerging.

### Inclusion and Exclusion Criteria

Clinical studies published in Greek or English were included, involving participants aged over 18 years who remained in prolonged horizontal bed rest, regardless of underlying pathology. No publication date restrictions were applied. Studies employing simulated microgravity conditions (e.g., 6° head-down tilt bed rest) and those limiting immobilization to a single limb or body segment were excluded due to physiological differences compared to the clinical reality of prolonged hospitalization.

### Quality Assessment

The methodological quality of the studies was evaluated using the PEDro scale, comprising 11 criteria related to internal validity, statistical sufficiency, and generalizability of findings. Each criterion scores 1 (yes) or 0 (no), with a maximum possible score of 11. Studies were classified as high quality (≥6), moderate quality (4–5), or low quality (≤3) based on the total score.

### Data Extraction and Analysis

Study selection was performed by two independent reviewers. Initially, titles were screened according to predefined inclusion and exclusion criteria, followed by abstract reviews where necessary. Final inclusion decisions were based on the full-text review. Data extracted from selected studies included parameters of WBV application, evaluation timelines from the onset to the completion of bed rest, intervention outcomes in control and experimental groups, and medium- to long-term findings following intervention discontinuation. Data extraction was performed regardless of each study's methodological quality; however, quality assessment was considered during the interpretation of findings and the formulation of final conclusions and limitations of this review.

## RESULTS

Article selection from the three electronic databases (PubMed, Cochrane, and Greynet), a total of 1237 articles were identified. Specifically, 826 articles were sourced from PubMed and 411 from Cochrane, while the Greynet search yielded no results. After removing 83 duplicates, the number decreased to 1154. Following the title screening, 1024 articles were excluded, leaving 130 articles for further evaluation through abstract review. Abstract screening led to the exclusion of 62 articles, resulting in 68 articles undergoing full-text review. Ultimately, based on predetermined inclusion and exclusion criteria, 17 studies were selected and included in this systematic review (Table 1).

Quality of Studies Based on the qualitative analysis, thirteen studies were classified as high quality (12 studies scoring 6/11 and 1 scoring 7/11), while four were considered moderate quality (3 studies scoring 5/11 and 1 scoring 4/11). The most frequent methodological limitation was the absence of participant blinding during allocation to intervention groups (Table 2).

1. Study - Article Analysis Based on Research Protocol Studies included in the review were categorized based on the mode of vibration application (active or passive participation), leading to the identification of three main experimental protocols: the Berlin Bed-Rest (BBR)[24] protocol (15 studies), WBV application in critically ill hospital patients[22] (1 study), and passive WBV application in a healthy population[23] (1 study).

A) Berlin Bed-Rest (BBR) - Active Participation

This protocol was part of a comprehensive study conducted in Berlin (2003–2004), aiming to investigate multisystem effects of prolonged bed rest and their potential mitigation through WBV [24]. Twenty healthy males aged 20–45 underwent strict bed rest for 8 weeks, randomly assigned equally to intervention and control groups. The intervention group performed lower limb closed kinetic chain resistance exercises on a bilateral oscillating vibration platform from a supine position twice daily, with adjustable intensity and frequency (19–26 Hz), using straps ensuring whole-body stimulus transmission. The control group remained inactive in the supine position throughout the 56-day study duration. Measurements occurred across three periods: baseline data collection, bed-rest period (56 days), and recovery phase, with follow-up up to 6 months post-study.

B) Passive Application of WBV in Critically Ill Patients

The second protocol evaluated the effects of WBV on critically ill patients receiving mechanical ventilation, without active participation.[22] The intervention was conducted in 19 patients. The vibration platform was placed under the patients' feet at the lower end of the bed, with knees and hips slightly flexed (approximately 20°). In this study, two different vibration devices were utilized, distinguished by the type of oscillation they provided (vertical or bilateral oscillation), and two distinct application protocols were configured accordingly. The device producing vertical oscillations was set at 26 Hz and applied nine times for 1 minute per session, whereas the bilateral oscillation device was set at 24 Hz and applied three times for 3 minutes per session. The total effective therapeutic time was 9 minutes for both vibration types. Data collection was carried out over five distinct time periods: (baseline, passive mobilization 6min, vibration, post-intervention periods). The total duration for data recording was 90 minutes.

C) Passive Application of WBV in Healthy Subjects Using a Wearable Device

The third protocol examined the physiological responses to passive application of WBV in healthy individuals in a supine position, simulating conditions of complete immobility as encountered in bedridden patients.[23] For this purpose, an innovative wearable vibration device (therapeutic vibration device - TVD) was used, equipped with four inertial actuators positioned at the shoulders and ankles. Participants (n=19) remained completely passive, while vibration was applied for 10 minutes, with frequencies set at 25 Hz on the lower limbs and 15 Hz at the shoulders. During the intervention, muscle activation, metabolic consumption, and regional tissue oxygenation parameters were assessed.

2. Analysis of Results Based on the Research Hypothesis

All 17 studies included in this review were categorized according to their primary research hypothesis into four major domains. Each category reflects targeted research efforts to evaluate the capacity of WBV to counteract the physiological alterations induced by prolonged immobilization.

2.1 Analysis of Results Related to the Muscular System

The study by Blottner et al. (2006) [8] investigated whether WBV, in combination with resistance exercises (intervention group), could preserve muscle size, fiber phenotype, and force output during long-term bed rest. In the control group, following 56 days of strict bed rest, MIPF decreased significantly by 18.9% in the morning ($p<0.001$) and by 32.9% in the evening of the first day of re-ambulation ($p=0.009$). The soleus muscle exhibited a marked phenotypic shift, with an increase of over 140% in the proportion of type II fibers, although no statistically significant reduction in cross-sectional area (CSA) was observed. No substantial phenotypic changes were found in the VL. Moreover, there was a notable reduction in the expression of endothelial nitric oxide synthase (eNOS/NOS1) in both type I and type II fibers in both muscles. Conversely, in the intervention group, MIPF was preserved during the first measurement on the day of re-ambulation (R1m), with only a 9.2% decrease recorded in the evening (R1e, $p=0.015$). In the SOL muscle, hypertrophy was observed in both type I and type II fibers, and the normal distribution ratio between fiber types was maintained. Additionally, NOS1 expression increased in type I fibers of both SOL and VL muscles. As in the control group, no significant changes were observed in the VL fiber distribution.

The study by Buehring et al. (2011)[18] investigated the effects of WBV under prolonged immobilization, with a focus on muscle strength, on power output and the overall function of the neuromuscular system. Results demonstrated a significant reduction in IPFF in the control group from the first recovery measurement (R1m), with further decline later that same day (R1e). Although gradual improvements were observed over the first week of recovery, strength values did not return to baseline ($p < 0.001$). In contrast, the intervention group maintained performance at R1m, showed improvement by day 4, and achieved near-complete recovery by day 7. Differences between groups were statistically significant ($p < 0.001$). EMG did not reveal statistically significant differences between groups ($p = 0.117$). However, on the first day post-reambulation, RMS amplitude decreased by 20% in the control group and 5% in the vibration group.

As for functional performance, the control group showed a significant decline in peak power (−24.1%, $p = 0.0004$) and jump height (−28.5%, $p = 0.0006$), compared to smaller losses in the vibration group (−12.2% and −14.2%, both $p < 0.0001$). While values in the exercise group remained stable in the early days post-bed rest, the control group began to show improvements from day 4 onward. Differences between groups in power and jump height remained significant ($p = 0.007$). Comparatively, functional decline in muscle performance was more pronounced than the loss in isometric strength. These differences were statistically significant in the vibration group (IPFF vs. peak power: $p = 0.014$; IPFF vs. jump height: $p = 0.0044$).

The study by Mulder et al. (2006)[9] examined the time course of adaptations in quadriceps muscle size, strength, and neuromuscular activation during long-term bed rest, as well as the potential protective role of WBV combined with resistive exercise. After 56 days of immobilization, the control group showed a significantly greater reduction in quadriceps CSA (−14.1% ± 5.2%, $p < 0.001$) compared to the intervention group (−3.5% ± 4.2%, $p < 0.05$). There was a trend toward asymmetrical muscle mass loss in the control group, with the left leg—untested during the intervention—exhibiting a greater decrease ($p = 0.091$), whereas the intervention group did not display significant interlimb differences. Maximum isometric torque was preserved in the intervention group, but decreased significantly in the control group by the end of the bed rest period ($p < 0.001$), with a more pronounced reduction in the left leg ($p < 0.05$). The knee angle at which peak torque was produced did not change significantly over time in either group (WBV: 62° ± 4° before vs. 61° ± 3° after; Control: 63° ± 5° both before and after).

In a follow-up to their 2006 study, Mulder et al. (2008)[12] investigated the explosive force production capacity and contractile properties of the quadriceps muscle under conditions of prolonged bed rest, focusing particularly on the integrity of neural drive. The results indicated that the maximal torque during explosive isometric contractions was preserved in both the control and intervention groups, suggesting that the ability of the nervous system to activate muscle fibers remained functionally intact during immobilization.

In a 2009 follow-up study, Mulder et al.[14] based on their earlier findings, hypothesized that maximum voluntary muscle activation of quadriceps, as assessed via RMS amplitude during maximal voluntary contractions, would remain unchanged in both groups. Instead, any EMG changes were expected to manifest primarily through shifts in median frequency (Fmed), reflecting muscular—not neural—alterations such as atrophy or reduced conduction velocity. The results revealed a significant reduction in maximum isometric torque in both groups ($p < 0.001$), with a notably greater decline in the control group by the end of bed rest ($p < 0.05$). In the intervention group, torque values stabilized after day 4 (BR4), whereas the control group demonstrated a continuous, statistically significant decline through day 56 ($p < 0.001$). With respect to RMS amplitude, the intervention group showed a significant increase over the course of the study ($p < 0.001$), particularly on days 10, 17, 24, and 56. Day 38 also showed a near-significant trend ($p = 0.054$). In contrast, RMS remained unchanged in the control group throughout the immobilization period. The RMS increase in the intervention group was evident during both maximal and submaximal contractions, with a stronger expression during the former.

Additionally, the control group exhibited a significant reduction in Fmed and conduction velocity across all activation levels ($p < 0.05$ and $p < 0.001$, respectively), pointing to intramuscular origin changes, likely due to atrophy or alterations in muscle membrane properties. These parameters remained stable in the WBV group, underscoring that whole-body vibration combined with resistance training not only preserves muscle strength, but also maintains the physiological and electrophysiological integrity of the muscle tissue.

In the prospective study by Mendis et al. (2009)[15] , the effects of long-term immobilization were investigated on both deep and superficial anterior hip muscles. During the immobilization period, a significant decrease in CSA was observed in the iliopsoas between day 14 and day 42 ($p = 0.01$), and in the sartorius from day 42 to day 56 ($p = 0.03$ and $p = 0.005$, respectively). Other muscle groups, including superficial stabilizers such as the rectus femoris, showed no statistically significant changes. Importantly, the patterns of atrophy were comparable between the control and intervention (WBV+CKC) groups, suggesting that the exercise countermeasure did not prevent muscle loss in these specific deep stabilizers. During the six-month follow-up, most muscle groups returned to their baseline size. However, the psoas and iliopsoas showed a persistent reduction in CSA, which remained statistically significant at 180 days post bed rest ($p = 0.003$ and $p = 0.001$, respectively). These findings highlight the vulnerability of deep hip stabilizers to long-term unloading and suggest a need for more targeted interventions to mitigate their decline.

The study by Belavý et al. (2008)[10] investigated both anatomical and functional adaptations in the lumbar spine (LS) resulting from prolonged bed rest, as well as the effectiveness of WBV. With respect to overall spinal structure, a general increase in lumbar spine length was observed during bed rest, most notably between vertebrae L2–L5. These changes coincided with increases in intervertebral disc height and area, particularly in the central discs (L2–L5), with lesser changes in L1–L2. Although the intervention group showed reduced variations, no statistically significant differences between groups were found at the segmental level. During reambulation, these parameters gradually decreased but did not return to baseline (BR1) values. Lumbar lordosis increased at the lower lumbar levels during recovery in both groups, with no statistically significant differences between them. Changes in intervertebral angles throughout the study were not significant.

Regarding the musculature, cross-sectional area (CSA) was evaluated for several muscles in the lumbar region. Statistically significant changes were found for the multifidus ($p = 0.021$), lumbar erector spinae ($p = 0.0003$), and rectus abdominis ($p = 0.0008$). The intervention group had a significantly larger baseline CSA in the psoas ($p = 0.0005$), and multifidus atrophy during bed rest and recovery was less pronounced compared to controls ($p = 0.101$), with some degree of preservation lasting up to three months post-intervention. The erector spinae muscles exhibited a trend toward decreased volume, though not statistically significant. Interestingly, the rectus abdominis showed an increase in CSA at the end of bed rest, possibly as a compensatory response to decreased posterior chain activation.

The study by Belavý et al.[19] evaluated the effects of prolonged bed rest on lumbopelvic motor control, as well as the potential protective role of WBV. The EMG results revealed a reduction in coordinated co-contraction between lumbar flexors and extensors in the control group, a change that approached statistical significance ($p = 0.058$). Conversely, a slight increase in co-contraction was observed in the WBV group, though it did not reach statistical significance. While within-group differences were not significant, the between-group comparison showed a trend toward significance ($p = 0.058$), suggesting potential preservation of motor coordination in the intervention group. In addition, changes in body composition were assessed, focusing on trunk fat accumulation, using whole-body scanning (Delphi W). The control group showed a statistically significant increase in trunk fat as early as day 17 of bed rest (BR17), with this trend intensifying by the end of immobilization and persisting throughout the recovery phase—up to one year post-intervention (R360)—relative to baseline values (BDC3). In contrast, the intervention group exhibited only a mild increase in trunk fat by day 55 (BR55, $p < 0.05$), with no further deterioration during the reambulation period.

The study by Sun et al. (2015)[21] focused on the biochemical assessment of the effects of prolonged immobilization on muscle tissue by monitoring three specific biomarkers: Pro-C6, C6M, and Pro-C3. Pro-C6, indicative of collagen type VI synthesis, exhibited a progressive increase from the first week of immobilization, reaching statistical significance between day BR19–R28 of the intervention, and peaking on day 47 ($p = 0.0002$). No significant differences were found between the intervention and control groups throughout the study. C6M, a marker of collagen type VI degradation mediated by MMP-2 and MMP-9, remained stable during the bed rest phase. However, a transient increase of 30–40% was observed at the onset of re-ambulation. This rise appeared to be independent of the intervention, suggesting that collagen type VI degradation is primarily driven by the transition from inactivity to resumed activity, rather than the presence of countermeasures. Pro-C3, representing type III collagen synthesis, decreased by approximately 20% in the early phase of immobilization (BR3–BR12, $p < 0.004$), followed by an increase near the end of the bed rest period (BR40, $p = 0.05$). A similar pattern emerged during remobilization, with statistically significant elevations from day 3 to day 28 of the recovery phase ( $p < 0.03$), possibly indicating connective tissue remodeling. Moreover, C6M and Pro-C3 levels were significantly associated with baseline lean body mass (LBM), supporting their role as indicators of muscle condition. In contrast, elevated Pro-C6 levels were linked to reduced muscle mass loss during bed rest and less muscle (re)gain during recovery.

The study by Salanova et al. (2008)[11] evaluated the efficacy of WBV as a countermeasure against muscle dysfunction induced by prolonged immobilization, with a specific focus on the expression and function of the ryanodine receptor type 1 (RyR1) in the soleus muscle. In the control group, RyR1 expression was reduced in both type I fibers ($-1.8 \pm 8.3\%$) and type II fibers ($-15.2 \pm 3.2\%$). Although these reductions did not reach statistical significance, the [$^3$H]ryanodine-binding capacity—a marker of RyR1 functionality—decreased significantly by 38% ($6.2 \pm 0.8$ pmol/mg protein vs. $10.0 \pm 1.3$, $p < 0.05$), indicating a diminished channel open probability. In contrast, the WBV group maintained normal RyR1 expression levels, and [$^3$H]ryanodine-binding capacity significantly increased by 62.9% ($13.2 \pm 3.1$ pmol/mg protein vs. $8.1 \pm 0.5$, $p < 0.05$). Immunohistochemical analysis showed a marked increase in RyR1 expression in both type I ($+41.0 \pm 13.3\%$) and type II ($+34.6 \pm 9.9\%$) fibers in the WBV group, suggesting balanced protection across fiber types. Furthermore, confocal microscopy revealed enhanced colocalization of RyR1 with neuronal nitric oxide synthase (NOS1) in the WBV group, indicating a potentially improved functional interaction. In the control group, RyR1 S-nitrosylation increased by $16.5 \pm 2.5\%$, a modification known to reduce channel activation. Conversely, S-nitrosylation decreased slightly in the WBV group ($-2.5 \pm 2.8\%$), though not significantly, aligning with the preservation of RyR1 functional status.

The study by Wollersheim et al. (2017)[22] , which applied WBV passively in critically ill patients, demonstrated significant changes in parameters associated with energy metabolism and physiological activation. A statistically significant increase in energy expenditure was observed during WBV application ($p = 0.007$), accompanied by increased oxygen consumption ($p = 0.012$) and carbon dioxide production ($p < 0.001$). These metabolic responses indicate skeletal muscle activation, despite the passive nature of the intervention. In comparison, during passive mobilization provided by physiotherapists, only an increase in $CO_2$ elimination was detected ($p = 0.041$), without corresponding increases in $O_2$ uptake or overall energy expenditure. This suggests a distinct physiological response profile between the two interventions. Notably, $CO_2$ output remained elevated during the early recovery phase following WBV, returning to baseline only in the later recovery phase. Respiratory rate increased significantly during both physiotherapy ($p < 0.01$) and WBV ($p < 0.001$), while the respiratory quotient (RQ) increased exclusively during physiotherapy ($p = 0.033$), reflecting the isolated rise in $CO_2$ production without a corresponding increase in $O_2$ uptake. Additionally, arterial blood gas analysis revealed a statistically significant increase in serum potassium levels during WBV ($p = 0.048$), a change not observed during physiotherapy. All other blood gas parameters, including glucose concentration, as well as levels of cortisol and insulin-like growth factor I (IGF-1), remained stable throughout the study.

The study by Saxena et al. (2020)[23] examined the effects of passive application of WBV using the therapeutic vibration device in healthy participants in a supine position, without active muscle engagement. The aim of the study was to evaluate muscle activity, peripheral tissue oxygenation ($rSO_2$), and metabolic parameters through indirect calorimetry.

Electromyographic (EMG) analysis revealed a statistically significant increase in muscle activity in six out of the eight muscle groups: soleus (SO, $p = 0.011$), tibialis anterior (TA, $p = 0.012$), gastrocnemius lateralis (GL, $p = 0.003$), vastus medialis (VM, $p < 0.001$), vastus lateralis (VL, $p < 0.0001$), and deltoid medius (DM, $p = 0.006$). In contrast, no statistically significant differences were recorded in the rectus femoris (RF, $p = 0.59$) and semitendinosus (ST, $p = 0.86$). The highest activation was observed in the distal muscles of the lower limbs, a finding attributed to the damping of vibration during its longitudinal transmission toward the proximal muscles.

Indirect calorimetry recorded statistically significant increases in oxygen consumption ($VO_2$, $p < 0.0001$), carbon dioxide production ($VCO_2$, $p < 0.0001$), total energy expenditure (EE, $p < 0.0001$), and minute ventilation (VE, $p < 0.0001$). Tidal volume (VT) did not show a statistically significant change ($p = 0.094$). These increases are interpreted as a result of the activation of the tonic vibration reflex (TVR), which induces passive muscle contractions and an increase in metabolic demands. Peripheral tissue oxygenation ($rSO_2$), as measured by near-infrared spectroscopy (NIRS), showed a significant increase in all evaluated areas: gastrocnemius lateralis (GL, $p < 0.0001$), rectus femoris (RF, $p < 0.0001$), and biceps brachii (BB, $p < 0.001$), indicating an increase in blood flow and local oxygenation through vasodilation.

2.2 Analysis of Results Related to the Skeletal System

The study by Armbrecht et al. (2010)[17] investigated the impact of WBV on metabolic and structural adaptations in the skeletal system during prolonged bed rest and subsequent re-ambulation. During bed rest, the control group showed mild or negligible increases in bone formation markers. In contrast, the WBV group exhibited significant increases in PINP (procollagen type I N-terminal propeptide, $p<0.05$) and bone-specific alkaline phosphatase (BAP) ($p<0.01$–$0.001$ depending on timepoint), indicating stimulation of bone formation. The CTX marker (C-terminal telopeptide of type I collagen), reflecting bone resorption, increased in both groups but to a lesser extent in the WBV group, though without statistically significant between-group differences ($p>0.05$).

The TRACP 5b marker (a measure of osteoclastic activity) remained unchanged in both groups throughout the immobilization period. Intact parathyroid hormone (iPTH) decreased in the control group but remained stable in the WBV group, although this difference did not reach statistical significance. Notably, urinary calcium excretion, assessed through 24-hour collections, was substantially higher in the control group and significantly attenuated in the WBV group during immobilization. In the re-ambulation phase, PINP levels remained elevated in both groups up to day R28 before declining. BAP remained low in the control group and elevated in the WBV group; however, post-R28, BAP levels in the control group rose, eventually aligning with those of the intervention group by R90. Conversely, CTX levels returned to baseline by R7 in both groups. iPTH levels rose during recovery, beginning from R3 in the control group and R1 in the WBV group. The urinary calcium loss observed in the control group during bed rest decreased sharply after R2, suggesting a reversal of the catabolic phase of calcium metabolism. Regarding bone mass composition, the control group experienced greater bone loss, particularly in the lower limbs, although this difference was not statistically significant ($p>0.91$). Furthermore, lean mass in the legs declined significantly only in the control group, while a compensatory increase was observed in the trunk region, possibly indicating a redistribution of muscle mass during immobilization.

The study by Rittweger et al. (2010)[16] investigated morphological and quantitative changes in bone tissue and muscle cross-sectional area (CSA) of the upper and lower limbs. A significant reduction in the CSA of the gastrocnemius muscle was observed in the control group following prolonged immobilization. Although muscle loss was also statistically significant in the WBV group ($p < 0.001$), the intergroup difference favored the vibration intervention. No significant differences were noted between right and left limbs ($p > 0.2$). At the 12-month follow-up, partial recovery of muscle CSA was evident only in the control group ($p = 0.004$), without further gain in the WBV group.

Regarding bone parameters, no significant changes were found in the WBV group, except in the tibial epiphysis, where a borderline significant reduction was noted ($p = 0.06$). In contrast, the control group exhibited peak bone loss at day R14 post-immobilization ($p = 0.008$ at the 38% tibial site; $p < 0.001$ for others). At 12 months, epiphyseal bone loss in the tibia remained significant in the control group ($p < 0.002$), while the WBV group showed slight increases in bone density at the 38% and 66% tibial sites. No significant differences were observed in lumbar spine measurements. Small, early losses (~2%) returned to baseline by day R14. Similarly, changes in hip bone mass were not statistically significant in either group, though WBV participants showed improved values at 12 months ($p < 0.038$). Importantly, no changes were detected in the forearm musculature or bone mass, nor in handgrip strength, in either group during or after bed rest.

### 2.3 Analysis of Results Related to the Endocrine System

The study by Belavý et al. (2012)[20] investigated endocrine and body composition adaptations during prolonged bed rest and the subsequent recovery phase in healthy male participants, with a particular focus on sex hormone regulation. During immobilization, the control group exhibited a statistically significant increase in fat mass ($p = 0.015$), which persisted throughout the recovery period up to day R360. In contrast, the WBV group showed a more moderate increase (6.2%, $p = 0.094$). Concurrently, the control group demonstrated a trend toward decreased lean mass between BR31 and BR55 ($p = 0.06$), while values remained stable in the intervention group. Although intergroup differences were not statistically significant ($p = 0.72$), lean mass increased significantly beyond baseline in the control group during recovery ($p = 0.0001$), while in the intervention group it did not exceed initial levels ($p = 0.014$).

SHBG levels gradually declined in the control group until one week post-bed rest, returning to baseline by R28. In contrast, the intervention group showed stable SHBG levels during bed rest and a significant increase during re-ambulation, with highly significant differences between the groups in both phases (BR: $p < 0.0001$; R: $p < 0.0001$). Prolactin decreased by 15% in the control group during bed rest, while it increased by 15.3% in the intervention group, with a significant between-group difference ($p = 0.021$). During recovery, prolactin declined similarly in both groups. Total testosterone followed a comparable trajectory across groups ($p \geq 0.10$), increasing until BR19, returning to baseline by the end of immobilization, and decreasing significantly during the first week of recovery (R1–R7), remaining suppressed thereafter. Estradiol showed a trend toward increase near the end of immobilization in both groups, but only the control group exhibited a sharp rise during early recovery, with a significant difference compared to WBV ($p = 0.0090$). TSH increased in both groups over the course of the study, without significant intergroup differences ($p \geq 0.015$). FT3 declined during the early phase of bed rest and returned to baseline by R7, following a similar pattern in both groups ($p \geq 0.25$). Similarly, cortisol levels decreased in the control group, particularly on BR5, BR12, and BR33, while they remained stable in the intervention group and showed a trend toward increase on R3 and R90. However, between-group differences were not statistically significant. Finally, creatine kinase (CK) levels declined in both groups during bed rest and increased during recovery, with a statistically significant rise only on R3 and only in the control group. Overall, CK behavior did not differ significantly between groups ($p = 0.65$).

### 2.4 Analysis of Results Related to the Vascular System

In the study by Bleeker et al. (2005)[7] , the effects of WBV on the functional capacity of the arterial system in both upper and lower limbs during prolonged bed rest were investigated. The researchers examined changes in vessel diameter and blood flow in the common and superficial femoral arteries, the brachial artery, and the common carotid artery—both at rest and following vascular occlusion and nitroglycerin administration—to assess endothelium-dependent (FMD) and endothelium-independent vasodilation.

During the period of bed rest, heart rate (HR) significantly increased in the control group but remained stable in the intervention group. Statistically significant differences were observed between the groups at both BR25 and BR52 ($p<0.05$), in favor of the intervention group. Blood pressure remained unchanged in both groups. The diameter of the common and superficial femoral arteries (CFA and SFA) decreased significantly only in the control group, while it remained nearly unchanged in the WBV group. The difference between the groups was statistically significant (CFA: $p=0.001$, SFA: $p<0.001$). Blood flow in these arteries did not show significant changes over the course of the study in either group. The brachial artery diameter decreased significantly in both groups ($p=0.016$), but there was no statistically significant difference between them. Blood flow in the brachial and carotid arteries remained stable in both groups. Additionally, no changes were recorded in the diameter or flow of the common carotid artery. Following vascular occlusion, FMD increased significantly in both groups. However, the FMD increase was significantly smaller in the WBV group compared to the control group on day BR25 ($p=0.008$), whereas no difference was found on BR52 ($p=0.55$). Similarly, endothelium-independent vasodilation, assessed via nitroglycerin administration, increased significantly in both groups, without differences between them.

Complementary to the study on arterial parameters, Van Duijnhoven et al. (2008)[13] investigated the effects of prolonged bed rest on the venous system and the potential protective role of vibration, focusing on morphological and functional changes in the popliteal vein—specifically diameter, capacitance, and compliance.

The diameter of the popliteal vein did not exhibit statistically significant changes, either between the two groups or within each group, under resting conditions or during venous occlusion at increasing pressures (20–80 mmHg). This finding remained consistent across all measurement intervals, suggesting that prolonged inactivity did not structurally affect the vein, regardless of intervention. In contrast, functional assessment revealed a significant reduction in venous capacitance in the control group following bed rest, whereas capacitance remained stable in the vibration group—highlighting a potential protective effect of the intervention. A statistically significant difference between the two groups was observed on day 25 of bed rest (BR25, $p < 0.01$), but this difference diminished by BR52 and was no longer statistically significant. Vein compliance showed a trend toward increase in both groups, although this change did not reach statistical significance, either within or between groups.

## DISCUSSION

Prolonged immobilization leads to significant adverse adaptations in various physiological systems of the human body, including the musculoskeletal, endocrine, cardiovascular and cellular metabolism systems. Remarkably, certain dysfunctions also persisted in participants who received vibration and/or exercise treatment. This observation suggests that vibration, while beneficial, may not be sufficient on its own to fully offset the effects of immobility.

This systematic review has shown that vibration may have effects beyond local musculoskeletal responses and provides initial evidence of a multisystemic effect. In particular, changes were found in the endocrine system (SHBG, prolactin, testosterone, oestradiol), metabolic parameters (oxygen consumption, $CO_2$ production, energy consumption and collagen turnover markers), venous function parameters (capacitance and compliance of the popliteal vein) and arterial structure and function (femoral artery diameter and wall thickness, endothelial performance).

This raises the critical question of whether the effects of vibration are localized to the specific anatomical regions of application or whether they extend systemically to the entire body. Analysis of the included studies, particularly those from the Berlin Bed Rest Protocols (BBR), suggests that vibration can also affect structures beyond the site of application. For example, in studies focusing on motor control in the lumbopelvic region[19] and on the multifidus muscle[10] , favorable neuromuscular adaptations were observed in areas not directly addressed by the vibration platform. These effects can be partly explained by the bilateral transmission of mechanical stimuli that can trigger movements in the pelvic region and activate the deep stabilizing muscles. Regarding endocrine responses, statistically significant differences in serum concentrations of SHBG and prolactin during immobilization were found in favor of the intervention group. Although similar trends were found in cortisol levels, they did not reach statistical significance. These results provide further evidence for the hypothesis that WBV may have systemic effects.

However, the lack of measurements at remote sites and the anatomical proximity of many structures make it difficult to draw firm conclusions regarding a systemic effect specifically on muscles that are not directly vibrated. Furthermore, in the vast majority of studies, vibration was administered in conjunction with closed kinetic chain resistance exercise. While this combined stimulus increases the overall effectiveness of the intervention, it also limits the ability to determine the specific contribution of vibration. An exception to this is studies in which WBV was applied in isolation, without concurrent exercise, in either healthy or clinical populations. For example, in the study by Saxena et al. (2020)[23] , passive WBV in the supine position resulted in significant muscle activation in the lower limbs and an increase in regional tissue oxygenation ($rSO_2$) and oxygen uptake ($VO_2$) near the sites where vibration was applied. Similarly, in the study by Wollersheim et al. (2017)[22] , WBV elicited an increase in energy expenditure and changes in metabolic markers in critically ill immobilized patients, even in the absence of voluntary exercise. While these results support the clinical relevance of WBV, they cannot be considered definitive evidence of a systemic effect on the musculoskeletal system due to the proximity between the measurement and application sites.

Interestingly, in the second phase of the Berlin Bed Rest Protocol (BBR2) —which was not included in the present review — participants underwent 6° head-down tilt. The combination of WBV with resistance exercise resulted in significant preservation of cortical bone mass[25,26] and endothelial function in the arteries[27,28] of the lower limbs. In contrast, resistance training alone failed to prevent the negative vascular adaptations. This finding supports the notion that vibration, when applied with sufficient duration and precision, can have effects beyond the target musculature.

A review of the literature shows that systemic effects similar to those of vibration can also be induced by other techniques that do not require the active participation of the patient. Specifically, the systematic review by Vollenweider et al. (2020)[29] examined the local and systemic effects of passive lower extremity exercise techniques — including simple passive exercise, exercise combined with blood restriction techniques (a technique that combines low intensity exercise with blood flow occlusion), continuous passive motion (CPM) and passive cycling— in patients who were bedridden for at least four days in a hospital setting. According to the results of the study, passive interventions showed a tendency to attenuate muscle atrophy and maintain microcirculation at the local level, similar to the vibration protocols. At a systemic level, certain techniques appeared to positively influence markers such as nitric oxide (NO) concentration, cytokine levels (decrease in TNF-α, increase in IL-10) and oxygen consumption ($VO_2$).

The meta-analysis by Li et al. (2024)[30] , which included 23 randomized controlled trials investigating the use of electrical stimulation (electrical muscle stimulation, neuromuscular electrical stimulation and functional electrical stimulation) in critically ill patients, also showed statistically significant improvements in muscle strength as assessed by the Medical Research Council (MRC) scale. In addition, the use of electrical stimulation appeared to be associated with a reduction in ICU length of stay, providing further evidence of possible systemic effects, although the authors emphasized that further research is needed to confirm these findings.

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As with whole-body vibration, parameters such as duration and intensity of stimulus application appear to be critical factors in the efficacy of passive mobilization and electrical stimulation. Thus, under appropriate conditions, passive therapeutic methods that do not require active patient participation could serve as valuable tools to prevent and manage the adverse consequences associated with prolonged immobilization.

Specifically with regard to the use of whole-body vibration, the present systematic review emphasizes the need for future high-quality studies that exclusively evaluate the effects of vibration to accurately determine whether vibration alone can serve as an alternative therapeutic intervention with systemic effects.

## CONCLUSIONS

This systematic review has shown that the use of whole-body vibration during prolonged immobilization can have protective effects not only on the musculoskeletal system but also on the endocrine and vascular systems. However, the data currently available do not allow definitive conclusions to be drawn about the systemic nature of these effects. Therefore, future research with more rigorous and targeted experimental designs is needed to clarify whether vibration is an independent therapeutic modality with demonstrable systemic effects.

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**ANNEX**

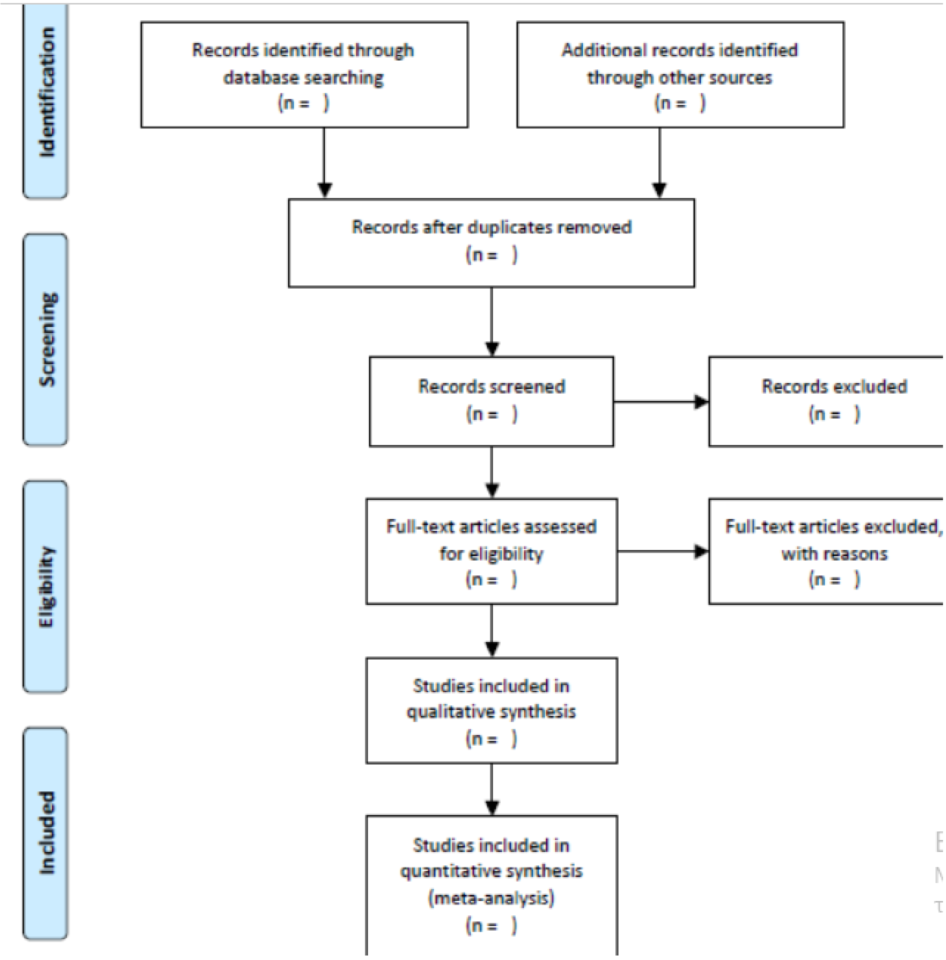


**FIGURE 1.** Flowchart illustrating the selection process of studies included in the systematic review.

**TABLE 1.** Quality assessment of the 17 studies based on the PEDro scale

| | Eligibility criteria | Random allocation | Concealed allocation | Baseline similarity | Blinding of subjects | Blinding of therapists | Blinding of assessors | Measures of key outcomes from more than 85% of subjects | Intention-to-treat | Between-groups statistical comparisons | Point measures and measures of variability | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Bleeker et al. 2005 [7] | • | • | | • | | | | • | | • | • | **6** |
| Blottner et al. 2006 [8] | • | • | | • | | | | • | | • | • | **6** |
| Mulder et al. 2006[9] | • | • | | • | | | | • | | • | • | **6** |
| Belavý et al. 2008 [10] | • | • | | • | | • | | • | | • | • | **7** |
| Salanova et al. 2008[11] | • | • | | • | | | | • | | • | • | **6** |
| Mulder et al 2008 [12] | • | • | | • | | | | • | | • | • | **6** |
| Van Duijnhoven et al. 2008 [13] | • | • | | • | | | | • | | • | • | **6** |
| Mulder et al 2009 [14] | • | • | | • | | | | • | | | • | **5** |
| Mendis et al. 2009 [15] | • | • | | • | | | | | | • | • | **5** |
| Rittweger et al. 2010 [16] | • | • | | • | | | | • | | • | • | **6** |
| Armbrecht et al. 2010 [17] | • | • | | • | | | | • | | • | • | **6** |
| Buehring et al. 2011 [18] | • | • | | • | | | | • | | • | • | **6** |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Belavý et al. 2012 [19] | • | • | | • | | | | • | | • | • | **6** |
| Belavý et al. 2012 [20] | • | • | | • | | | | • | | • | • | **6** |
| Sun et al. 2015 [21] | • | • | | • | | | | • | | • | • | **6** |
| Wollersheim et al.2017[22] | • | • | | • | | | | • | | | • | **5** |
| Saxena et al. 2020[23] | • | | | • | | | | • | | | • | **4** |