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Effectiveness of assisted standing on bone mineral density in children with cerebral palsy. A systematic review

Fernando Valenzuela-Aedo[a], Camila Reyes-Moreno[b], Teresa Balboa-Castillo[c]

ABSTRACT

Cerebral palsy is associated with complications such as low bone mineral density, which is more severe in patients with greater motor involvement. Assisted standing helps to prevent or delay this complication; however, its effect is controversial because the type of stander, the type of standing (dynamic or static), and its dosage are not clear.

The objective of this study was to determine the effectiveness of assisted standing on bone mineral density in children with cerebral palsy. A systematic review was carried out in compliance with the PRISMA guidelines, using 5 databases. The results were presented using tables, a risk of bias analysis, and a narrative synthesis. Four studies met the inclusion criteria. Assisted standing generates positive changes in bone mineral density, but further research is required, with studies that have greater methodological rigor, longer follow-up periods, and a larger number of patients.

Keywords: *cerebral palsy; bone density; standing; physical medicine and rehabilitation; disability assessment.*

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[a] Department of Rehabilitation Science, School of Medicine, Universidad de La Frontera, Temuco, Chile; [b] Student of the Master's Program in ABA Intervention Assessment in Autism Spectrum Disorder, Universidad Autónoma de Chile, Santiago, Chile; [c] Department of Public Health, Research Center for Nutrition and Cardiovascular Epidemiology (Centro de Investigación en Epidemiología Cardiovascular y Nutricional, EPICYN), School of Medicine, Universidad de La Frontera, Temuco, Chile.

Correspondence to *Fernando Valenzuela-Aedo: fernando.valenzuela@ufrontera.cl*

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INTRODUCTION

Cerebral palsy (CP) is the most common form of infant disability, with a prevalence of 1.5 to 3.8 per 1000 live births, and an incidence of 12 to 64 preterm births in 1 year.[1] Many children with cerebral palsy will develop a decreased range of motion and alterations in strength and endurance, which lead to complications, such as contractures, fractures, scoliosis, hip dislocation, talipes equinovarus, among others.[2] These complications increase in patients with greater motor involvement, which is classified according to the Gross Motor Function Classification System (GMFCS).[3] Studies show that children who walk less than 2 hours a day are more likely to experience these complications, which directly affect their quality of life and also translate into a high cost for families and health systems.[4,5] It has been proven that the higher the GMFCS level, the higher the degree of osteopenia.[6]

The bone remodeling process is activated and controlled by mechanical forces, apoptosis, hormones, cytokines, and local factors.[7] The transformation of mechanical stress into biochemical signals is mediated by stretching and loading.[8]

Children who walk little lack exposure to mechanical forces to initiate and maintain the remodeling process.[9] Supplements, such as calcium,[10] and drugs, such as bisphosphonates,[11] are commonly used as therapy for the management of bone mineral density (BMD) loss. As a non-drug therapy, assisted standing delivers loads that may favor the intrinsic capacity of the bone to adapt its morphology and avoid its degradation due to disuse.[12]

There is much controversy about the effectiveness of assisted standing on BMD in children with CP. Protocols and different types of standers have been proposed considering dynamic and static standing systems, standing associated with therapeutic exercises, and different time dosage options. In addition, there is little evidence available in systematic reviews, including experimental designs that summarize available information in terms of dosage, method or schedule of standing, and its effects on BMD in children with CP. Therefore, the objective of this study was to determine the effectiveness of assisted standing on BMD in children with CP.

METHODS

This systematic review was based on the recommendations of the Cochrane Guidelines for Systematic Reviews and was written in accordance with the PRISMA guidelines.[13] It was registered and approved in PROSPERO (CRD420223653379).

Review question

What is the effectiveness of assisted standing on BMD in children with CP?

Eligibility criteria

Randomized clinical trials (RCTs) and quasi-experiments in children younger than 18 years diagnosed with CP, who were classified according to GMFCS level IV or V and who used any method of dynamic or static assisted standing were included. Studies that described in detail the intervention to increase and/or maintain BMD and studies that included BMD as one of their outcome measures were also considered.

Duplicate publications or articles with missing data, studies that did not have a Digital Object Identifier (DOI), and studies in which at least 1 description was not found in order to classify the GMFCS level of participants were excluded. In addition, studies that included patients with previous lower extremity fracture, severe spinal deformity, hip dislocation, spinal or lower extremity surgery or nerve block in the previous 3 months, or uncontrolled epilepsy were excluded.

Bibliographic search

A systematic bibliographic search was performed using 5 biomedical databases from 2003 onwards: MEDLINE (https://pubmed.ncbi.nlm.nih.gov/), EMBASE (https://www.embase.com), LILACS (https://lilacs.bvsalud.org/es), WOS (https://www.webofscience.com), and SciELO (https://scielo.org/es/). The gray literature search was done using OPENGRAY (https://opengrey.eu/), GOOGLE SCHOLAR (https://scholar.google.com/), and unpublished theses. Articles included in other systematic reviews were also used in the search. The search included free terms, key terms, MeSH terms, and Emtree terms; there were no language restrictions; and the patient, intervention, comparison, outcome (PICO) mnemotechnical structure was used. For patient, intervention, and outcome terms, the Boolean operator "OR" was used. For the final search phrase, the Boolean operator "AND" was used (*Table 1*). The last search was performed on March 20th, 2023.

Study selection

Collected data were entered and analyzed using the RAYYAN© 2022 software (https://www.rayyan.ai/); duplicates were removed. Two blinded reviewers screened the titles and abstracts of potentially eligible studies, and eligibility criteria were applied. The full text of eligible articles was read; controversial articles were considered by the reviewers, who defined their inclusion or exclusion.

Data extraction and analysis

Data extraction and management of selected primary studies were performed independently by a primary reviewer. A secondary reviewer resolved any doubts that arose during the data extraction process. A narrative synthesis was done of the findings from included studies according to the study type, the study objective, the characteristics of participants, the variables measured according to BMD, the intervention and type of stander used, and the main results. Using the available data, we estimated the percentage change in BMD pre- and post-intervention for the 2 quasi-experiments and the percentage change in BMD in the intervention group for the RCTs using the Review Manager (RevMan) software v.5.4.1 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration).

Assessment of study quality and publication bias

Two reviewers independently assessed the risk of bias of included studies. The RoB 2 tool and the ROBINS 1 tool were used to assess the risk of bias of clinical trials[14] and quasi-experiments, respectively.[15]

RESULTS

A. Qualitative synthesis

1. Description of studies

The total number of studies identified after conducting the search is shown in *Figure 1*. After screening them, 4 articles were selected for qualitative synthesis: 2 clinical trials and 2 quasi-experiments.

A summary of the study characteristics is shown in *Table 2*. The 4 studies included in the analysis were published in English. The RCTs were conducted in 2 countries (England and South Korea), while the quasi-experiments were carried out in the United States. The 4 studies included a total of 71 children aged 2.25 to 12 years classified as GMFCS level IV and V. All did assisted standing (in 1 of its modalities); dynamic in 2 studies[16,17] and static in the other 2,[18,19] differentiated by the type of stander: supine or prone. The dosage of standing was detailed in each of the included studies by hours or minutes per day and days per week, and follow-up ranged from 6 to 15 months.

Table 1. Terms included in the search strategy

PICO		MeSH terms	Free terms
P	Patient	*Cerebral palsy*	*Cerebral palsy* *Children*
I	Intervention	*Standing position* *Supine position* *Prone position*	*Standing* *Stander* *Prone table* *Whole body* *Vibration* *Tilt table* *Standing frame** *Standing support* *Assisted standing*
C	Comparison	…	…
O	Outcome	*Bone density*	*Bone mineral density*

MeSH: *Medical Subject Headings. Final search phrase ((("Cerebral Palsy" [Mesh]) OR ("cerebral palsy children")) AND ((((((((((("Standing Position" [Mesh]) OR ("STANDING")) OR ("stander")) OR ("prone table")) OR ("Prone Position" [Mesh])) OR ("Supine Position"[Mesh])) OR ("whole body vibration")) OR ("tilt table")) OR ("standing frame*")) OR ("standing support")) OR ("assisted standing"))) AND (("Bone Density"[Mesh]) OR ("Bone mineral density")).*
Study type filter: clinical trials and quasi-experiments.

Table 2. Characteristics of individual studies

Reference	Type of study	Participants	Variables	Intervention	Stander
Caulton et al. 2003[17]	RCT	26 children with CP, nonwalkers. Aged between 4.3 and 10.8 years.	Spine BMD measured by CT scan (mg/cm^3).	Increased of usual standing by 50% for 9 months.	Static prone and supine
Wren et al. 2010[18]	Quasi-experiment	17 children with CP, GMFCS IV and V, aged 6 to 12 years (mean: 9.4, SD: 1.4).	Spine BMD and cross-section of the spine with CT scan (mg/cm^3).	10 minutes of dynamic standing per day for 6 months. Follow-up or 6 and 12 months.	Supine vibration platform
Damcott et al. 2013[16]	Quasi-experiment	21 children with CP, aged 4 to 9 years, GMFCS IV and V.	Femur BMD measured by DXA (mg/cm^2).	30 minutes of standing, 5 days per week for 15 months. Follow-up at 3, 6, 9, 12, and 15 months.	Dynamic supine stander
Han et al. 2017[19]	RCT	7 children with CP, aged 2.25 to 6.4 years, GMFCS V.	Femur BMD measured by DXA (mg/cm^2).	Assisted standing for more than 2 hours per day, more than 5 days per week for 6 months.	Static supine stander

RCT: randomized clinical trial, CP: cerebral palsy, BMD: bone mineral density, SD: standard deviation, CT: computed tomography, DXA: dual x-ray absorptiometry, GMFCS: Gross Motor Function Classification System.

2. Changes in bone mineral density according to the type of stander.

Dynamic supine stander

The study conducted by Wren et al.[18] obtained positive results in spine BMD with an increase of 1.6% (95% confidence interval [CI]: 7.7–10.9, $p = 0.73$), with a stander vibration of 30 hertz (Hz) and an acceleration of 0.3 g.

The data obtained by Damcott et al.[16] showed an increase in femur BMD of 9.5%, without the possibility of estimating the CI; they mentioned a p value < 0.044, with a stander vibration of 1 Hz, imitating the hertz of the gait cadence. Both studies demonstrated positive changes in BMD; the results obtained by Damcott et al. are statistically significant.[16]

Static supine stander

The study by Han et al.[19] obtained positive results in femur BMD with an increase of 3.61% (95% CI: 2.59–4.63, $p = 0.713$).

Static supine/prone stander

The study by Caulton et al.[17] obtained positive results for spine BMD with an increase of 6% (95% CI: 1.93–14.39, $p = 0.01$). However, they did not observe changes in tibia BMD, which is reported only descriptively.

3. Changes in bone mineral density according to the time of the intervention

Included studies had varying treatment periods, from minutes to hours on the stander. The minimum total intervention time was 6 months and the maximum time was 15 months; the longer time obtained the best results in terms of BMD increase (*Table 3*).

B. Quantitative synthesis

It was not possible to combine individual results given the heterogeneity among study subjects and the different standing protocols and dosage described in the selected articles.

Risk of bias in the studies

Included studies had a high risk of allocation, measurement, and reporting bias. Most notably, there were missing data for the interpretation of results in all studies. The risk of bias was described using a graphic representation (*Figures 2* and *3*) developed with the REV-MAN 5.4.1 software (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration).

DISCUSSION

The results show statistically significant changes in femur BMD[17,19] and spine BMD[16] when using static and dynamic standers, respectively.

There is still controversy about the effectiveness of assisted standing in relation to BMD. Caulton et al.[17] and Damcott et al.[16] found statistically significant differences in the increase in spine and femur BMD; however, Wren et al.[18] and Han et al.[19] found no differences for femur and spine BMD.

When comparing our results with those obtained by Paleg et al.,[4] they are consistent to a certain extent because an increase in BMD was observed, but the studies included not only measured BMD in children, but also in adults, who had different levels of motor involvement. In addition, the level of risk of bias in the studies was high. Also, Occhipintti,[20] in their results regarding BMD, concluded that further evidence and prospective studies with longer follow-up periods are required to obtain valid results.

The difference in the results may be due to various factors, e.g., age at the start of standing, dosage, type of stander, or GMFCS level. The age at the start of standing is an important characteristic that has not been taken into account in the studies reviewed. In their study, Macias-Merlo et al.[21] recommend starting treatment at 12–14 months of age, while in the studies reviewed, standing programs began at an age ranging from 2 to 6 years. This may have clearly influenced the results obtained.

The dosage varies considerably in each of the studies. Damcott et al. (2013),[16] who obtained the best results, used a protocol that established standing on a dynamic stander for 30 minutes, 5 days per week, for 15 months. Wren et al. (2010),[18] who obtained the most discrete results, implemented 10 minutes of dynamic standing per day for 6 months. Other authors described effective standing times for other variables: 90 minutes per day, 7 days per week, divided into 2 periods of 45 minutes.[21] In view of the results, it would be advisable to implement protocols of standing for more than 30 minutes, 7 days per week, to generate changes in BMD.

The GMFCS level directly influences the results of various treatments.[22] Children with GMFCS level IV and V are more likely to develop osteoporosis,[23] in addition to having an increased risk of bone density loss due to anticonvulsant use[24] when they do not receive calcium and vitamin D supplementation.[25] In this review, all children were receiving such supplementation.

Another important element that is not mentioned in any of the studies is the position on the stander and the joint ranges necessary to maintain an adequate standing position or the use of orthoses to accompany this standing position.[21]

The objective of this review was to determine the effect of assisted standing on BMD in children with cerebral palsy. There is still little evidence published on this subject due to the difficulty of conducting a long-term treatment, the insufficient number of users, and several intrinsic factors that may modify the results.

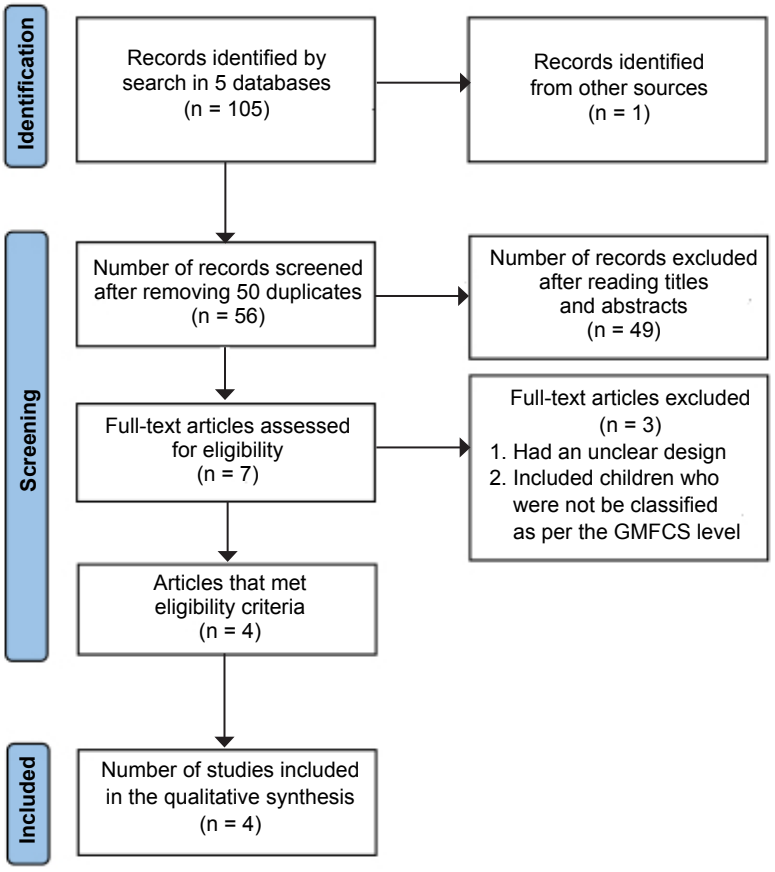
This systematic review summarizes the current evidence on this issue and provides quality

Table 3. Summary of results

Reference	Sample size	Intervention	Stander	Body site for BMD measurement	% of change in BMD after the intervention
Caulton et al. 2003[17]	26 children	Increased of usual standing by 50% for 9 months.	Static prone and supine	Spine	6% (95% CI: 1.93–14.39, $p = 0.01$)
Wren et al. 2010[18]	17 children	10 minutes of dynamic standing per day for 6 months. Follow-up for 6 and 12 months.	Dynamic supine stander	Spine	1.6% (95% CI: 7.7–10.9, $p = 0.73$)
Damcott et al. 2013[16]	21 children	30 minutes of standing, 5 days per week of static standing for 15 months. Follow-up at 3, 6, 9, 12, and 15 months.	Dynamic supine stander	Femur	9.5%, $p < 0.044$
Han et al. 2017[19]	7 children	Standing for more than 2 hours per day, more than 5 days per week for 6 months.	Static supine stander	Femur	3.61% (95% CI: 2.59–4.63, $p = 0.713$)

BMD: bone mineral density.

Figure 1. PRISMA flow chart



Figures 2 and 3. Summary of risk of bias

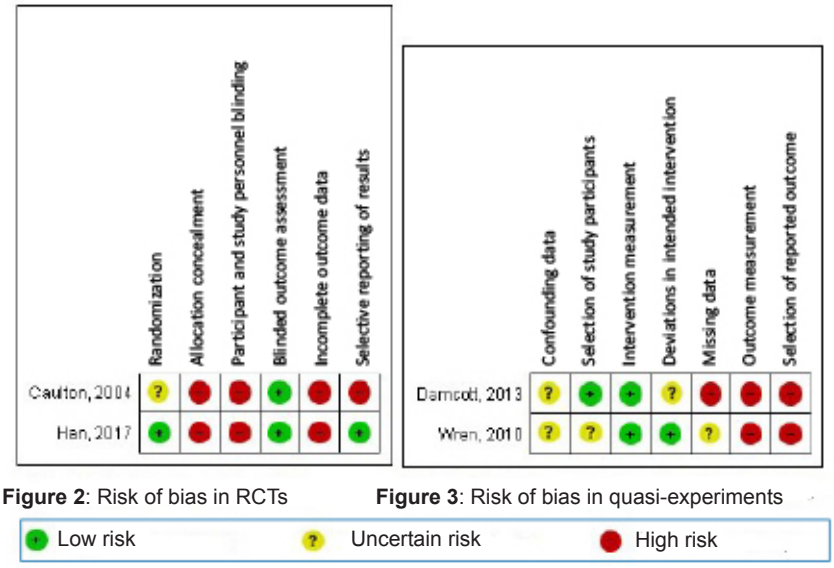


Figure 2: Risk of bias in RCTs **Figure 3**: Risk of bias in quasi-experiments

Summary of risk of bias as per the opinion of reviewers considering each element in the risk of bias for each study included, both RCTs and quasi-experiments.
RCT: randomized clinical trial.

evidence from randomized controlled clinical trials and quasi-experiments to guide clinical practice and provide guidance for healthcare providers. There are no other studies of similar characteristics published in recent years that specifically analyzed the effect of assisted standing on BMD in children with CP.

Among the main limitations of this study, we found a great heterogeneity among study subjects and different standing protocols and dosage described in the selected articles. For this reason, recommendations should be taken with moderation, as it is not possible to suggest a single assisted standing protocol with all that this implies. In addition, it is difficult to conduct blinded clinical trials with interventions; all included studies had a high risk of bias in terms of blinding and outcome reporting with confounding or missing data.

For clinical practice purposes, the recommendation is that all nonwalkers be helped with artificial standing.[16–19] This review allowed to identify that there are still gaps regarding the effect of standing on BMD. New primary studies should be carried out to corroborate the good results observed in this review and to strengthen a therapy that is widely used worldwide in children's rehabilitation.

CONCLUSIONS

Assisted standing in children with cerebral palsy leads to positive changes in BMD. The best results were described by Damcott et al. (2013),[16] who considered the recommendation of a dynamic stander at 1 Hz for a minimum of 30 minutes, for 5 days per week and for at least 6 months. Based on the evidence reviewed and given the limitations of this study, it is not possible to recommend the most effective type and dosage of standing to generate the expected changes in BMD. Therefore, further research is required, with studies that have a greater methodological rigor, avoid bias as much as possible, establish longer follow-up periods, include a larger number of users, and provide full reporting of data obtained. ■

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