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REVIEW



# Low bone mineral density in ambulatory persons with cerebral palsy? A systematic review

Cindy T. R. Mus-Peters[a], Bionka M. A. Huisstede[b], Suzie Noten[c], Minou W. M. G. C. Hitters[a], Wilma M. A. van der Slot[c,d] and Rita. J. G. van den Berg-Emons[a,c]

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**ABSTRACT**

**Purpose:** Non-ambulatory persons with cerebral palsy are prone to low bone mineral density. In ambulatory persons with cerebral palsy, bone mineral density deficits are expected to be small or absent, but a consensus conclusion is lacking. In this systematic review bone mineral density in ambulatory persons with cerebral palsy (Gross Motor Function Classification Scales I–III) was studied.

**Materials and methods:** Medline, Embase, and Web of Science were searched. According to international guidelines, low bone mineral density was defined as *Z*-score $\leq -2.0$. In addition, we focused on *Z*-score $\leq -1.0$ because this may indicate a tendency towards low bone mineral density.

**Results:** We included 16 studies, comprising 465 patients aged 1–65 years. Moderate and conflicting evidence for low bone mineral density (*Z*-score $\leq -2.0$) was found for several body parts (total proximal femur, total body, distal femur, lumbar spine) in children with Gross Motor Function Classification Scales II and III. We found no evidence for low bone mineral density in children with Gross Motor Function Classification Scale I or adults, although there was a tendency towards low bone mineral density (*Z*-score $\leq -1.0$) for several body parts.

**Conclusions:** Although more high-quality research is needed, results indicate that deficits in bone mineral density are not restricted to non-ambulatory people with cerebral palsy.

**➤ IMPLICATIONS FOR REHABILITATION**

- Although more high-quality research is needed, including adults and fracture risk assessment, the current study indicates that deficits in bone mineral density are not restricted to non-ambulatory people with CP.
- Health care professionals should be aware that optimal nutrition, supplements on indication, and an active lifestyle, preferably with weight-bearing activities, are important in ambulatory people with CP, also from a bone quality point-of-view.
- If indicated, medication and fall prevention training should be prescribed.

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## Introduction

Cerebral palsy (CP) occurs in 1.5–3.0 out of every 1000 live births and is the most common cause of physical disability in pediatric rehabilitation medicine [1]. CP describes a group of permanent disorders in the development of movement and posture causing limitations in activity that are attributable to non-progressive disturbances which occurred in the fetal or infant brain [2]. There are three CP subtypes: spastic, ataxic, and dyskinetic [1]. Motor disorders of CP are often accompanied by disturbances of sensation, perception, cognition, communication, and behavior, as well as epilepsy and secondary musculoskeletal problems [2]. Moreover, persons with CP often have nutritional problems [3,4].

Persons with CP are prone to low bone mineral density (BMD) [3,5] because of low calcium and vitamin D intake [3,5,6] as well as use of anticonvulsant medication [3,7], which can lead to vitamin D deficiency [5]. Furthermore, persons with CP are generally known to have inactive lifestyles [8–11], which may adversely affect BMD [7].

Several studies [3,12–17], including two systematic reviews [16,17], have suggested the presence of low BMD in children, adolescents, and adults with CP. However, these studies mainly focused on non-ambulatory persons with moderate to severe CP (Gross Motor Function Classification System (GMFCS) levels IV–V [18]). Because nutritional deficiencies, epilepsy [19], and inactivity [10] occur less frequently or less severely in persons with CP who are ambulatory or mildly affected (GMFCS levels I–III), it may be expected that BMD deficits are smaller or absent in these subgroups. Furthermore, ambulatory persons perform more weight-bearing activities compared to non-ambulatory persons, which

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Supplemental data for this article can be accessed here.

may prevent development of low BMD [9]. However, evidence for the magnitude of BMD deficits in ambulatory persons with CP is, as far as we know, lacking. BMD information in this subgroup is important because it may have treatment implications.

The aim of this systematic review was to provide an overview of the current scientific literature on BMD in ambulatory persons (children and adults) with mild to moderate CP (GMFCS levels I–III).

## Materials and methods

### Literature search

This study focusing on BMD in ambulatory persons with CP (GMFCS levels I–III) was a computer-aided literature study performed using Medline, Embase, and Web of Science up to June 2017. Key words representing CP and BMD were included in the literature search. The complete search strategy is shown in Supplementary Table S1.

### Inclusion criteria

Full-text original studies (i.e., no abstracts, reviews or editorials) were included in this study if they fulfilled all of the following criteria: (1) study of a diagnostic group of CP classified as GMFCS levels I–III. Studies also including GMFCS levels IV and V were permitted if results for GMFCS levels I–III were presented separately or results for GMFCS levels I–III could be calculated separately; (2) BMD was included as an outcome measure; (3) the study had to be an observational study (cohort study or case–control study) or concern baseline measurements of an intervention or experimental study; (4) results on BMD had to be compared with reference data and presented as average *Z*-score (standard deviation (SD)). A *Z*-score is the difference between a patient's value and an age-specific mean value, divided by the reference group's SD. Alternatively, the average *Z*-score (SD) for persons with CP could be calculated from results of BMD in a simultaneously measured control group of typically developing persons (case control studies). For proper calculation, a minimum sample size of typically developing persons was set at 15; and (5) the study had to be written in English, German, French, or Dutch.

### Study selection

Two reviewers (C. M. and R. v. d. B.) independently selected potentially relevant studies using the inclusion criteria to evaluate titles, abstracts, and full text articles (Figure 1). A consensus method was used when there was any disagreement regarding the inclusion of the data between the two reviewers. When any disagreement persisted, a third reviewer (B. H.) was consulted. In the case of multiple articles by the same authors, we contacted corresponding authors to clarify whether the articles used different study samples.

### Data extraction

The same two reviewers independently extracted the data from included studies. Any disagreement about data extraction was resolved by the same consensus process as previously described. Characteristics of the included studies can be found in Supplementary Table S2.

### Methodological quality assessment

The two reviewers (C. M. and R. v. d. B.) independently assessed the methodological quality of the included studies using a constructed quality assessment list (Table 1), which included criteria adapted from the New Castle-Ottawa scale [20], the Dutch Cochrane Centre [21], as well as the studies of Huisstede et al. [22,23], Van Rijn et al. [24,25], and Hombergen et al. [26] and modified to cover the topic of this review. The list consisted of ten items within three themes (study population/selection, outcome measurements, and study design). The reviewers scored each item as positive (+), negative (−), or unclear (?). A consensus procedure was used to resolve disagreements between reviewers. A study was considered high-quality when the score exceeded 50% of the maximum attainable score.

### Data analysis

We considered pooling of data in a meta-analysis when patient characteristics and outcome measures used to evaluate BMD were homogeneous. If pooling of data was not possible, a best-evidence synthesis was performed to summarize the results of the included studies. For the best-evidence synthesis, we used *Z*-score to compare the results between persons with CP and typically developing persons. According to the International Society For Clinical Densitometry [6,27], low BMD was defined as a *Z*-score-$\leq -2$ for our primary evidence synthesis. We adopted this definition for both children and adults with CP. In addition, we focused on *Z*-score $\leq -1.0$, because this may indicate a tendency towards low BMD. For (case–control) studies that did not provide *Z*-score, we calculated average (SD) *Z*-score based on average BMD level in the CP group and average (SD) BMD level in the simultaneously measured control group of typically developing persons (the minimum requested sample size of typically developing persons was set at 15). If levels of significance were not provided for the comparisons of our interest, we calculated *p* values using means, SDs, and sample sizes.

The level of evidence for low BMD in persons with CP was ranked as follows [26]: (1) Strong evidence: $\geq 2$ high-quality studies in which CP results meet the criteria for low BMD (i.e., an average BMD *Z*-score $\leq -2.0$) and differ significantly ($p \leq 0.05$) from typically developing persons results; (2) moderate evidence: $\geq 2$ low-quality studies or 1 high-quality study in which CP results meet criteria for low BMD (i.e., an average BMD *Z*-score $\leq -2.0$) and differ significantly ($p \leq 0.05$) from typically developing persons results; (3) limited evidence: 1 low-quality study in which CP results meet the criteria for low BMD (i.e., an average BMD *Z*-score $\leq -2.0$) and differ significantly ($p \leq 0.05$) from typically developing persons results; (4) conflicting evidence: conflicting findings between studies (less than 75% of studies report low BMD in the CP group compared with the typically developing persons group and a significant difference between the results in the CP and the typically developing persons group); (5) no evidence: studies available, but no low BMD or no significant differences between the CP and typically developing persons groups are reported; (6) no studies found.

In addition, as a secondary best-evidence synthesis, we applied the above ranking method for the cutoff level of *Z*-score $\leq -1.0$, since this level may indicate a tendency towards low BMD.

Results (mean and SD, where necessary, SD was calculated from standard error [SE]) were described for each body site separately (lumbar spine [comprising several spinal levels], total proximal femur, femur neck, distal femur, calcaneus, radius, and tibia), and for the total body. Furthermore, we reported results for

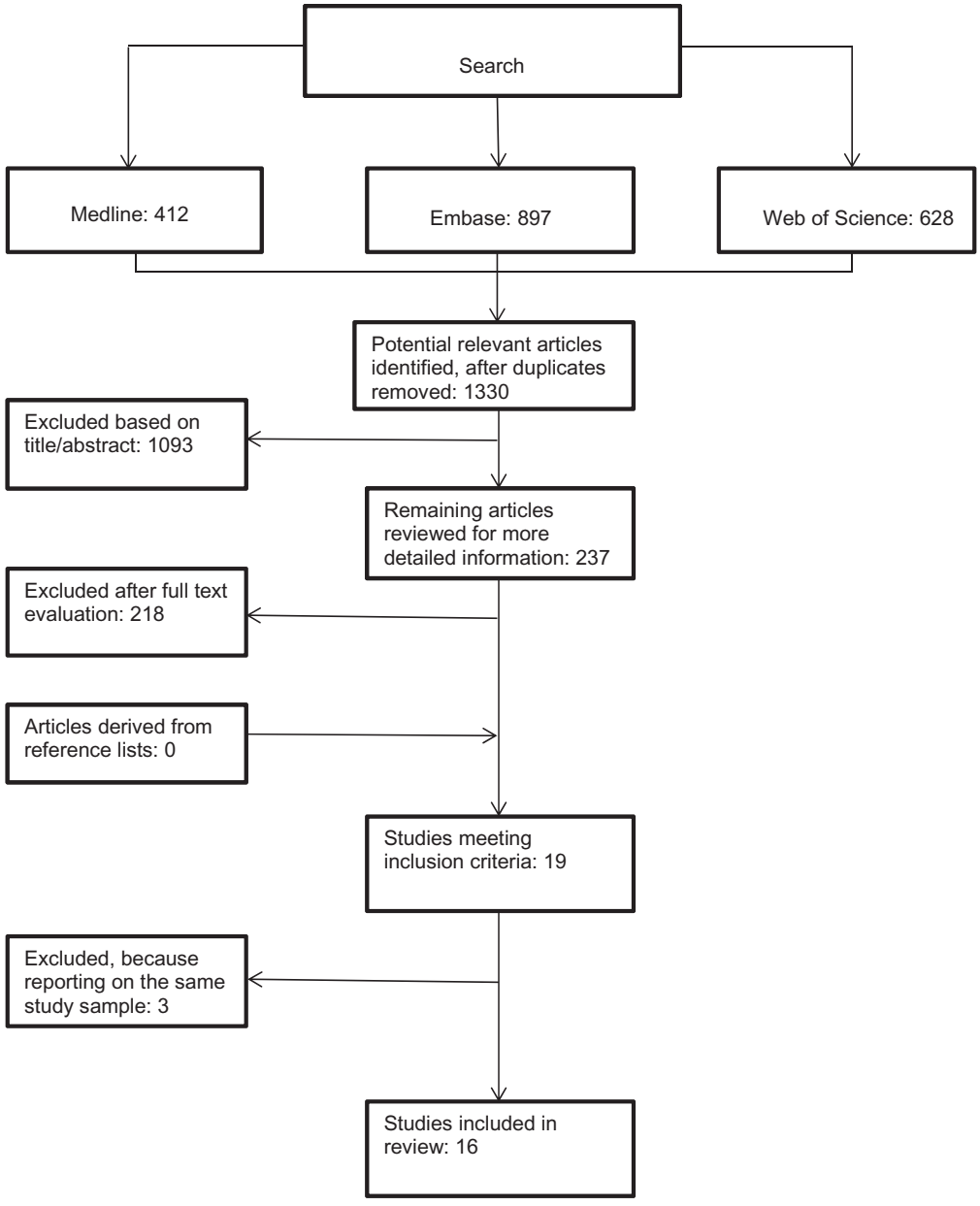


**Figure 1.** Flowchart of the included studies.

children (age 0–17 years) and adults (≥18 years) and for each GMFCS level separately. If this was not possible, we described results for combined age (including both children and adults) and combined ambulatory levels (GMFCS levels I and II or GMFCS levels I–II–III). To enhance readability, we only reported *Z*-scores ≤ −2.0 and *Z*-scores ≤ −1.0 in the results section. Of course, the best-evidence syntheses were based on all *Z*-scores, including those > −1.0; an overview of all *Z*-scores can be found in Tables 4–6. Because of small sample sizes, results at the alpha level of 0.10 were reported.

## Results

### *Characteristics of included studies*

The literature search resulted in 1330 potentially eligible studies. After reviewing titles, abstracts, and full text-articles, 19 studies met our inclusion criteria (Figure 1). For three studies by Henderson et al. [3,13,28] and three studies by Chen et al. [29–31], there was uncertainty about whether these studies reported on the same study sample. Consultation with the authors revealed that the studies of Henderson et al. reported on one study sample; therefore, only one study [3] was included in this review. We did not succeed in contacting the group of Chen. We decided to include the GMFCS level I and II results for the lumbar spine and femur, as reported in one of their studies [31]. Furthermore, we included part of another study by Chen et al. [30] that focused on GMFCS level III and the calcaneus results. In total, 16 studies were included in the analysis.

The study of Esen et al. [32] reported *Z*-score for four different adjustment methods (decimal age, bone age, height age, and height-for-age). According to the recommendation of the International Society for Clinical Densitometry [27] to use if possible the *Z*-score adjusted for height, we decided to report only the *Z*-score adjusted for height. The Society also recommends measuring BMD in the total proximal femur or femur neck and not in the greater trochanter or Ward's triangle [6,27]. Therefore, we did not report the results measured in these latter regions in the study of Han et al. [33] and Kim et al. [34]. Because most

**Table 1.** Quality assessment criteria.

| Study population/selection |
|---|
| 1. Positive if samples are consecutive or an obviously representative series of persons with cerebral palsy (recruitment from more than one hospital or rehabilitation centre) |
| 2. Sufficient description of characteristics of persons with CP<br>Positive if at least four out of six requirements are reported<br>(a) Age (mean and standard deviation or range)<br>(b) Sex (number or percentage)<br>(c) Type of cerebral palsy<br>(d) Distribution of cerebral palsy<br>(e) Level of ambulation<br>(f) Level of intelligence/education |
| 3. Sufficient description of characteristics of typically developing persons<br>Positive if at least two out of three requirements are reported:<br>(a) Age (mean and standard deviation or range)<br>(b) Sex (number or percentage)<br>(c) Level of intelligence/education |
| 4. Positive if participation in bone mineral density (BMD) measurements is $\geq$70% in persons with CP and typically developing persons |
| 5. Positive if the total number of cases is $\geq$50 (25 persons with CP and 25 typically developing persons) |
| Outcome measurements |
| 6. Positive if BMD measurements are obtained in a standardized valid way |
| Study design |
| 7. Positive if inclusion and exclusion criteria are described for persons with CP |
| 8. Positive if inclusion and exclusion criteria are described for typically developing persons |
| 9. Positive if potential confounders are described (medication for epilepsy, nutrition and sports activity) and BMD data are matched/adjusted for these confounders |
| 10. Positive if persons with CP and typically developing persons are matched for age and sex in the design or adjusted for these factors in the analysis |

CP: cerebral palsy; BMD: bone mineral density.

studies of the distal femur measured BMD in region 2 (mixture of cortical and trabecular bone), we report only results for region 2.

Characteristics of the included studies are presented in Supplementary Table S2. The included studies comprised a total of 465 persons with CP (GMFCS I–III) ranging in age from 1 to 65 years. Ten studies used reference data to interpret BMD in CP (*Z*-score) and six studies had a case–control design from which we calculated *Z*-score. Pooling of the results was not possible because of heterogeneity in patient characteristics and outcome measurements. Fourteen studies reported BMD results of the lumbar spine [3,12,30–41], nine of the femur [3,12,30,31,33,34,37,38,42], two of the calcaneus [30,36], two of the total body [37,42], and one of the radius and tibia [43]. Most studies focused on children, but five focused on adults [34,38,39] or a mixed age group [3,43]. The countries from which the participants were recruited were: Canada [3,12,42], Taiwan [30,31], USA [3,39], England [36], Turkey [32], Norway [37], Korea [33], Israel [43], and Pakistan [41]. Four studies did not report the country from which the participants were recruited [34,35,38,40]. Five studies [12,30,31,40,42] reported only on persons with spastic CP, three studies [34,37,38] on other types of CP, and seven studies [3,32,33,35,36,39,41,43] did not report CP type.

Almost all studies used dual X-ray absorptiometry scan for measuring BMD. Three studies used quantitative computed tomography (QCT) [35,36,39] and three studies used ultrasound of the calcaneus [30,36], or radius and tibia [43].

### Methodological quality

The methodological quality results are shown in Table 2. Ten studies (63%) were classified as high-quality [3,12,30,31,35,37,38,40–42] and six (37%) as low-quality [32–34,36,39,43]. The most common methodological shortcomings were (1) study samples that were not consecutive or an obviously representative series of cases (88%); and (2) the total number of cases was less than 50 (63%).

### Bone mineral density results

#### Lumbar spine

***GMFCS I.*** Five high-quality studies [12,31,35,37,41] reported BMD results of the lumbar spine in children classified as GMFCS level I (Tables 3 and 4). An exact lumbar spine level was not reported. According to *Z*-score $\leq -2.0$, there was no low BMD noted. However, Akhter et al. [41] reported an average *Z*-score of $-1.30$ (SD 0.09, $p < 0.0001$). According to the best-evidence synthesis regarding *Z*-score $\leq -2.0$, there was no evidence for low BMD. Regarding *Z*-score $\leq -1.0$, there was conflicting evidence for low BMD of the lumbar spine in children with GMFCS level I.

We found no studies of BMD of the lumbar spine in adults with GMFCS level I (Tables 5 and 6).

***GMFCS II.*** Five high-quality studies [12,31,35,37,41] reported BMD results of the lumbar spine in children classified as GMFCS level II (Tables 3 and 4). According to *Z*-score $\leq -2.0$, none of these studies found low BMD. However, Akhter et al. [41] reported an average *Z*-score of $-1.68$ (SD 0.33, $p < 0.0001$) and Finbråten et al. [37] of $-1.4$ (SD 1.3, $p < 0.01$). According to the best-evidence synthesis regarding *Z*-score $\leq -2.0$, there was no evidence for low BMD. Regarding *Z*-score $\leq -1.0$, there was conflicting evidence for low BMD of the lumbar spine in children with GMFCS level II. We found no studies of BMD of the lumbar spine in adults with GMFCS level II (Tables 5 and 6).

***GMFCS III.*** Four high-quality studies [12,30,35,41] and two low-quality studies [33,36] reported BMD of the lumbar spine in children with GMFCS level III (Tables 3 and 4). Regarding *Z*-score $\leq -2.0$, the low-quality study of Wilmshurst et al. [36] reported low BMD at T12-L3 (*Z*-score $-2.12$, SD 1.2, $p < 0.05$). Furthermore, the high-quality studies of Akhter et al. [41] (*Z*-score $-1.86$, SD 0.20, $p < 0.0001$) and Chen et al. [30] (*Z*-score $-1.1$, SD 0.6, $p < 0.01$; L1–L4) reported *Z*-score $\leq -1.0$. According to the best-evidence synthesis regarding *Z*-score $\leq -2.0$ and regarding *Z*-score $\leq -1.0$, there was conflicting evidence for low BMD of the lumbar spine in children with GMFCS level III (Table 3).

Table 2. Methodological quality of the studies.

| Study | Year | Persons with CP are representative | Sufficient description of persons with CP | Sufficient description of typically developing persons | Participation in BMD measurement ≥70% | Number of cases ≥50 | Standardised And valid measurements | Inclusion and exclusion criteria described for CP | Inclusion and exclusion criteria described for typically developing persons | Consideration for confounders | matched for sex and age | Score maximum | Score study | % |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Chen [30] | 2011 | - | + | + | + | + | + | + | + | + | + | 10 | 9 | 90 |
| Chen [31] | 2011 | - | + | + | + | + | + | + | + | - | + | 10 | 8 | 80 |
| Wren [35] | 2011 | - | + | + | + | + | + | + | + | - | + | 10 | 8 | 80 |
| Henderson [12] | 1995 | - | + | ? | + | + | + | + | ? | - | + | 10 | 7 | 70 |
| Finbråten [37] | 2015 | - | + | ? | + | + | + | + | ? | + | + | 10 | 7 | 70 |
| Ünay [40] | 2000 | ? | + | + | + | - | + | + | - | + | + | 10 | 7 | 70 |
| Akhter [41] | 2017 | - | - | + | + | + | + | - | - | - | + | 10 | 6 | 60 |
| Chad [42] | 2000 | + | + | + | + | - | + | - | - | - | + | 10 | 6 | 60 |
| Fowler [38] | 2015 | ? | + | - | + | ? | + | + | - | + | + | 10 | 6 | 60 |
| Henderson [3] | 2002 | + | - | - | - | - | + | + | + | + | + | 10 | 6 | 60 |
| Esen [32] | 2011 | - | - | ? | + | - | + | - | ? | + | + | 10 | 4 | 40 |
| Hartman [43] | 2004 | - | + | ? | + | - | - | - | ? | + | + | 10 | 4 | 40 |
| Kim [34] | 2015 | ? | + | - | + | ? | + | - | - | - | + | 10 | 4 | 40 |
| Wilmshurst [36] | 1996 | - | - | + | - | - | + | - | + | - | + | 10 | 4 | 40 |
| Peterson [39] | 2015 | - | - | - | + | - | + | - | - | - | + | 10 | 3 | 30 |
| Han [33] | 2012 | ? | - | - | ? | - | + | - | - | - | - | 10 | 1 | 10 |

In the high-quality study by Henderson et al. [3], which included persons up to 19 years of age, BMD lumbar spine results were reported for GMFCS level III (Tables 3 and 5). Regarding $Z$-score $\leq -2.0$, no low BMD of the lumbar spine was noted. However, Henderson et al. [3] reported a $Z$-score of $-1.5$ (SD 0.9, $p < 0.001$; lumbar spine level was not reported). According to the best-evidence synthesis regarding $Z$-score $\leq -2.0$, there was no evidence for low BMD. Regarding $Z$-score $\leq -1.0$, there was moderate evidence for low BMD of the lumbar spine in a combined group of children and adults up to 19 years of age at GMFCS level III.

The high-quality study by Fowler et al. [38] reported BMD results of the lumbar spine (spine level not reported) in adults with GMFCS level III (Tables 3 and 6); no low BMD was reported, neither regarding $Z$-score $\leq -2.0$ nor regarding $Z$-score $\leq -1.0$). According to the best-evidence synthesis (both regarding $Z \leq -2.0$ and regarding $Z \leq -1.0$), there was no evidence for low BMD of the lumbar spine in adults with GMFCS level III.

***GMFCS I – II combined.*** Two low-quality studies [33,36] reported BMD of the lumbar spine in children with combined GMFCS levels I and II (Tables 3 and 4). None of these studies reported low BMD according to $Z$-score $\leq -2.0$. However, Wilmshurst et al. [36] reported a $Z$-score of $-1.08$ (SD 0.9, $p < 0.05$; T12-L3). According to the best-evidence synthesis regarding $Z$-score $\leq -2.0$, there was no evidence for low BMD. Regarding $Z$-score $\leq -1.0$, there was conflicting evidence for low BMD of the lumbar spine in children within the combined GMFCS levels I and II group.

The high-quality study by Fowler et al. [38] reported BMD results of the lumbar spine (lumbar spine level not reported) in adults with GMFCS levels I and II combined (Tables 3 and 6); no low BMD was reported according to $Z$-score $\leq -2.0$; however, they reported a $Z$-score of $-1.07$, (SD 1.0, $p < 0.001$). According to the best-evidence synthesis regarding $Z$-score $\leq -2.0$, there was no evidence for low BMD. Regarding $Z$-score $\leq -1.0$, there was moderate evidence for low BMD of the lumbar spine in adults of a group with GMFCS levels I and II combined.

***GMFCS I–II–III combined.*** Two high-quality studies [37,40] and one low-quality study [32] reported BMD results of the lumbar spine in a combined group of children with GMFCS levels I, II, and III (Tables 3 and 4). None of the studies reported low BMD according to $Z$-score $\leq -2.0$. However, the low-quality study of Esen et al. [32] reported an average $Z$-score of $-1.21$ at L1–L4 (SD 1.4, $p < 0.001$). According to the best-evidence synthesis regarding $Z$-score $\leq -2.0$, there was no evidence for low BMD. Regarding $Z$-score $\leq -1.0$, there was conflicting evidence for low BMD of the lumbar spine in a combined group of children with GMFCS levels I, II, and III.

Two low-quality studies [34,39] reported BMD results of the lumbar spine in adults with GMFCS levels I, II, and III combined (Tables 3 and 6). Kim et al. [34] reported the results separately for the spastic type and dyskinetic type of CP without mentioning if the BMD was measured in trabecular or in cortical bone of the lumbar vertebras. The study of Peterson et al. [39] reported the results separately for trabecular and cortical bone without mentioning the type of CP. No low BMD was noted, neither regarding $Z$-score $\leq -2.0$ nor regarding $Z$-score $\leq -1.0$. According to the best-evidence synthesis (both regarding $Z$-score $\leq -2.0$ and regarding $Z$-score $\leq -1.0$), there was no evidence for low BMD of the lumbar spine in adults with GMFCS levels I, II, and III combined.

**Table 3.** Evidence for low bone mineral density.

| Study | | Year | GMFCS | Lumbar spine | Total proximal femur | Femur neck | Distal femur (region 2) | Distal femur (no region) | Calcaneus | Radius | Tibia | Total body |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Akhter [41] | HQ | 2017 | I | *NE* | – | – | – | – | – | – | – | – |
| | | | II | *NE* | – | – | – | – | – | – | – | – |
| | | | III | *NE* | – | – | – | – | – | – | – | – |
| Chad [42] | HQ | 2000 | I–II | – | NE | NE | – | – | – | – | – | NE |
| Chen [31] | HQ | 2011 | I | NE | – | – | NE | – | – | – | – | – |
| | | | II | NE | – | – | NE | – | – | – | – | – |
| Chen [30] | HQ | 2011 | I–II | – | – | – | – | – | NE | – | – | – |
| | | | III | *NE* | – | – | – | NE | *NE* | – | – | – |
| Finbråten [37] | HQ | 2015 | I | NE | – | – | NE | – | – | – | – | *NE* |
| | | | II | *NE* | – | – | E | – | – | – | – | E |
| | | | I–II–III | NE | – | – | *NE* | – | – | – | – | – |
| Fowler [38] | HQ | 2015 | I–II | *NE* | NE | NE | – | – | – | – | – | – |
| | | | III | NE | *NE* | NE | – | – | – | – | – | – |
| Henderson [12] | HQ | 1995 | I[a] | NE | NE | – | – | – | – | – | – | – |
| | | | II[a] | NE | NE | – | – | – | – | – | – | – |
| | | | III[a] | NE | E | – | – | – | – | – | – | – |
| Henderson [3] | HQ | 2002 | III | *NE* | – | – | *NE* | – | – | – | – | – |
| Ünay [40] | HQ | 2003 | I–II–III[a] | NE | – | – | – | – | – | – | – | – |
| Wren [35] | HQ | 2011 | I | NE | – | – | – | – | – | – | – | – |
| | | | II | NE | – | – | – | – | – | – | – | – |
| | | | III | NE | – | – | – | – | – | – | – | – |
| Esen [32] | LQ | 2011 | I–II–III | *NE* | – | – | – | – | – | – | – | – |
| Han [33] | LQ | 2012 | I–II[a] | NE | – | *NE* | – | – | – | – | – | – |
| | | | III[f] | NE | – | NE | – | – | – | – | – | – |
| Hartman [43] | LQ | 2004 | I | – | – | – | – | – | – | *NE* | NE | – |
| | | | II | – | – | – | – | – | – | NE | NE | – |
| Kim [34] | LQ | 2015 | I–II–III spastic | NE | *NE* | NE | – | – | – | – | – | – |
| | | | I–II–III dyskinetic | NE | NE | NE | – | – | – | – | – | – |
| Peterson [39] | LQ | 2015 | I–II–III trabecular | NE | – | – | – | – | – | – | – | – |
| | | | I–II–III cortical | NE | – | – | – | – | – | – | – | – |
| Wilmshurst [36] | LQ | 1996 | I–II[a] | *NE* | – | – | – | – | *NE* | – | – | – |
| | | | III[a] | E | – | – | – | – | *NE* | – | – | – |

NE: no evidence for low BMD; E: evidence for low BMD ($Z$-score $\leq -2.0$); *NE (Italics)*: no evidence for low BMD, but a tendency for low BMD ($Z$-score $\leq -1.0$); –: no studies included in this category; HQ: high-quality study; LQ: low-quality study; GMFCS: Gross Motor Function Classification Scale.
[a]GMFCS level inferred from descriptions.

### *Femur*

***Total proximal femur.*** Two high-quality studies, one by Henderson et al. [12] and one by Chad et al. [42], reported BMD of the total proximal femur in children with different GMFCS levels (Tables 3 and 4). Regarding $Z$-score $\leq -2.0$, Henderson et al. [12] reported low BMD in children with GMFCS level III ($Z$-score of $-2.3$ SD 1.2, $p < 0.001$). For GMFCS level I, GMFCS level II, and GMFCS levels I and II combined, no low BMD was reported, neither regarding $Z$-score $\leq -2.0$ nor regarding $Z$-score $\leq -1.0$ [12,42]. According to the best-evidence synthesis regarding $Z$-score $\leq -2.0$ and regarding $Z$-score $\leq -1.0$, there was moderate evidence for low BMD of the total proximal femur in children with GMFCS level III. There was no evidence (not regarding $Z$-score $\leq -2.0$ nor regarding $Z$-score $\leq -1.0$) for low BMD of the total proximal femur in children with GMFCS level I, II, or in a group with GMFCS levels I and II combined.

One high-quality study by Fowler et al. [38] and one low-quality study by Kim et al. [34] reported BMD results of the total proximal femur in adults with different GMFCS levels (Tables 3 and 6). None of these studies reported low BMD according to $Z$-score $\leq -2.0$. However, the high-quality study of Fowler et al. [38] reported in GMFCS level III a $Z$-score of $-1.23$ (SD 0.9, $p < 0.01$) and the low-quality study of Kim et al. [34] reported in GMFCS levels I–II–III combined (spastic type) a $Z$-score of $-1.2$, (SD 1.0, $p = 0.001$). According to the best-evidence synthesis regarding $Z$-score $\leq -2.0$, there was no evidence for low BMD in the group of adults with GMFCS levels I and II combined, GMFCS level III, and adults with spastic and dyskinetic type of CP with GMFCS levels I, II, and III combined. According to the best-evidence synthesis regarding $Z$-score $\leq -1.0$, there was moderate evidence for low BMD of the total proximal femur in adults with GMFCS level III and limited evidence for low BMD of the total proximal femur in adults with spastic type of CP with GMFCS levels I, II and III combined. In addition, according to the best-evidence synthesis regarding $Z$-score $\leq -1.0$, there was no evidence for low BMD of the total proximal femur in adults in a group with GMFCS level I and II combined, as well as in adults with dyskinetic type of CP with GMFCS levels I, II, and III.

***Proximal femur: femur neck.*** The high-quality study by Chad et al. [42] and the low-quality study by Han et al. [33] reported BMD of the femur neck in children with different GMFCS levels (Tables 3 and 4). The low-quality study of Han et al. [33] reported in a group with GMFCS levels I and II combined a $Z$-score of $-1.0$ (SD 0.6, $p = 0.05$). According to the best-evidence synthesis regarding $Z$-score $\leq -2.0$, there was no evidence for low BMD of the femur neck in children with GMFCS levels I and II combined or with GMFCS level III. According to the best-evidence synthesis regarding $Z \leq -1.0$, there was conflicting evidence for low BMD of the femur neck in children with GMFCS levels I and II combined and no evidence for children with GMFCS level III.

One high-quality study by Fowler et al. [38] and one low-quality study by Kim et al. [34] reported BMD of the femur neck in adults with different GMFCS levels (Tables 3 and 6). No low BMD was reported, neither regarding $Z$-score $\leq -2.0$ nor regarding $Z$-score $\leq -1.0$. According to the best-evidence synthesis, there was no evidence for low BMD of the femur neck in adults with GMFCS level III, levels I and II combined, or levels I, II, and III combined, both regarding $Z$-score $\leq -2.0$ and regarding $Z$ score $\leq -1.0$.

**Table 4.** Bone mineral density results for children.

| Measurement location | Ambulation and/or GMFCS | Study | *Z*-score (SD) | *p* value |
|---|---|---|---|---|
| Proximal femur | | | | |
| Total proximal femur | Normal (I) | *Henderson [12] | −0.23 (1.1[c]) | >0.05[c] |
| | Community (II) | *Henderson [12] | −0.8[b] (1.2[c]) | ≤0.001[c] |
| | Household (III) | *Henderson [12] | **−2.3[b] (1.2[c])** | <0.001[c] |
| | Independent (I–II) | *Chad [42] | −0.23 (1.5) | >0.05[c] |
| Femoral neck | Independent (I–II) | *Chad [42] | 0.13 (1.7) | >0.05[c] |
| | Independent (I–II) | Han [33] | *−1[c] (0.6[c])* | =0.05[c] |
| | Walker (III) | Han [33] | −0.85[c] (0.3[c]) | <0.10[c] |
| Distal femur | | | | |
| Region 2 | I | *Chen [31] | −0.38[c] (0.6[c]) | <0.10[c] |
| | | *Finbråten [37] | −0.7 (1.2) | <0.05[c] |
| | II | *Chen [31] | −0.43[c] (0.5[c]) | <0.10[c] |
| | | *Finbråten [37] | **−2.8 (1.2)** | <0.001[c] |
| | I–III | *Finbråten [37] | *−1.6 (1.8)* | <0.001[c] |
| Region not reported | III | *Chen [30] | −0.77[c] (0.6) | =0.05[c] |
| Lumbar spine | | | | |
| T12–L3 | Mobile with abnormal gait (I–II) | Wilmshurst [36] | *−1.08 (0.9[c])* | <0.05[c] |
| | Mobile with frame or rollator (III) | Wilmshurst [36] | **−2.12 (1.2[c])** | <0.05[c] |
| L1–L4 | I | *Chen [31] | −0.28[c] (0.8[c]) | >0.05[c] |
| | II | *Chen [31] | −0.5[c] (0.8[c]) | <0.10[c] |
| | Independent (I–II) | Han [33] | −0.14[c] (1.4[c]) | >0.05[c] |
| | III | *Chen [30] | *−1.1[c] (0.6[c])* | <0.01[c] |
| | Walker (III) | Han [33] | 0.29[c] (1.6) | >0.05[c] |
| | I–II–III | Esen [32] | *−1.21 (1.4)* | <0.001 |
| L2–L4 | Ambulant (I–III) | *Ünay [40] | −0.43[c] (1.1) | >0.05[c] |
| L3 | I | *Wren [35] | −0.04[ac] (1.1[a,c]) | >0.05[a,c] |
| | II | *Wren [35] | −0.37[ac] (1.2[a,c]) | >0.05[a,c] |
| | III | *Wren [35] | −0.45[ac] (0.9[a,c]) | =0.05[a,c] |
| Not reported | Normal (I) | *Henderson [12] | −0.3[b] (1.2[c]) | >0.05[c] |
| | I | *Finbråten [37] | −0.4[d] (1.1) | >0.05[c] |
| | | *Akhter [41] | *−1.30 (0.09)* | <0.0001 [c] |
| | Community (II) | *Henderson [12] | −0.6[b] (0.7[c]) | <0.001[c] |
| | II | *Finbråten [37] | *−1.4[d] (1.3)* | <0.01[c] |
| | | *Akhter [41] | *−1.68 (0.33)* | <0.0001[c] |
| | III | *Akhter [41] | *−1.86 (0.20)* | <0.0001[c] |
| | Household (III) | *Henderson [12] | −0.8[b] (0.9[c]) | <0.05[c] |
| | I–II–III | *Finbråten [37] | −0.8 (1.2) | <0.01[c] |
| Calcaneus | Mobile with abnormal gait (I–II) | Wilmshurst [36] | *−1.07 (1.0[c])* | <0.01[c] |
| | I–II | *Chen [30] | −0.59[c] (0.5[c]) | <0.05[c] |
| | Mobile with frame or rollator (III) | Wilmshurst [36] | *−1.85 (1.0)* | <0.05[c] |
| | III | *Chen [30] | *−1.71[c] (0.7[c])* | <0.001[c] |
| Total body | I | *Finbråten [37] | *−1.5[d] (0.9)* | <0.001[c] |
| | II | *Finbråten [37] | **−2.2[d] (1.1)** | <0.001[c] |
| | Independent (I–II) | *Chad [42] | −0.25 (1.4) | >0.05[c] |

[a]Obtained from first author.
[b]Inferred from figure.
[c]Calculated based on mean, standard deviation and sample size.
[d]Adjusted for height; studies indicated with a * demonstrate a high-quality study. *Z*-score ≤ −2.0 are in bold. Additional *Z*-score ≤ −1.0 are in italics; distal femur region 2: transition between metaphysis and diaphysis (mixture of cortical and trabecular bone); GMFCS: Gross Motor Function Classification System [18].

**Table 5.** Bone mineral density results for combined groups of children and adults.

| Measurement location | GMFCS | Study | *Z*-score (SD) | *p* value |
|---|---|---|---|---|
| Distal femur | | | | |
| Region 2 | III | *Henderson [3] | *−1.8 (1.3[b])* | <0.001[b] |
| Tibia | | | | |
| Midshaft | I[a] | Hartman [43] | −0.6 (1.6) | >0.05[b] |
| | II[a] | Hartman [43] | −0.5 (1.4) | >0.05[b] |
| Lumbar spine | | | | |
| Not reported | III | *Henderson [3] | *−1.5 (0.9[b])* | <0.001[b] |
| Radius | | | | |
| Distal third | I[a] | Hartman [43] | *−1.7 (0.5)* | <0.01[b] |
| | II[a] | Hartman [43] | −0.9 (1.3) | <0.05[b] |

[a]Obtained from first author.
[b]Calculated based on mean, standard deviation and sample size; studies indicated with a * demonstrate a high quality study. Additional *Z*-score ≤ −1.0 are in italics; distal femur region 2: transition between metaphysis and diaphysis (mixture of cortical and trabecular bone); GMFCS: Gross Motor Function Classification System [18].

***Distal femur.*** Three high-quality studies [30,31,37] reported BMD of the distal femur in children with different GMFCS levels (Tables 3 and 4). Two studies [31,37] reported BMD results in region 2 (mixture of cortical and trabecular bone); one study [30] did not report the specific region of BMD measurement. For GMFCS level I, no low BMD was reported, neither regarding *Z*-score ≤ −2.0 nor regarding *Z*-score ≤ −1.0. For GMFCS level II, Finbråten et al. [37] reported low BMD (*Z*-score −2.8, SD 1.2, $p < 0.001$), whereas Chen et al. [31] reported no low BMD according to *Z*-score ≤ −2.0. For GMFCS levels I, II, and III combined, Finbråten et al. [37] reported no low BMD according to *Z*-score ≤ −2.0 (*Z*-score −1.6, SD 1.8, $p < 0.001$). According to the best-evidence synthesis regarding *Z*-score ≤ −2.0 and *Z*-score ≤ −1.0, there was conflicting evidence for low BMD of the distal femur in children with GMFCS level II. Furthermore, there was no evidence for low BMD of the distal femur in children with GMFCS level I, GMFCS level III, or in a group

**Table 6.** Bone mineral density results for adults.

| Measurement location | GMFCS | Study | Z-score (SD) | *p* value |
|---|---|---|---|---|
| Proximal femur | | | | |
| Total proximal femur | I–II | *Fowler [38] | −0.86 (1.0) | <0.01[a] |
| | III | *Fowler [38] | *−1.23 (0.9)* | <0.01[a] |
| | I–II–III (spastic) | Kim [34] | *−1.2 (1.0)* | =0.001[a] |
| | I–II–III (dyskinetic) | Kim [34] | −0.4 (1.0) | >0.05[a] |
| Femur neck | I–II | *Fowler [38] | −0.75 (1.1) | <0.05[a] |
| | III | *Fowler [38] | −0.54 (1.5) | >0.05[a] |
| | I–II–III (spastic) | Kim [34] | −0.7 (0.9) | <0.05[a] |
| | I–II–III (dyskinetic) | Kim [34] | −0.2 (1.0) | >0.05[a] |
| Lumbar spine | | | | |
| Not reported | I–II | *Fowler [38] | *−1.07 (1.0)* | <0.001[a] |
| | III | *Fowler [38] | −0.98 (0.8) | <0.01[a] |
| L1–L4 | I–II–III (spastic) | Kim [34] | −0.9 (1.3) | <0.05[a] |
| | I–II–III (dyskinetic) | Kim [34] | −0.1 (1.1) | >0.05[a] |
| L4 | I–II–III (cortical) | Peterson [39] | −0.69[a] (1.1[a]) | <0.05[a] |
| | I–II–III (trabecular) | Peterson [39] | −0.56[a] (1.1[a]) | <0.05[a] |

[a]Calculated based on mean, standard deviation and sample size; studies indicated with a * demonstrate a high quality study. Additional *Z*-score $\leq -1.0$ are in italics; GMFCS: Gross Motor Function Classification System [18].

combining GMFCS levels I, II, and III regarding *Z*-score $\leq -2.0$. According to the best-evidence synthesis regarding *Z*-score $\leq -1.0$, there was moderate evidence for low BMD of the distal femur in a group combining GMFCS levels I, II and III and no evidence for low BMD for GMFCS levels I and III.

The high-quality study of Henderson et al. [3] reported distal femur results (region 2, a mixture of cortical and trabecular bone) in a sample that included persons up to 19 years of age with GMFCS level III. Regarding *Z*-score $\leq -2.0$, no low BMD was reported; however, Henderson et al. [3] reported a *Z*-score of −1.8, (SD 1.3, $p < 0.001$). According to the best-evidence synthesis regarding *Z*-score $\leq -2.0$, there was no evidence for low BMD of the distal femur in a combined group of children and adults up to 19 years of age with GMFCS level III. According to the best-evidence synthesis regarding *Z*-score $\leq -1.0$, there was moderate evidence for low BMD of the distal femur in a group combining children and adults up to 19 years of age with GMFCS level III.

### *Calcaneus*

The high-quality study of Chen et al. [30] and the low-quality study of Wilmshurst et al. [36] reported BMD results of the calcaneus in children with different GMFCS levels (Tables 3 and 4). In a group with GMFCS levels I and II combined, Wilmshurst et al. [36] and Chen et al. [30] reported no low BMD regarding *Z*-score $\leq -2.0$. However, Wilmshust et al. [36] reported a *Z*-score of −1.07, SD 1.0, $p < 0.01$. Likewise, no low BMD was reported regarding *Z*-score $\leq -2.0$ in the GMFCS level III group, but the studies by Wilmshurst et al. [36] (*Z*-score −1.85, SD 1.0, $p < 0.05$) and Chen et al. [30] (*Z*-score −1.71, SD 0.7, $p < 0.001$) reported low BMD regarding *Z*-score $\leq -1.0$. According to the best-evidence synthesis regarding *Z* score $\leq -2.0$, there was no evidence for low BMD of the calcaneus in children in a combined group with GMFCS levels I and II or GMFCS level III group. According to the best-evidence synthesis regarding *Z*-score $\leq -1.0$, there was conflicting evidence for low BMD of the calcaneus in children in a combined group with GMFCS level I and II. In addition, there was moderate evidence for low BMD of the calcaneus in children with GMFCS level III.

We found no studies regarding BMD of the calcaneus in adults (GMFCS I–III) (Tables 5 and 6).

### *Radius*

The low-quality study of Hartman et al. [43] reported BMD results of the radius in a sample of persons up to 29 years of age with GMFCS levels I and II (Tables 3 and 5). According to *Z*-score $\leq -2.0$, no low BMD was reported for GMFCS level I (*Z*-score –1.7, SD 0.5, $p < 0.01$) or GMFCS level II. According to the best-evidence synthesis regarding *Z*-score $\leq -2.0$, there was no evidence for low BMD of the radius in a group of children and adults up to 29 years of age with GMFCS level I or GMFCS level II. According to the best-evidence synthesis regarding *Z*-score $\leq -1.0$, there was limited evidence for low BMD of the radius in a group of children and adults up to 29 years of age with GMFCS level I and no evidence for GMFCS level II.

### *Tibia*

The low-quality study by Hartman et al. [43] reported BMD results for the tibia in a sample that included persons aged 1–29 years with GMFCS levels I and II (Tables 3 and 5). No low BMD was reported, not regarding *Z*-score $\leq -2.0$ nor regarding *Z*-score $\leq -1.0$ in GMFCS level I or GMFCS level II. According to the best-evidence synthesis regarding *Z*-score $\leq -2.0$ and $Z \leq -1.0$, there was no evidence for low BMD of the tibia in a combined group of children and adults up to 29 years of age with GMFCS level I and GMFCS level II.

### *Total body*

Two high-quality studies [37,42] reported BMD results of the total body for children with different GMFCS levels (Tables 3 and 4). Regarding *Z*-score $\leq -2.0$, for GMFCS level I, Finbråten et al. [37] reported no low BMD (*Z*-score −1.5, SD 0.9, $p < 0.001$). However, the same study showed low BMD for GMFCS level II (*Z*-score −2.2, SD 1.1, $p < 0.001$). In a group combining GMFCS levels I and II, Chad et al. [42] reported no low BMD. According to the best-evidence synthesis regarding *Z*-score $\leq -2.0$, there was moderate evidence for low BMD of the total body for children with GMFCS level II. There was no evidence for low BMD of the total body in children with GMFCS level I or in a combined group with GMFCS levels I and II. According to the best-evidence synthesis regarding *Z*-score $\leq -1.0$, there was moderate evidence for low BMD of the total body in children with GMFCS levels I and II and no evidence for BMD of the total body in a combined group with GMFCS levels I and II.

We found no studies regarding BMD of the total body in children with GMFCS III and in adults (GMFCS I–III) (Tables 5 and 6).

## Discussion

According to our primary best-evidence synthesis regarding a *Z*-score $\leq -2$, which follows the International Society For Clinical Densitometry [6,27], we found moderate evidence for low BMD of the total proximal femur in children with GMFCS III and of the total body in children with GMFCS level II. Furthermore, we found conflicting evidence for low BMD of the distal femur in children with GMFCS level II and of the lumbar spine in children with GMFCS level III. We found no evidence for low BMD in children with GMFCS I, in adults, or in other parts of the body. However, *Z*-scores $\leq -1$ were found in several parts of the body and in several groups. Although this cutoff value is not in accordance with the criteria of the International Society for Clinical Densitometry [6,27], it may indicate a tendency towards low BMD and may be clinically important considering timely prevention. In addition, it is unknown whether BMD *Z*-score $> -2$ is associated with more fragility or increased fracture risk [6,27].

The moderate evidence we found for low BMD of the total proximal femur in children with GMFCS level III is consistent with our expectations, as the duration and number of standing and walking activities decreases with worsening gross motor functioning [9]. In contrast, there was no evidence for low BMD of the total proximal femur for adults with GMFCS level III. However, the best-evidence synthesis regarding *Z*-score $\leq -1.0$ suggests a tendency towards low BMD of the total proximal femur in adults with GMFCS level III. In addition, this secondary analysis showed limited evidence for a tendency towards low BMD of the total proximal femur in a combined group of adults with spastic type CP with GMFCS I–II–III.

The finding of moderate evidence for low BMD of the total body in children with GMFCS II was surprising, because we did not find evidence for low BMD in children with GMFCS II in most parts of the body except for the distal femur (conflicting evidence, same result for the best-evidence synthesis regarding *Z*-score $\leq -1.0$). This finding of conflicting evidence for the distal femur was also remarkable because we found no evidence for low BMD in the same region in children with GMFCS level III .However, the best-evidence syntheses regarding *Z*-score $\leq -1$ pointed at a tendency towards low BMD in several groups and in several regions, which may explain the above discrepancy.

Several studies explored BMD in non-ambulatory persons with CP (GMFCS IV–V), [3,16,17,30,32,35,37,44]. These studies focused primarily on BMD of the femur and lumbar spine in children, and generally showed that low BMD is a serious problem in children with severe CP [3,16,17,32,42]. The BMD *Z*-score in these studies ranged from $-2.4$ to $-3.8$ for the femur and from $-1.8$ to $-2.2$ for the lumbar spine. Compared with these studies, the average BMD deficits we found in ambulatory persons with CP were less severe. It is worth mentioning that this study focuses on mean *Z*-scores from various studies, while variability between subjects within a study exists, as some individuals will have lower *Z*-scores than the mean while others will have higher scores. Our findings are in line with our expectations, as nutritional problems, epilepsy, and inactivity (including fewer weight-bearing activities) occur less frequently in ambulatory persons with CP [9,10,19,30,38].

For non-ambulatory children at risk for low BMD, regular BMD evaluation and vitamin D and calcium intake optimization is advised [16]. One might argue to also use a similar strategy in ambulatory children with CP (particularly for GMFCS II and III). However, although nutritional adaptations may improve BMD, it is yet unclear whether this results in fewer fractures [45]. It is also unclear to what extent nutritional problems and medication determine low BMD in ambulatory persons with CP. Given the generally low activity levels in ambulatory persons with CP, a more active lifestyle with more weight-bearing activities is a potential strategy to improve BMD as well. Because the literature on BMD in ambulatory persons with CP, particularly adults, is scarce, more research is required before specific recommendations can be made for treatment in this population. Future research should also address fracture risk because the literature on the relationship between low BMD and fractures is limited and conflicting, and is primarily based on retrospective self-reports [12,46,47].

The strength of our systematic review is that we retrieved and combined data from available studies on BMD from various countries. However, some limitations should be mentioned: (1) dual X-ray absorptiometry was the most frequently used method for measuring BMD, but other methods were also used. The International Society for Clinical Densitometry stated in 2013 that dual X-ray absorptiometry is the preferred method for clinical densitometry evaluation in children and adults [27]. However, the dual X-ray absorptiometry scan has limitations. The bone is a three-dimensional structure that is measured two-dimensionally by dual X-ray absorptiometry; this can lead to underestimation of BMD in small bones and overestimation of BMD in large bones [26,48–50]. The QCT measures volumetric BMD but, because of limited reference data and higher radiation dose, this method is not regularly used [26,48,49]. There are also limited reference data for ultrasound. (2) Muscle and joint contractures may have influenced BMD measurements. McDowell et al. [51] reported a significant reduction of the passive range of motion with increasing functional limitation. Scoliosis and metallic implants may also have limited BMD measurements. The risk of developing scoliosis also increases with increasing functional limitations [52]. (3) In most studies, participants were recruited from only one hospital or rehabilitation center, which may have resulted in selection bias. Only the high-quality study of Henderson et al. [3] included participants from multiple centers. Furthermore, studies focused primarily on children. (4) Because of the heterogeneity of CP, we decided to present the evidence as much as possible by GMFCS level. This grouping often resulted in small sample sizes per level. Because not all studies used the GMFCS classification, we had to infer GMFCS level in some studies. (5) Some research groups have published several articles on BMD, so we had to use our own judgment regarding study inclusion in those cases. (6) Most studies did not focus on differences in BMD between ambulatory persons with CP (GMFCS I–III) and typically developing persons, but on differences between persons with CP across all GMFCS levels, including non-ambulatory persons, and typically developing persons. Therefore, we had to calculate significance levels for several studies. (7) Finally, five of the included studies only presented average BMD (SD) levels in persons with CP and typically developing persons. Thus, we had to calculate average (SD) *Z*-score from these data. Because we only included studies containing a typically developing group $\geq$15 persons, we expect only a minor effect of this procedure on our conclusions.

In conclusion, we found moderate and conflicting evidence for low BMD of several body parts (total proximal femur, total body, distal femur, and lumbar spine) in children with GMFCS II and III. This suggests that mainly children with GMFCS II and III are vulnerable to low BMD. However, the results of the secondary best-evidence syntheses for *Z*-score $\leq -1.0$, suggest a tendency towards low BMD in other regions than the above in children with GMFCS II and III and also in children with GMFCS I and adults. Although more high-quality research is needed, including

adults and fracture risk assessment, the current study indicates that deficits in BMD are not restricted to non-ambulatory people with CP.

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