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REVIEW ARTICLE

Whole-body vibration in children with disabilities demonstrates therapeutic potentials for pediatric cancer populations: a systematic review

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Abstract

Purpose Low levels of physical activity often observed in pediatric oncology might be attributed to various functional deficits, especially those of the lower limbs as these affect gait, mobility, and, consequently, physical activity. In the past few years, whole-body vibration (WBV) has emerged as a new therapy modality for improving physical functioning. Although WBV is increasingly applied in children with disabilities, its impact on lower limb function in pediatric cancer patients and survivors has not yet been investigated.

Methods To establish whether there is evidence that WBV may be beneficial for pediatric cancer patients and survivors, this review summarizes current data on WBV studies among children with disabilities and extracts relevant information for the pediatric cancer population. Two independent reviewers performed a systematic literature search following the PRISMA guidelines.

Results Nine studies were included in the analysis. Results demonstrate that WBV is a safe, highly compliant, and effective approach in cohorts of children with disabilities. The largest effects of WBV were observed in lower extremity muscle mass and strength, balance control, gait, and walking ability. Furthermore, we were able to develop first recommendations for WBV protocols.

Conclusions WBV seems to be feasible and effective for improving parameters that may be relevant to the pediatric cancer population. Efforts are needed to conduct first WBV interventions in children with cancer proving the effects. The developed recommendations for WBV protocols might help to implement these intervention studies.

Keywords WBV · Vibration · Children with disabilities · Pediatric cancer · Pediatric oncology

Introduction

Physical inactivity is a major concern in pediatric oncology. Various studies report low levels of physical activity (PA) in pediatric cancer patients [1–3], which do often not recover after cessation of medical treatment and can even persist well into children's adulthood [4–7]. These low levels of PA might be attributed to various functional deficits often observed in the pediatric cancer population, especially those of the lower limbs as these affect gait, mobility, and, consequently, PA. The most commonly reported deficits of the lower limbs include decreased muscle strength [8–14], impaired joint range of motion [10, 13, 15–17], reduced balance control [9, 12, 18, 19], and limitations in functional mobility [11, 13], gait, and walking ability [20–23]. The cause and extent of lower limb deficits can vary within the population, as they may be due to both cancer disease and medical treatment. In patients with acute

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lymphocytic leukemia, for example, these deficits are often caused by vincristine-induced peripheral neuropathy [24]. In children with brain tumors, the location of the lesion as well as the choice of treatment including surgery and/or radiation may contribute to the ambulatory problems [18, 25].

In the past few years, whole-body vibration (WBV) has emerged as a new training method and therapeutic modality for improving physical functioning [26]. WBV describes a neuromuscular training method in which participants stand or exercise on a vibrating platform that produces oscillating vibrations. As such, mechanical stimuli are transmitted to the feet and, accordingly, to the rest of the body [27]. Thereby, the vibratory load of WBV depends on different variables including frequency, amplitude, acceleration, and duration [28]. The underlying mechanisms regarding the effects of WBV remain to be elucidated. The "tonic vibration reflex," a stimulation of the muscle spindles which induces reflexive muscle contractions, seems to be a trigger mechanism for several physical responses [27], also including muscular contraction [29]. In addition, several other mechanisms such as metabolic, neuronal, or circulatory mechanisms may play a role here, but, to date, they are not well understood [30, 31]. Rittweger et al. (2010) previously described the physical and physiological principles of WBV in more detail [30].

To date, several studies have been conducted with physically disabled children and adolescents suffering from congenital disorders [32]. These studies promote WBV as a safe training method that can be of benefit for improving single physical fitness parameters including strength and gait variables [32–34]. In pediatric oncology, by contrast, WBV has only received very little attention so far [35], and its impact on lower limb function has not yet been investigated. Both populations, however, children with cancer and patients with disabilities, suffer from lower limb deficits that interfere with their autonomy. Despite different derivations of these deficits, it is therefore possible that WBV could be of benefit for pediatric cancer populations as well. WBV might be a beneficial adjunct to conventional exercise therapy interventions as conventional programs could not always achieve the desired effect of improved lower limb function [36–38].

To establish whether there is evidence that WBV may be beneficial to improve lower limb function in pediatric cancer populations, this review aims to analyze WBV intervention studies conducted in children with disabilities that affect the physical functioning of the lower limbs and as a result limit their ability to be physically active. We hypothesized that WBV is a safe and compliant approach in cohorts of children with disabilities and at the same time could effectively improve functional and physical parameters relevant in the pediatric cancer populations, including lower extremity muscle mass and strength, joint range of motion, balance control, functional mobility, gait, and walking ability.

Methods

A literature search was conducted in October 2016 by two independent researchers (V.R., J.D.) searching three electronic databases (PUBMED, LIVIVO, SportDiscus) as well as screening reference lists of articles and related reviews. Based on the preferred reporting items for systematic reviews and meta-analysis (PRISMA) 2009 statement [39], this review was conducted in four steps. After identifying all records through database search and reference list screening (Step 1—identification), two reviewers independently analyzed all records by examining titles and abstracts against inclusion and exclusion criteria listed below (Step 2—screening). After that, relevant full texts were assessed for eligibility (Step 3—eligibility) and finally all relevant studies were included (Step 4—inclusion) in this review (Fig. 1). Inter-reviewer disagreement was resolved by a third reviewer (F.S.). The keywords used for database search (Table 1) were defined based on the PICOS approach [39] focusing on children with disabilities that affect the physical functioning of the lower limbs (P—participants) receiving a WBV intervention (I). No restrictions were made regarding comparisons (C) as comparing to placebo interventions, usual care and no intervention were allowed. Reported outcomes (O) were defined as parameters relevant in pediatric oncology, and all kinds of study designs (S) were included except for case reports with less than 10 study participants.

The following inclusion and exclusion criteria were applied: Articles were included if they were peer-reviewed original work, written in English language, published within the last 15 years (starting from 2001), including at least 10 study participants, investigating study participants 18 years old and younger, focusing on the effects of a WBV intervention period on outcomes relevant in pediatric oncology including muscle mass and strength, joint range of motion, balance control, functional mobility, as well as gait and walking ability. Muscle mass and strength were required to either refer to the whole body or the lower limbs. Records were excluded if studies included solely healthy children/adolescents, they were animal studies, they were study protocols, review articles or meta-analysis or if the study results were not explicitly related to the intervention period.

Results

After removing duplicates, a total of 308 titles were initially identified. Nine studies were included in this review after reviewing titles, abstracts, and full texts. Detailed descriptions and statistical results of all included studies are displayed in Table 2. Also, a comprehensive summary of the descriptive study results is given in Supplementary Table 1. Seven out of nine studies included an intervention as well as a control group and were designed as randomized controlled trials

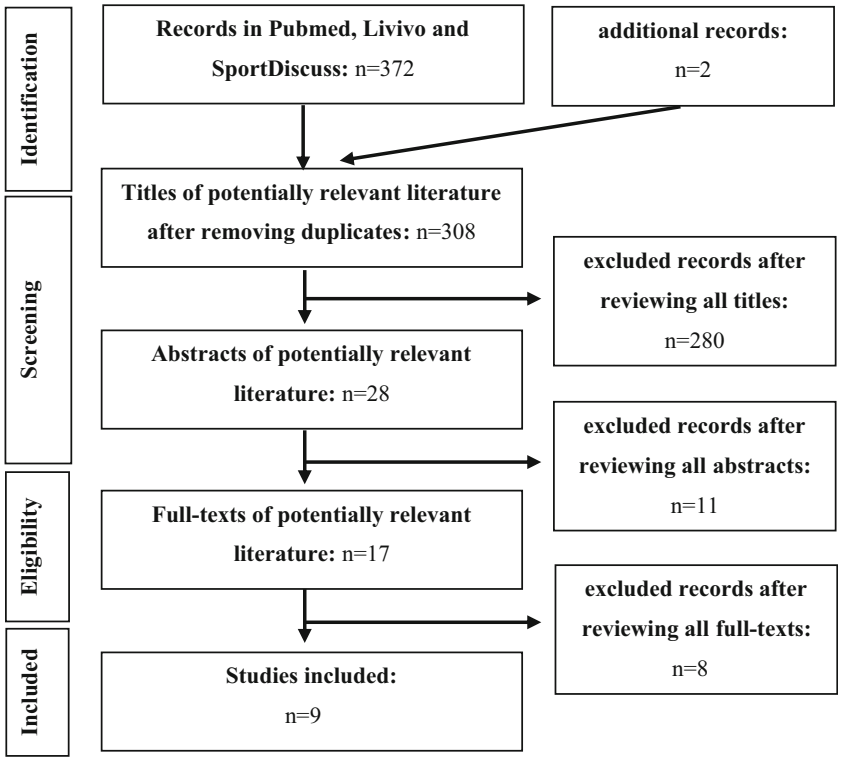

Fig. 1 Flow chart of literature search and study selection based on PRISMA 2009 flow diagram [39]

(RCTs) [40, 41, 43, 44, 46–48] including two cross-over design studies [40, 48]. One study was a double-arm non-randomized study [45], and one study was single-armed [42]. Out of all seven RCTs, five studies investigated a combined WBV training and physical therapy or passive muscle stretching in comparison to physical therapy or muscle stretching without WBV [40, 41, 43, 44, 46]. One study compared WBV with a placebo intervention [48] and another study investigated WBV in comparison to a group not receiving any intervention [47]. One study included two intervention groups receiving WBV [45]. Except for one of all nine studies [42], all trials were prospective studies. Two studies conducted additional follow-up analysis [42, 45]; however, this data is not presented in this review.

In total, 274 study participants (aged 5 to 18), all diagnosed with a specific congenital disorder, were included. Most frequently, studies included children diagnosed with cerebral palsy [40, 43, 44, 46–48]. In addition, single studies investigated children with Down syndrome [41], spina bifida [42] as well as Duchenne muscular dystrophy and spinal muscular atrophy [45].

Intervention designs and WBV protocols

The intervention designs and WBV protocols demonstrated a wide heterogeneity across studies. Intervention designs varied in overall duration (6 weeks [40] to 6 months [41, 42, 47, 48]) and in training frequency (3×/week [41, 44, 46] to 10×/week [42, 45]). Session durations ranged from 40 [40] to 80 min [41] for combined interventions (including 10 [40] to 20 min [41] of WBV training) and from 10 [48] to 15 min [42, 45, 47] for interventions based solely on WBV. In terms of WBV protocol, side-alternating vibration [41–47] was used more frequently than vertical vibration [40, 48] and interval training (3–6 series of 1–3 min WBV and 3 min rest [42–47] or 10 series of 30–60 s WBV and 60 s rest [40, 41]) was applied more frequently than single bouts of WBV (bouts of 10 min) [48]. Moreover, the applied vibration frequencies mostly ranged from 12 to 30 Hz ($n = 6$) [40, 41, 43, 44, 47, 48]. Three studies used lower frequencies starting from 5 Hz [42, 46] or 10 Hz [45]. Regarding amplitude, peak-to-peak displacements were mainly found between 2 mm [44, 43, 47]

Table 1 Search terms used to identify relevant studies

Participants	pediatr* OR child* OR adolescent AND
	disabilities OR novel entities OR cerebral palsy OR Diplegia OR Down Syndrome OR Down's Syndrome OR Osteogenesis Imperfecta OR adolescent idiopathic scoliosis OR Duchenne muscular dystrophy OR muscular dystrophy OR Spina Bifida OR Spinal muscular atrophy OR muscular atrophy OR ataxia OR fragile X syndrome OR osteopenia OR osteoporosis OR cancer OR oncology AND
Intervention	vibration OR vibration therapy OR whole-body vibration OR whole body vibration OR whole body vibration therapy OR WBV OR mechanical loading

Table 2 Detailed description and statistical results of all included WBV intervention studies for children with disabilities

Authors	Study design	Subjects	Demographic and medical data	Setting	Intervention protocol	WBV intervention	Results[a]
Tupimai et al. (2016) [40]	Prospective, double-arm (PG/PG), cross-over, randomized controlled trial	IG and CG: children and adolescents with cerebral palsy, $n = 12$	IG and CG: Age: 10.58 ± 2.35 years Sex (M/F): not mentioned Height: 127.25 ± 9.72 cm Weight: 26.48 ± 7.95 kg Pathology information: MAS Score ≥ 1	At school, supervised	IG: 6 weeks, 5×/week, 40 min/session, passive muscle stretching (30 min) and WBV (10 min) CG: 6 weeks, 5×/week, 40 min/session, passive muscle stretching	Device: AIKO vibrator Protocol: 10 × 60 s, 60 s rest Vibration form: vertical Frequency: 20 Hz Amplitude: not mentioned Peak acceleration: not mentioned Progression: no progression Support device: holding onto a handle-bar was allowed Footwear: not mentioned Position: standing with equal weight-bearing on both feet, legs shoulder-width apart Exercises: none	IG (changes during intervention): Balance control: balance (PBS) ↑ IG and CG (changes during intervention): Functional mobility: FTSST ↑ IG vs. CG (changes during intervention): Functional mobility: FTSST → Balance control: balance (PBS) →
Eid et al. (2015) [41]	Prospective, double-arm (PG/PG), randomized controlled trial	IG: children and adolescents with Down syndrome, $n = 15$ CG: children and adolescents with Down syndrome, $n = 15$	IG: Age: 8.93 ± 0.7 years Sex (M/F): 8/7 Height: 118.0 ± 2.27 cm Weight: 29.20 ± 3.40 kg CG: Age: 9.26 ± 0.79 years Sex (M/F): 9/6 Height: 119.06 ± 2.81 cm Weight: 29.53 ± 3.22 kg IG and CG: Pathology information: Down syndrome with mild hypotonia, independent standing and walking, balance problems	Supervised by therapist	IG: 6 months, 3×/week, 75–80 min/session, physical therapy (60 min) and WBV (15–20 min) CG: 6 months, 3×/week, 60 min/session, physical therapy	Device: VibraFlex Home Edition II Protocol: 10 × 30–60 s; 60 s rest Vibration form: side-alternating Frequency: 25–30 Hz Amplitude: 2 mm Peak acceleration: not mentioned Progression: in frequency and duration, every 8 weeks Support device: not mentioned Footwear: gymnastic shoes Position: standing, knees bent about 30°, equal weight-bearing on both feet Exercises: none	IG and CG (changes during intervention): Balance control: stability ↑ Muscle mass/strength: strength of knee flexors ↑, strength of knee extensors ↑ IG vs. CG (changes during intervention): Balance control: stability ↑ Muscle mass/strength: strength of knee flexors ↑, strength of knee extensors ↑
Stark et al. (2015) [42]	Retrospective, single-arm (PG)	IG: children and adolescents with spina bifida, $n = 60$	Age: 8.71 ± 4.7 years Sex (M/F): 28/32 Height: 119.0 ± 21.65 cm Weight: 26.69 ± 17.37 kg Pathology information: Hoffer criteria (community walker, 10.3%; household walker, 36.2%; exercise walker, 41.4%; non-walker, 12.1%)	Inpatient supervised and non-supervised at home	6 months, 10×/week, 15 min/session, WBV, two short inpatient stays with intensive therapeutic program	Device: System Galileo® Protocol: 3 × 3 min, 3 min rest Vibration form: side-alternating Frequency: 5–27 Hz Amplitude: 0 ± 3.9 mm Peak acceleration: not mentioned Progression: not mentioned Support device: lying on a tilt-table if necessary; tilt angle 0–90° according to weight-bearing ability Footwear: not mentioned Position: standing Exercises: none	IG (changes during intervention): Walking ability/gait: speed ↑, path length ↑
El-Shamy (2014) [43]	Prospective, double-arm (PG/PG), randomized controlled trial	IG: children with cerebral palsy, $n = 15$ CG: children with cerebral palsy, $n = 15$	IG: Age: 9.66 ± 1.2 years Sex (M/F): 12/3 Height: 1.34 ± 0.51 m Weight: 32.23 ± 0.45 kg	Supervised by physiotherapist	IG: 3 months, 5×/week, 75 min/session, physical therapy (60 min)and WBV (15 min) CG: 3 months, 5×/week, 60 min/session, physical therapy	Device: VibraFlex Home Edition II Protocol: 3 × 3 min, 3 min rest Vibration form: side-alternating Frequency: 12–18 Hz Amplitude: 2–4 mm peak-to-peak displacement Peak acceleration: 2.6 g (targeted)	IG vs. CG (changes during intervention): Muscle mass/strength: strength of knee extensors ↑ Balance control: stability ↑

Table 2 (continued)

Authors	Study design	Subjects	Demographic and medical data	Setting	Intervention protocol	WBV intervention	Results[a]
			Pathology information: GMFCS level I ($n = 7$), GMFCS level II ($n = 8$) CG: Age: 9.93 ± 1.1 years Sex (M/F): 11/4 Height: 1.34 ± 0.40 m Weight: 32.43 ± 0.70 kg Pathology information: GMFCS level 1 ($n = 6$), GMFCS level II ($n = 9$)			Progression: in frequency and amplitude, individually Support device: not mentioned Footwear: not mentioned Position: standing, hip and knees bent 10° to 45° Exercises: shifting weight, alternation of knee flexion, trunk rotation	
Ibrahim et al. (2014) [44]	Prospective, double-arm (PG/PG), randomized controlled trial	IG: children with cerebral palsy, $n = 15$ CG: children with cerebral palsy, $n = 15$	IG and CG: Age: 9.63 ± 1.41 years Sex (M/F): not mentioned Height: not mentioned Weight: not mentioned Pathology information: MAS score 1 and 2	Supervised	IG: 12 weeks, 3×/week, 75 min/session, physical therapy (60 min) and WBV (15 min) CG: 12 weeks, 3×/week, 60 min/session, physical therapy	Device: vibration platform Protocol: 3 × 3 min, 3 min rest Vibration form: side-alternating Frequency: 12–18 Hz Amplitude: 2–6 mm peak-to-peak displacement Peak acceleration: not mentioned Progression: in frequency and amplitude Support device: supervising person could stabilize children if necessary Footwear: gymnastic shoes Position: standing, knees slightly bent Exercises: none	IG (changes during intervention): Muscle mass/strength: strength of knee extensors ↑ Walking ability/gait: 6MWT ↑ IG and CG (changes during intervention): Functional mobility: TUG →
Vry et al. (2014) [45]	Prospective, double-arm (PG/PG) non-randomized trial	IG[1]: children and adolescents with Duchenne muscular dystrophy, $n = 14$ IG[2]: children and adolescents with spinal muscular atrophy, $n = 8$	IG[1]: Age: ± 8.8 years Sex (M/F): 14/0 Height: not mentioned Weight: not mentioned IG[2]: Age: ± 9.9 years Sex (M/F): 3/5 Height: not mentioned Weight: not mentioned IG[1] and IG[2]: Age: 5.7–16.2 years Pathology information: ambulatory, independent standing and 10 m walking, ability to perform specific exercises during training	Inpatient supervised and non-supervised at home	IG[1] and IG[2]: 8 weeks, 5×/week, 2×/day, 15 min/session, WBV	Device: Galileo[a] MedM Protocol: 3 × 3 min, 3 min rest Vibration form: side-alternating Frequency: 10–24 Hz Amplitude: 4 mm Peak acceleration: not mentioned Progression: in frequency every 4 weeks Support device: holding onto wall bars was allowed Footwear: not mentioned Position: standing Exercises: mild squatting, stretching the gastrocnemius muscle, alternating, slight weight shift	IG[1] and IG[2] (changes during intervention): Walking ability/gait: speed → Functional mobility: climbing 4 stairs →, rising from a supine position → Muscle mass/strength: strength of hip flexors →, strength of hip extensors →, strength of hip abductors →, strength of knee flexors →, strength of knee extensors →, strength of ankle dorsiflexors →, strength of ankle plantarflexors →, strength of lower limb → Flexibility/range of motion: AROM of ankle → IG[1] (changes during intervention): Walking ability/gait: 6MWT → IG[2] (changes during intervention): Walking ability/gait: 6MWT ↑
Lee & Chon (2013) [46]	Prospective, double-arm (PG/PG), randomized controlled trial	IG: children and adolescents with cerebral palsy, $n = 15$	IG: Age: 10.00 ± 2.26 years Sex (M/F): 6/9 Height: 130.59 ± 12.04 cm Weight: 27.91 ± 8.14 kg	Supervised by physiotherapist	IG: 8 weeks, 3×/week, 60 min/session, physical therapy and WBV	Device: Galileo system Protocol: 6 × 3 min, 3 min rest Vibration form: side-alternating Frequency: 5–25 Hz Amplitude: 1–9 mm	IG (changes during intervention): Walking ability/gait: speed ↑, stride length ↑, cadence ↑ Muscle mass/strength: muscle thickness of tibialis anterior ↑,

Table 2 (continued)

Authors	Study design	Subjects	Demographic and medical data	Setting	Intervention protocol	WBV intervention	Results[a]
		CG: children and adolescents with cerebral palsy, $n = 15$	Pathology information: GMFM score 78.40 ± 2.82 CG: Age: 9.66 ± 2.58 years Sex (M/F): 9/6 Height: 128.26 ± 13.77 cm Weight: 29.17 ± 7.27 kg Pathology information: 79.53 ± 4.19 IG and CG: Pathology information: walking without walking aids, inability to rise from a chair		CG: 8 weeks, 3×/week, 30 min/session physical therapy	Peak acceleration: not mentioned Progression: in frequency and amplitude, individually Support device: holding onto handlebars if necessary Footwear: barefoot Position: squat position (30–100° knee flexion) with heels being slightly off the ground Exercises: none	muscle thickness of soleus ↑, muscle thickness of gastrocnemius → Flexibility/range of motion: ankle angle ↑, hip angle →, knee angle → IG vs. CG (changes during intervention): Walking ability/gait: speed ↑, stride length ↑, cadence ↑ Muscle mass/strength: muscle thickness of tibialis anterior ↑, muscle thickness of soleus ↑, muscle thickness of gastrocnemius → Flexibility/range of motion: ankle angle ↑, hip angle →, knee angle →
Ruck et al. (2010) [47]	Prospective, double-arm (PG/PG), randomized controlled trial	IG: children with cerebral palsy, $n = 10$ CG: children with cerebral palsy, $n = 10$	IG: Age: ± 8.3 years (6.6–9.6 years) Sex (M/F): 8/2 Height: 118 (109–131) cm Weight: 21.8 (16.7–25.1) kg Pathology information: GMFCS level 1 ($n = 1$), GMFCS level 2 ($n = 5$), GMFCS level 3 ($n = 4$) CG: Age: ± 8.1 years (7.3–10.6 years) Sex (M/F): 6/4 Height: 121 (110–132) cm Weight: 22.3 (17.3–26.0) kg Pathology information: GMFCS level 1 ($n = 1$), GMFCS level 2 ($n = 4$), GMFCS level 3 ($n = 5$)	At school, supervised by physiotherapist	IG: 6 months; 5×/week, 15 min/session, WBV CG: no intervention	Device: Vibraflex Home Edition II® Protocol: 3 × 3 min, 3 min rest Vibration form: side-alternating Frequency: 12–18 Hz Amplitude: 2–4 mm peak-to-peak displacement Peak acceleration: 2.6 g (targeted) Progression: in frequency and amplitude every 2 sessions Support device: lying on a tilt table initially and continuously if necessary; attached with straps at pelvis and knees; initial tilt table angle 35° with continuous increase of angle if possible; use of walker if necessary Footwear: shoes Position: standing, hip/knee flexion of 10–45° Exercises: weight shifting, rotation of the trunk, flexion/extension of knees	IG vs. CG (changes during intervention): Walking ability/gait: speed ↑
Wren et al. (2010) [48]	Prospective, double-arm (PG/PG), cross-over, randomized controlled trial	IG and CG: children with cerebral palsy, $n = 31$	IG and CG: Age: 9.4 ± 1.4 years Sex (M/F): 18/13 Height: 127 ± 10 cm Weight: 29 ± 9 kg Pathology information: GMFCS level 1 ($n = 10$), GMFCS level 2 ($n = 4$), GMFCS level 3 ($n = 15$), GMFCS level 4 ($n = 2$)	At home, non-supervised	IG[b]: 6 months, 7×/week, 10 min/session, WBV CG[c]: 6 months, 7×/week, 10 min/session, placebo fintervention	Device: Juvent Medical Inc. Protocol:1 × 10min Vibration form: vertical Frequency: 30 Hz Amplitude: not mentioned Peak acceleration: 0.3 g Progression: no progression Support device: ankle–foot orthoses if necessary	IG (changes during intervention): Muscle mass/strength: concentric strength of calf muscle ↑ IG and CG (changes during intervention): Muscle mass/strength: muscle area of calf muscle →, eccentric strength of calf muscle ↑ IG vs. CG (changes during intervention):

Table 2 (continued)

Authors	Study design	Subjects	Demographic and medical data	Setting	Intervention protocol	WBV intervention	Results[a]
						Footwear: ankle–foot orthoses if necessary Position: standing Exercises: none	Muscle mass/strength: muscle area of calf muscle →, concentric strength of calf muscle →, eccentric strength of calf muscle →

↑, significant improvement; →, no significant changes; %, percentage; 6MWT, 6 min walk test; AROM, active range of motion; CG, control group; FTSST, five-times-sit-to-stand test; g, (fraction of) gravitational acceleration; GMFCS, Gross Motor Function Classification System; GMFM, Gross Motor Function Measure; HG, healthy group; IG, intervention group; IG vs. CG, intervention group in comparison to control group; MAS Score, Modified Ashworth Scale Score; MECP2, gene encoding methyl CpG binding protein 2; *n*, sample size; PBS, pediatric balance score; PG, patient group; TUG, Timed-Up-and-Go test; WBV, whole-body vibration

[a] This table solely presents results of relevant parameters according to the aim of this review including muscle mass/strength, flexibility/joint range of motion, functional mobility, balance control, gait/walking ability. Follow-up results are not presented in this review

[b] Results refer to both vibration periods performed during this cross-over trial

[c] Results refer to both standing (placebo) periods performed during this cross-over trial

Brand names: Galileo®, Novotec Medical, Pforzheim, Germany; Power Plate® Pro5, Power Plate, Netherlands; AIKO vibrator, ETF-001CG, Thailand; VibraFlex Home Edition II, Orthometrix Inc., White Plains, NY; Juvent 1000 Dynamic Motion Device, Juvent Medical, Inc. UK

and 8 mm [45] for side-alternating vibration platforms. For vertical vibration platforms, no amplitude was reported. Peak acceleration was indicated as 0.3 g [48] and 2.6 g (targeted) [43, 47], respectively. To allow for training progression, frequency and amplitude or duration were increased in most studies ($n = 6$) [41, 43, 44–47] either individually according to the participants' response to WBV [43, 46] or after a defined time period (i.e., every 4 or 8 weeks) [41, 45, 47]. Except for one study [48], all interventions were fully or partially supervised and additional home-based WBV training was requested in two studies [42, 45]. External support [42, 47] and stabilization [40, 44, 45] were allowed during WBV if needed. WBV was performed either with shoes [41, 44, 47] or barefoot [46]. Participants were allowed to wear foot orthosis in one study [48]. Moreover, study participants were either asked to stand on the vibration platform with their knees bent to a certain degree [41, 44, 46] or to perform exercises such as shifting weight, squatting, trunk rotation, or stretching the gastrocnemius [43, 45, 47].

Safety and compliance

One of five studies analyzing adverse events did not report any [43]. Two studies described itching and redness of the extremities (feet/ankle area) [44, 47], and one reported muscle weakness, soreness, and cramps [45]. One study revealed that 11 out of 937 training sessions had to be interrupted because of fatigue or pain (i.e., stomach ache, headache, or back pain) [47]. Moreover, Vry et al. (2014) reported that two children dropped out because of a creatine kinase increase of > 100%, which was a defined stop criterion of the study protocol, and one child dropped out because of a talus fracture that had been detected during the study period (not clearly related to the WBV intervention) [45]. Stark et al. (2015) described that 12 out of 60 children mentioned orthopedic problems regarding increased contractures of the hips or knees, three participants reported spontaneous bladder emptying, and one child each described the development of a symptomatic tethered cord, a shunt revision, and a femur fracture while standing in a standing frame (not part of the study program) [42]. Compliance with WBV was relatively high with three studies documenting adherence rates of 78–94% [41, 44, 47]. One study reported a wide range of compliance (24–99%) [48].

Efficiency

Muscle strength and mass

Regarding the impact of WBV on muscle parameters, significant beneficial effects on muscle strength of knee flexors [41], knee extensors [41, 43, 44], and calf muscle [48], as well

as the thickness of tibialis anterior and soleus muscle [46] were shown. Only a few studies were not able to detect significant positive effects of WBV on either muscle strength [45] or single muscles (muscle thickness of gastrocnemius [46] and muscle area of calf muscle [48]). Additionally, the positive effects found by the intervention group did not always vary significantly to those found by the control group when being compared to a placebo intervention [48]. While muscle strength was investigated using a handheld/isokinetic dynamometer [41, 43, 44, 45, 48] or the modified Medical Research Council scale, muscle mass was examined using ultrasonography [46] or CT/QCT [48].

Joint range of motion

Mixed results were found for range of motion. While significant positive effects were observed for ankle angle measured with a gait analysis system [46], no effects were found on active ankle range of motion measured with a goniometer [45]. No significance was observed for hip and knee angle [46].

Balance control

WBV showed significant beneficial effects on balance control, assessed in three studies [40, 41, 43]. Balance/pressure distribution platforms [41, 43], as well as the pediatric balance scale (PBS) [40], were applied to examine balance control.

Gait and walking ability

Significant positive effects of WBV were observed regarding walking distance [44], assessed using the 6 min walk test, and regarding gait economy (speed, stride length, cadence) [42, 46, 47], determined using the 10 m walk test and/or a gait analysis system. Solely, Vry et al. (2014) were not able to prove significant positive effects of WBV on gait speed [45].

Functional mobility

In terms of functional mobility, results are contradictory across studies. While significant positive effects of WBV were detected assessed with the five-times-sit-to-stand test [40], no significant effects were found using the Timed-Up-and-Go test (TUG) [44], functional tests measuring the time to climb four stairs [45], as well as the time to rise from a supine position [45].

Discussion

Since the impact of WBV on lower limb function has not yet been investigated in children with cancer but all the more in children with disabilities, the main objective of the present review was to analyze WBV intervention studies in children with disabilities to establish whether relevant findings may be transferred into the pediatric oncology setting. In this respect, the present review demonstrates WBV to be a safe and highly compliant approach in cohorts of children with disabilities which is effective for improving parameters which may be relevant for the pediatric cancer population as well. The present findings indicate that the largest effects of WBV seem to be observed in lower extremity muscle strength and mass, balance control, gait, and walking ability. For lower extremity joint range of motion and functional mobility, the effect was limited.

Because of the large number of randomized controlled trials ($n = 7$) found in this review of nine studies, the authors ranked the overall level of evidence as level 2 according to the Levels of Evidence of the Oxford Centre for Evidence-Based Medicine (OCEBM 2011) [49]. However, most studies were conducted with patients suffering from cerebral palsy and reported the effects on muscle mass and strength or gait and walking ability. Consequently, best evidence exists for these conditions.

Our findings are in line with previous reviews summarizing the effects of WBV in children (and adults) with cerebral palsy [33, 34] and children with disabilities [32]. Previous reviews present safety [32] as well as positive impacts of WBV on gait and walking ability [32–34], muscle strength and mass [32, 33] and coordination (balance) [33]. However, recent reviews did not consider range of motion as part of their analysis. Regarding functional mobility, as this term includes a wide range of movements such as walking, climbing stairs, or turning, various parameters and instruments were used in the measurement of functional mobility which leads to difficulties in interpreting data.

In contrast to previous review papers, our review highlights the efficiency of WBV on functional outcomes that may also be relevant for children with cancer. Adequate functional performance is an essential condition for activities of daily living (ADL) [50] and active lifestyles. Improving lower limb performance is consequently a key importance during rehabilitation in pediatrics [46, 47]. However, many children with cancer lack these important performance skills. Functional deficits often emerge during medical treatment of pediatric cancer which can last for several months and may request prolonged hospital stays. During this period, many patients are immobile and very inactive [2] due to, i.e., reduced health conditions leading to activity restrictions and bed rest. A survey carried out among 130 pediatric cancer patients (mean age of ~ 12 years, diagnoses—leukemia, bone tumor, lymphoma, brain tumor, other solid tumors) demonstrated that 50% of patients during medical treatment do not leave their bed for more than 1 h per day while being admitted to hospital [1]. Moreover, many children with cancer remain inactive even after

cessation of medical treatment [6]. As such, applying WBV to children with cancer could be of benefit in order to set optimal functional conditions, which may allow the children to be physically active. It must be noted, however, that it seems to be difficult for children to automatically convert functional improvements, achieved through WBV, into complex movement patterns, as demonstrated in the poor results regarding functional mobility. Thus, WBV seems to mainly serve as a therapy method specifically designed to counteract functional impairments. This indicates that WBV should be applied as a complementary adjunct to exercise therapy programs, pursuing the overall objective to offer holistic care and to promote an active lifestyle. Integrating WBV into existing programs or applying additional WBV training to patients does not seem to be too burdensome for children. As demonstrated in the results, WBV is a low-time-consuming (10 to 20 min) training method to enhance lower limb function and, moreover, is low fatiguing [27] as WBV does not evoke cardiovascular stress [30].

With compliance rates averagely ranging from 74 to 94% among children with disabilities, WBV training is in line with the compliance rates of traditional exercise interventions in pediatric oncology (67–98%) [51] and, moreover, exceeds the compliance detected in hospital-based programs (59–85%) [52]. Also, WBV appears to be a safe training method in pediatric populations as only minor adverse events were reported, mainly described as itching and reddening [44, 47]. Itching and reddening are well-known reactions to WBV [44], possibly caused by vasodilation of arteries [30] and appeared to have occurred mainly in WBV interventions which applied longer bouts (3 min) of side-alternating and low-frequency (12–20 Hz) vibrations [44, 47]. Even though there is a relatively high probability that itching and reddening might occur, these data support the idea of investigating the effect of WBV in the pediatric oncology population.

To implement initial WBV intervention studies into the pediatric oncology setting, respecting existing WBV protocols among children with disabilities might be helpful, always taking into consideration the children's individual treatment factors, overall health status, and the common precautions for physical activity and exercise in pediatric oncology [53, 54]. With this objective, the beneficial WBV protocols among children with disabilities are summarized in Table 3, including the relevant information that needs to be specified when describing WBV interventions [26]. Moreover, an initial outcome-orientated analysis was undertaken aiming to improve the understanding of WBV in children with disabilities. As such, effective protocols for improving muscle strength and mass, as well as walking ability and gait, appeared to be quite similar. However, the protocols dealing with improving balance control differed to the above mentioned. These differences mainly concern vibration type, duration, and frequency as shown in Table 4. More precise recommendations, however, that would describe optimal methods for improving specific outcomes in children with disabilities cannot yet be provided due to sparse and partly ambiguous data.

By applying WBV to patients with pediatric cancer, it must be taken into account that the pathology and mechanisms differ to those of congenital disabilities. This could potentially also allow for WBV to express different effects and/or target other mechanisms and structures in our population. To date, the understanding of the precise impact of WBV in different populations requires further clarification. However, positive results of WBV intervention studies could also already be demonstrated in various populations including adult patients with different diseases as well as healthy subjects and older adults [30, 55, 56]. Providing more background information for children with cancer, offering supervised WBV seems of high importance, especially during anticancer treatment as (1) the medical situation may change abruptly and as (2) supervised programs in pediatric oncology show higher compliance in general [51]. Moreover, as experience in adult oncology has shown, neuropathic patients should avoid exercising barefoot as adequate footwear (shoes with a thin sole, i.e., gymnastic shoes) can help to reduce friction and blistering [31]. Importantly, pediatric cancer-specific contraindications of WBV still need to be determined. Common precautions that typically need to be considered when prescribing physical activity or exercise include, i.e., anemia, thrombocytopenia, and neutropenia [53].

Table 3 Preliminary recommendations for WBV in pediatric oncology extracted from studies with children with disabilities

1.	WBV can be administered very frequently, even up to twice a day
2.	Side-alternating vibration should be used preferably, although vertical vibration can be applied
3.	Interval training is recommended, although single bouts of vibration lasting several minutes are possible
4.	Vibration frequencies should range between 12 and 30 Hz
5.	Peak-to-peak displacements up to 8 mm for side-alternating platforms might be used
6.	Progression may be achieved by increasing amplitude, frequency, and/or duration
7.	Children should be given the possibility to hold onto something in case of loss of balance
8.	Children stand on the platform with knees bent to a certain degree and/or performing exercises
9.	Children can exercise either with or without shoes
10.	WBV training should be fully or partly supervised; training at home is feasible

Table 4 Summary of the main differences and similarities in effective WBV protocols for improving muscle strength/mass, walking ability/gait, and balance control in children with disabilities

Effective WBV protocols for improving muscle strength/mass and walking ability/gait in children with disabilities
• Interval training delivered on side-alternating platforms generally applying three (to six) bouts of about 3 min vibrations seem to be particularly beneficial
• Low vibration frequencies were generally applied even starting from 5 Hz [42, 46]
• An increase in vibration frequencies up to 30 Hz for muscle strength/mass [41, 48] and up to 27 Hz for walking ability/gait [42] was made during the course of interventions
Effective WBV protocols for improving balance control in children with disabilities
• Interval training on vertical ($n = 1$) and side-alternating platforms ($n = 2$) was applied
• Interval training comprised shorter vibration bouts lasting from about 30 to 60 s which were repeated more frequently [40, 41]
• Higher vibration frequencies were applied, even starting at 20 Hz [40] or 25 Hz [41] in two of three studies

Our review is of relevance for pediatric oncology as it provides first hints for WBV being a possible adjunct to the conventional exercise therapy regimes. The review's focus was on establishing whether there is evidence that WBV may be beneficial to improve lower limb function in pediatric cancer populations. However, the extent of the improvements is still unclear and needs to be assessed in future research. Moreover, within the reviewed studies, limitations exist in terms of study designs, WBV protocols and study cohorts. Regarding study designs, there are considerable methodological differences manifesting in wide ranges of intervention duration and training frequency as well as in different realizations of training (i.e., combined interventions such as physiotherapy and WBV vs. interventions solely based on WBV, standing vs. performing exercises on the vibration platform, different types of comparisons such as standard care or placebo), which makes comparison between studies and the interpretation of the effects of WBV difficult. Regarding WBV protocols, protocols are characterized by large heterogeneity and missing data. Regarding study cohorts, the included trials comprise small sample sizes with patients of wide age ranges. Demographic data of study participants were not always described sufficiently. Furthermore, although a systematic literature search was conducted, not all relevant studies might have been identified.

In conclusion, WBV interventions in children with various disabilities were shown to be safe and at the same time present a highly compliant training method that can positively impact physical function especially in terms of lower extremity muscle strength and mass, balance control as well as gait and walking ability. As such, WBV seems to be feasible and, moreover, effective for improving parameters that may be relevant to the pediatric cancer population. Efforts are needed to conduct first WBV interventions in the pediatric cancer population proving the effects.

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Compliance with ethical standards

Conflicts of interest The authors declare that they have no competing interests. Moreover, the authors have no final relationships to declare. The authors allow the journal to review the used data if required.

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