

# Bone mass in male and female children and adolescents with Down syndrome

A. González-Agüero · G. Vicente-Rodríguez ·  
L. A. Moreno · J. A. Casajús

Received: 13 July 2010 / Accepted: 13 September 2010

© International Osteoporosis Foundation and National Osteoporosis Foundation 2010

## Abstract

**Summary** Children and adolescents with Down syndrome (DS) have lower levels of bone mass compared with youths without DS. Their sexual dimorphism in bone mass also differs from that observed in children and adolescents without Down syndrome.

**Introduction** This study aimed to compare bone mass and sexual dimorphism in bone mass between male and female youths with DS and age- and sex-matched controls without DS.

**Methods** Bone mineral density (BMD), volumetric BMD, bone mineral apparent density (BMAD), BMD/height (BMDH), and total lean mass were measured or calculated from DXA. Thirty-two youths (15 females) with DS and 32 youths (13 females) without DS participated in the study.

**Results** ANOVA tests showed lower BMAD and BMDH in females with DS compared with females without DS. ANCOVA tests revealed lower BMD in the whole body of males and females as well as BMD in the hip region of the females with DS compared with their counterparts without DS. Within the group with DS, females had greater lumbar spine BMD than the males.

**Conclusions** The low values of BMD and related parameters, together with the differences in the sexual dimorphism, indicate a non-standard bone development in this specific population of children and adolescents with DS.

**Keywords** Body composition · DXA · Hip · Lumbar spine · Sexual dimorphism · Trisomy 21

A. González-Agüero · G. Vicente-Rodríguez · L. A. Moreno ·  
J. A. Casajús (✉)

GENUD (Growth, Exercise, Nutrition and Development)  
research group, University of Zaragoza,  
Ed. Cervantes. Corona de Aragón St. 42, 2nd floor,  
50009 Zaragoza, Spain  
e-mail: joseant@unizar.es

A. González-Agüero  
e-mail: alexgonz@unizar.es

G. Vicente-Rodríguez  
e-mail: gervicen@unizar.es

L. A. Moreno  
e-mail: lmoreno@unizar.es

A. González-Agüero · G. Vicente-Rodríguez · J. A. Casajús  
Faculty of Health and Sport Sciences, Huesca,  
University of Zaragoza,  
Zaragoza, Spain

L. A. Moreno  
School of Health Sciences, University of Zaragoza,  
Zaragoza, Spain

## Introduction

Life expectancy in Down syndrome (DS) population has increased over the last 70 years, rising from 9 years of age to as much as 55 years and older, and this trend is expected to continue [1–3]. As the life expectancy of populations with DS increases, a reasonable prediction would show an increased incidence in osteoporosis, bone fragility and related problems (which appear mainly with age) over the coming years.

High bone mass acquisition during childhood and adolescence is a key determinant for adult skeletal health [4, 5], and populations with DS have shown decreased bone mass compared with subjects without intellectual disabilities (ID) [6–11] as well as others with ID but without DS [12, 13]. However, only a few of these studies have included children and adolescents with DS [7, 8], or specifically examined a pediatric population [10, 13], that commonly display lower values of bone mineral content (BMC) and bone mineral density (BMD) compared with peers without

DS. Despite these studies, information concerning bone mass in pediatric population with DS is scarce [14] and should therefore be given greater attention, since low bone mass (osteopenia or osteoporosis) in adulthood may be a direct result of low acquisition during growth.

Previous studies showed sexual dimorphism in bone mass during growth in healthy populations [15]. In adults with DS, lower lumbar spine BMC, BMD, and volumetric BMD (vBMD) in males compared with females [6, 8, 12] have been observed; however, there is a lack of information in children or adolescents with DS. Since adult population with DS generally possess low bone mass, it would be of significant benefit to elucidate whether the acquisition of bone mass could be identified earlier, for example, in childhood and adolescence. Furthermore, one crucial aspect of such a study would investigate and detect sensitive growth periods that could correspond to a reduced level of bone mass acquisition.

The law of Wolff postulates that bones adapt to mechanical loads [16], and bone development seems to be site-specific [17, 18]. Consequently, it is very important to describe bone mass for the different regions of the body, which have not been previously studied in children and adolescents with DS. A study of this latter population could help to detect critical zones with low BMD in populations with DS in order to establish targeted interventions to improve bone mass. The aim of this study is to describe the total and regional (lumbar spine, hip, and femoral neck) bone mass in male and female children and adolescents with DS compared with age-matched subjects without DS.

## Materials and methods

### Subjects

A total sample of 32 children (15 females, 17 males) and adolescents with DS living at home, between 10 and 19 years were recruited from different special schools and institutions within the same region of Aragón in Spain. Another individually age-matched sample of 32 subjects (13 females, 19 males) without DS was also recruited from regular schools in this region. All the children without DS were healthy and without known illness, and all subjects had been medication-free for at least 3 months before the tests. A full clinical history, including illnesses or surgical interventions and stays in a hospital, was collected for each individual. Eight participants with DS had been diagnosed of hypothyroidism in the past; however, during the study, they were taking medication (levothyroxine sodium: four of them taking Levothroid and the other four, Eutirox). Both parents and children were informed about the aims and procedures of the study, as well as the possible risks and

benefits, and then, a letter of written informed consent was obtained from all the included subjects and their parents or guardians. The study was performed in accordance with the Helsinki Declaration 1961 (revised in Edinburgh, 2000) and was approved by the Research Ethics Committee of the Government of Aragón (CEICA, Spain).

### Anthropometric

All subjects were measured with a stadiometer without shoes and the minimum clothes to the nearest 0.1 cm (SECA 225, SECA, Hamburg, Germany), and weighted to the nearest 0.1 kg (SECA 861, SECA, Hamburg, Germany). WC was measured to the nearest 0.1 cm with an anthropometric tape (Rosscraft, Canada). Body mass index (BMI) was calculated as weight (in kilograms) divided by height (square meters).

### Pubertal status assessment

Pubertal development was determined by direct observation according to the five stages proposed by Tanner and Whitehouse [19].

### Bone and lean masses

The bone and lean masses of the subjects were measured with dual-energy X-ray absorptiometry (DXA) using a pediatric version of the software QDR-Explorer (Hologic Corp. Software version 12.4, Waltham, MA). DXA equipment was calibrated with a lumbar spine phantom and step densities phantom following the Hologic guidelines. Subjects were scanned in supine position, and the scans were performed in high resolution. Osseous area (square centimeters), BMC (in grams), and lean mass (in kilograms) were calculated from total and regional analysis of the whole body scan. BMD (grams per square centimeter) was calculated using the formula  $BMD = BMC/area^{-1}$ .

Two additional examinations were conducted to estimate bone mass at the lumbar spine (L<sub>1</sub>–L<sub>4</sub>) and proximal region of the femur (hip and femoral neck). Volumetric BMD (vBMD) was estimated for the lumbar spine and femoral neck using simple geometric cylindrical models [20], previously used with this population [8]. Bone mineral apparent density (BMAD) was calculated as previously described [21], using the formula whole body BMAD = BMC/(area<sup>2</sup>/body height). The expression BMD/height (BMDH) was calculated to adjust bone mass for whole body bone size [22].

### Statistical analysis

Mean and standard deviation are given as descriptive statistics, otherwise stated.

The variables showed normal distributions. ANOVA was used to test hypothesis regarding the equality of the means between groups for the following characteristics: age, weight, height, BMI, total lean mass, vBMD of the lumbar spine and femoral neck, BMAD, and BMDH. Analyses of covariance were performed to evaluate differences in BMD, entering Tanner stage, height, and whole body lean mass as covariates. The use of these covariates is based on evidence identifying pubertal status, height, and total lean mass as influential factors on muscle mass and bone mass in the growing skeleton [23–25]. Effect size statistics using Cohen's *d* (standardized mean difference) were calculated [26]. Taking into account the cutoff established by Cohen, the effect size can be small (~0.2), medium (~0.5), or large (~0.8).

The SPSS 15.0 software for Windows (SPSS Inc. Chicago, IL) was used for the analyses and the significance level was 5%.

## Results

All the analyses were conducted from the whole sample, and, in addition, excluding the eight subjects that reported past disease of hypothyroidism (data not shown); as results did not substantially change, the data presented herein correspond to the whole sample to keep sample size. Additionally, no differences were observed in any of the studied variables between DS subjects with and without past disease of hypothyroidism within our sample (data not shown).

### Physical characteristics

The characteristics of the groups with and without DS are summarized in Table 1. In general, subjects, both male and female with DS were lighter, smaller, and had lower lean mass compared with non-DS peers (all  $p < 0.05$ , Table 1).

### Bone mass

Appendix 1 summarizes the raw values of BMD of the subjects.

After adjusting the raw values by Tanner stage, height, and total lean mass, females and males with DS showed lower BMD in whole body than their counterparts without DS; females with DS also presented lower BMD in the hip (all  $p < 0.05$ ; Fig. 1).

Females with DS showed lower BMAD and BMDH than the females without DS (all  $p < 0.05$ ; Table 2). However, no differences were found in vBMD of lumbar spine or femoral neck between females or males with and without DS (Table 2).

### Differences between sexes within the same group

Figure 2 shows the differences in BMD between females and males within the groups with and without DS after adjusting by Tanner stage, height, and total lean mass. Lumbar spine BMD was higher in females than in males in the group with DS (both  $p < 0.05$ ; Fig. 2a).

All the previous comparisons exhibited large effect sizes (Cohen's *d* ranged from 0.9 to 1.5).

## Discussion

The principal finding of the present study is that children and adolescents with DS showed lower values of BMD and related parameters compared with age-matched subjects without DS. In doing so, it also shows that males with DS have lower BMD in lumbar spine than females with DS.

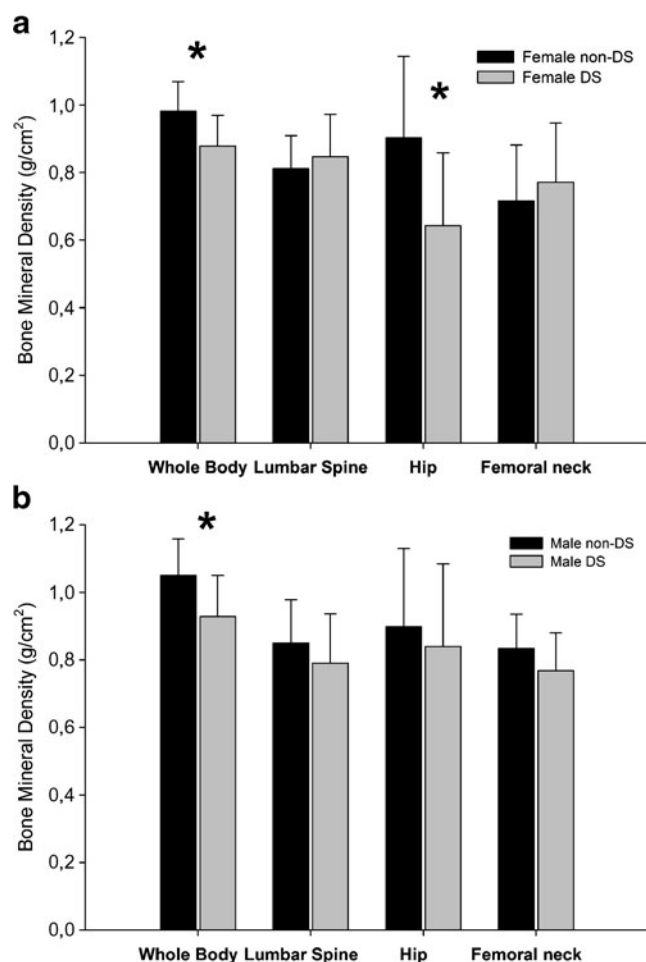
### Differences between with and without DS

To date, several studies have described lower bone mass in populations with DS compared with others without DS, with or without ID [6–13]. Osteoporotic problems in

**Table 1** Subject age, anthropometrics, total lean, and maturation status results (mean±standard deviation)

	Down syndrome			Without Down syndrome		
	All ( <i>n</i> =32)	Female ( <i>n</i> =15)	Male ( <i>n</i> =17)	All ( <i>n</i> =32)	Female ( <i>n</i> =13)	Male ( <i>n</i> =19)
Age (years)	15.3±2.9	14.9±3.2	15.6±2.7	14.7±2.3	14.6±2.4	14.8±2.2
Sexual maturation: Tanner (%) stages I/II/III/IV/V	16/6/22/9/47			13/6/13/19/50		
Weight (kg)	46.0*±11.8	42.8±12.5	48.7*±10.9	55.6±13.1	53.2±13.8	57.3±12.7
Height (cm)	145.2*±11.8	138.5*†±10.1	150.7*±10.3	163.3±12.3	156.7†±9.6	167.8±12.1
Body mass index (kg/m <sup>2</sup> )	21.5±3.4	21.8±4.0	21.2±2.8	20.6±3.6	21.4±4.5	20.1±2.7
Total lean mass (kg)	32.6*±8.3	27.7*†±7	36.6*±7.2	39.4±9.8	34.2†±6.7	42.9±10.2

\* $p < 0.05$  between groups; † $p < 0.05$  between genders within the same group



**Fig. 1** **a** Females bone mass. Tanner stage-, total lean mass-, and height-adjusted BMD from the whole body, lumbar, and femoral scans in females with and without DS. \* $p < 0.05$ . **b** Males bone mass. Tanner stage-, total lean mass-, and height-adjusted BMD from the whole body, lumbar, and femoral scans in males with and without DS. \* $p < 0.05$

populations with DS are well documented in adults [6, 9, 11, 12]; however, very few studies have included children or adolescents [7, 8], and even fewer have studied them specifically [10, 13].

The current investigation analyzes the biggest sample of children and adolescents with DS to date and considering bone regions in the analysis. Our results showed lower BMD in male and female children and adolescents with DS compared with children and adolescents without DS. The results also suggest that differences in height—therefore in bone size—between children and adolescents with and without DS are largely responsible for the differences in BMD.

The studies from Sepulveda et al. [9] and Guijarro et al. [11] described lower BMD in the pelvic region and whole body, respectively, in individuals with DS compared with those without DS. Our results corroborate these findings as we also found lower values of BMD in the whole body of males and females with DS compared with those without DS.

Previous studies in individuals with DS [6–11] clearly observed lower BMD in the lumbar spine of adults and young adult females with DS compared with females without DS. From all of them, only Kao et al. [10] studied an exclusive sample of only ten children with DS. Baptista et al. [8] divided their sample in age groups older and younger than 20 years and did not find differences in lumbar spine BMD in the younger group. In agreement with Baptista et al. [8], we found no observable differences in the lumbar spine of children and adolescents with DS compared with children and adolescents without DS. Most of the previous studies in adults with DS observed lower BMD in lumbar spine compared with adults without DS, which may therefore suggest that this decreased BMD could appear after puberty, since this period may be a key moment to enhance bone mass.

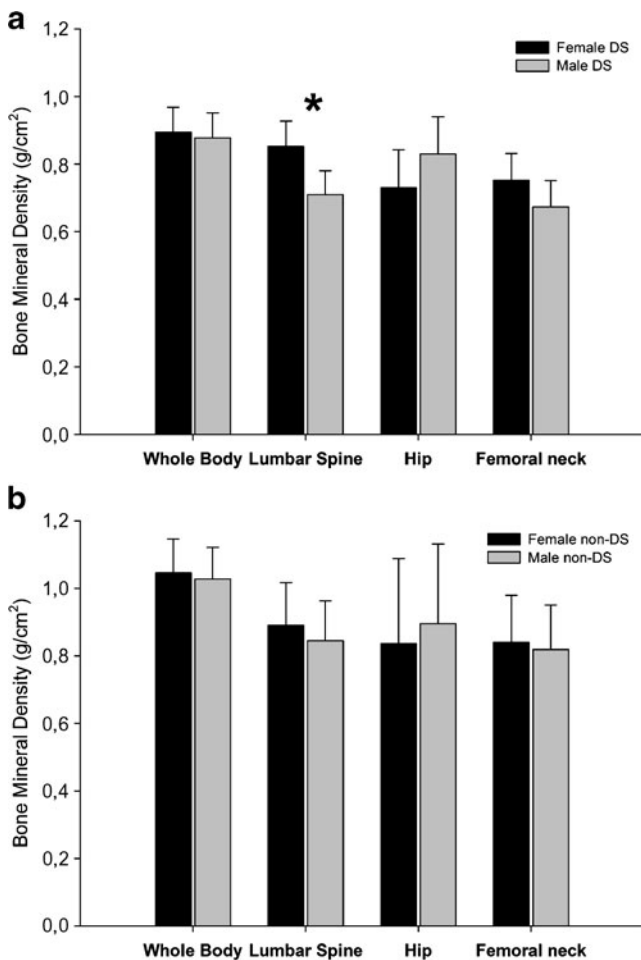
Regions such as the hip, especially the femoral neck, are very important areas to be studied because they are considered as ‘risk regions’ for osteoporosis and bone fracture. Guijarro et al. [11] found lower values of BMD in the femoral neck and total hip in the group with DS compared with the group without DS. Our results reinforce these, as we also described lower values of

**Table 2** Calculated variables of bone mass (mean±standard deviation)

	Down syndrome			Without Down syndrome		
	All ( $n=32$ )	Female ( $n=15$ )	Male ( $n=17$ )	All ( $n=32$ )	Female ( $n=13$ )	Male ( $n=19$ )
Lumbar spine vBMD (g/cm <sup>3</sup> )	0.26±0.05	0.24±0.05	0.27±0.05	0.27±0.05	0.27±0.06	0.27±0.04
Femoral neck vBMD (g/cm <sup>3</sup> )	0.32±0.04	0.33±0.03	0.32±0.04	0.32±0.05	0.33±0.06	0.31±0.03
Bone mineral apparent density (g/cm <sup>3</sup> )	0.088*±0.008	0.085*±0.008	0.090±0.008	0.092±0.006	0.092±0.004	0.092±0.006
BMDH (g/cm <sup>3</sup> )	0.61±0.05	0.61*±0.04	0.61±0.06	0.63±0.05	0.64±0.04	0.62±0.06

vBMD volumetric bone mineral density, BMDH bone mineral density/height

\* $p < 0.05$  between groups



**Fig. 2** **a** Down syndrome bone mass. Tanner stage-, total lean mass-, and height-adjusted BMD from the whole body, lumbar, and femoral scans in males and females with DS. \* $p < 0.05$ . **b** Controls bone mass. Tanner stage-, total lean mass-, and height-adjusted BMD from the whole body, lumbar, and femoral scans in males and females without DS. \* $p < 0.05$

BMD in the hip of females with DS compared with their peers without DS.

Although BMD has been shown to be a useful predictor of future fracture risk, vBMD provides a better approach to the real bone due to the limitations of the projected bone when very different populations (differences in height) are evaluated [27]. Guijarro et al. [11] and Baptista et al. [8] found lower vBMD at lumbar spine and femoral neck of adults with DS; as we did not find this, it is plausible to think that the lower vBMD in the population with DS appears with age and is not present during childhood and adolescence possibly due to impaired mineralization. To the best of our knowledge, the bone parameters BMAD and BMDH had not been used previously in populations with DS; these better reflect bone apparent density and take into account the height of the subjects [21, 22]. In the present study, females with DS showed lower levels of BMAD and

BMDH. This tends to suggest that young females with DS have a poorer bone development than young males with DS when each sex is separately compared with their counterparts without DS. Therefore, low BMD is already detected in females and partially in males with DS, although this disadvantage clinical situation may aggravate with growth. Several authors described childhood and adolescence as the most important periods to accumulate BMD in the skeleton [24] and, specifically, peak BMD is reached between 20 and 25 years. As children and adolescents with DS already have lower values of BMD, efforts to develop physical activity programs, which may enhance bone mass, should be considered. Strength or plyometric exercise may be beneficial for this population, although more detailed research on this topic is required.

#### Sexual dimorphism in children and adolescents with DS

Previous comparisons between bone mass of males and females, mainly in adults, with DS have been conducted [6, 8]. Angelopoulou et al. [6] and Baptista et al. [8] observed higher values of BMD in lumbar spine in adult females with DS compared with males with DS. Our study shows that those findings are already detectable in children and adolescents, showing higher values of BMD in the females with DS at the lumbar spine compared with males with DS.

Additionally, the differences between males and females in the group without DS were not the same of that observed between males and females with DS. These results indicate that bone mass acquisition during puberty seems to be different in children and adolescents with DS than in those without, also in terms of sexual dimorphism. Therefore, an independent study of this population is required in order to understand specific bone development and growth within the group.

Some limitations should be recognized. Despite that the number of participants is bigger than the majority of the previous published studies in children and adolescents with DS, the specificity of the condition and the age range become complicated, increasing the sample size. Therefore, the group may not be large enough to generalize the results of gender comparison. As strength of our study, the large effect size observed in the differences (between groups and between sexes) indicates a substantial biological magnitude of the results, which, in turn, may point out the direction of future research. The cross-sectional design is another limitation of this study; therefore, bone development cannot be studied. A longitudinal research of children with DS could help to corroborate the hypothesis that the low bone mass observed is due to a lower acquisition in the population with DS during the most important years of accumulation. However, this is the first investigation assessing BMD,

estimated vBMD, and apparent density in whole body and key subregions in a relatively large sample of male and female children and adolescents with DS and could serve as a starting point for further, even more detailed research.

## Conclusions

The current study provides evidence that children and adolescents with DS have a clear tendency towards lower BMD and vBMD in several regions of their bodies compared with age- and sex-matched subjects without DS. The lower values in BMAD and BMDH suggest that young females with DS are poorer at acquiring bone mass than young males with DS, when compared with their age- and sex-matched controls. Importantly, this is the first time that differences in bone mass between male and female children and adolescents with DS have been studied and compared. These results show that sexual dimorphism in bone mass is evident, and it is different than that observed in the children and adolescents without DS. The low levels of BMD, together with the differences in the sexual dimorphism, indicate a different bone

development in this specific population of children and adolescents with DS.

Longitudinal studies aiming to identify critical periods of bone development specifically in population with DS may corroborate the hypothesis presented in this study.

Further studies assessing other factors related to bone mass development during puberty, such as physical activity, physical fitness, or diet, could be beneficial in helping us understand the importance of lifestyle on the lower bone mass observed in populations with DS.

**Acknowledgment** The authors want to thank all the children and their parents who participated in the study, for their understanding and dedication to the project. Special thanks are given to Fundación Down Zaragoza and Special Olympics Aragon for their support. We also thank Scott G. Mitchell from the University of Glasgow for his work of reviewing the English style and grammar, and Paula Velasco from the University of Zaragoza for her great technical assistance. This work was supported by Gobierno de Aragón (Proyecto PM 17/2007) and Ministerio de Ciencia e Innovación de España (Red de investigación en ejercicio físico y salud para poblaciones especiales-EXERNET-DEP2005-00046/ACTI). There are no potential conflicts of interest that may affect the contents of this work.

**Conflicts of interest** None.

## Appendix 1

**Table 3** Mean and standard deviation in raw values of bone mineral density of children and adolescents with and without Down syndrome

	Female		Male	
	DS ( <i>n</i> =15) mean±SD	Non-DS ( <i>n</i> =13) mean±SD	DS ( <i>n</i> =17) mean±SD	Non-DS ( <i>n</i> =19) mean±SD
Bone mineral density (g/cm <sup>2</sup> )				
Whole body	0.845±0.086	1.014±0.109	0.928±0.127	1.049±0.128
Lumbar spine	0.762±0.118	0.873±0.154	0.788±0.146	0.857±0.151
Hip zone	0.697±0.086	0.847±0.198	0.834±0.115	0.888±0.177
Femoral neck	0.680±0.070	0.786±0.153	0.741±0.113	0.858±0.112

DS Down syndrome, non-DS without Down syndrome, SD standard deviation

## References

- Bittles AH, Glasson EJ (2004) Clinical, social, and ethical implications of changing life expectancy in Down syndrome. *Dev Med Child Neurol* 46:282–286
- Glasson EJ, Sullivan SG, Hussain R, Petterson BA, Montgomery PD, Bittles AH (2002) The changing survival profile of people with Down's syndrome: implications for genetic counselling. *Clin Genet* 62:390–393
- Smith DS (2001) Health care management of adults with Down syndrome. *Am Fam Physician* 64:1031–1038
- Rizzoli R, Bonjour JP (1999) Determinants of peak bone mass and mechanisms of bone loss. *Osteoporos Int* 9(Suppl 2):S17–S23
- Rizzoli R, Bianchi ML, Garabedian M, McKay HA, Moreno LA (2010) Maximizing bone mineral mass gain during growth for the prevention of fractures in the adolescents and the elderly. *Bone* 46:294–305
- Angelopoulou N, Souftas V, Sakadamis A, Mandroukas K (1999) Bone mineral density in adults with Down's syndrome. *Eur Radiol* 9:648–651
- Sakadamis A, Angelopoulou N, Matziari C, Papameletiou V, Souftas V (2002) Bone mass, gonadal function and biochemical

- assessment in young men with trisomy 21. *Eur J Obstet Gynecol Reprod Biol* 100:208–212
8. Baptista F, Varela A, Sardinha LB (2005) Bone mineral mass in males and females with and without Down syndrome. *Osteoporos Int* 16:380–388
  9. Sepulveda D, Allison DB, Gomez JE, Kreibich K, Brown RA, Pierson RN Jr, Heymsfield SB (1995) Low spinal and pelvic bone mineral density among individuals with Down syndrome. *Am J Ment Retard* 100:109–114
  10. Kao CH, Chen CC, Wang SJ, Yeh SH (1992) Bone mineral density in children with Down's syndrome detected by dual photon absorptiometry. *Nucl Med Commun* 13:773–775
  11. Guijarro M, Valero C, Paule B, Gonzalez-Macias J, Riancho JA (2008) Bone mass in young adults with Down syndrome. *J Intellect Disabil Res* 52:182–189
  12. Angelopoulou N, Matziari C, Tsimaras V, Sakadamis A, Souftas V, Mandroukas K (2000) Bone mineral density and muscle strength in young men with mental retardation (with and without Down syndrome). *Calcif Tissue Int* 66:176–180
  13. Halaba Z, Pyrkosz A, Adamczyk P, Drozdowska B, Pluskiewicz W (2006) Longitudinal changes in ultrasound measurements: a parallel study in subjects with genetic disorders and healthy controls. *Ultrasound Med Biol* 32:409–413
  14. González-Agüero A, Vicente-Rodríguez G, Moreno LA, Guerra-Balic M, Ara I, Casajus JA (2010) Health-related physical fitness in children and adolescents with Down syndrome and response to training. *Scand J Med Sci Sports* 20:716–724
  15. Nguyen TV, Maynard LM, Towne B, Roche AF, Wisemandle W, Li J, Guo SS, Chumlea WC, Siervogel RM (2001) Sex differences in bone mass acquisition during growth: the Fels Longitudinal Study. *J Clin Densitom* 4:147–157
  16. Wolff J (1892) *The law of bone formation*. Hirschwald, Berlin
  17. Vicente-Rodríguez G, Jimenez-Ramirez J, Ara I, Serrano-Sanchez JA, Dorado C, Calbet JA (2003) Enhanced bone mass and physical fitness in prepubescent footballers. *Bone* 33:853–859
  18. Vicente-Rodríguez G, Ara I, Perez-Gomez J, Serrano-Sanchez JA, Dorado C, Calbet JA (2004) High femoral bone mineral density accretion in prepubertal soccer players. *Med Sci Sports Exerc* 36:1789–1795
  19. Tanner JM, Whitehouse RH (1976) Clinical longitudinal standards for height, weight, height velocity, weight velocity, and stages of puberty. *Arch Dis Child* 51:170–179
  20. Gravholt CH, Lauridsen AL, Brixen K, Mosekilde L, Heickendorff L, Christiansen JS (2002) Marked disproportionality in bone size and mineral, and distinct abnormalities in bone markers and calcitropic hormones in adult Turner syndrome: a cross-sectional study. *J Clin Endocrinol Metab* 87:2798–2808
  21. Katzman DK, Bachrach LK, Carter DR, Marcus R (1991) Clinical and anthropometric correlates of bone mineral acquisition in healthy adolescent girls. *J Clin Endocrinol Metab* 73:1332–1339
  22. Bachrach LK, Hastie T, Wang MC, Narasimhan B, Marcus R (1999) Bone mineral acquisition in healthy Asian, Hispanic, Black, and Caucasian youth: a longitudinal study. *J Clin Endocrinol Metab* 84:4702–4712
  23. Faulkner RA, Bailey DA, Drinkwater DT, McKay HA, Arnold C, Wilkinson AA (1996) Bone densitometry in Canadian children 8–17 years of age. *Calcif Tissue Int* 59:344–351
  24. Vicente-Rodríguez G (2006) How does exercise affect bone development during growth? *Sports Med* 36:561–569
  25. Slemenda CW, Miller JZ, Hui SL, Reister TK, Johnston CC Jr (1991) Role of physical activity in the development of skeletal mass in children. *J Bone Miner Res* 6:1227–1233
  26. Nakagawa S, Cuthill IC (2007) Effect size, confidence interval and statistical significance: a practical guide for biologists. *Biol Rev Camb Philos Soc* 82:591–605
  27. Carter DR, Boussein ML, Marcus R (1992) New approaches for interpreting projected bone densitometry data. *J Bone Miner Res* 7:137–145