



## **Influence of Adolescents' Physical Activity on Bone Mineral Acquisition: A Systematic Review Article**

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### **Abstract**

**Background:** This study conducted to examine and to provide a systematic literature over the influence of adolescents' physical activity (PA) in maximizing's peak bone mass (PBM). PBM or the 'bone bank' is an important determinant in achieving healthy bone. PA is one of the bone's lifestyle contributors and high PBM is one of the major strategies for preventing osteoporosis.

**Methods:** A computerized literature search using Medline (Ovid) and Scopus were conducted to identify relevant observational studies on the influence of different level of PA on bone acquisition among the healthy adolescent population. All articles included, were limited to original articles and English language.

**Results:** Nine studies met the inclusion criteria. Reported bone outcomes were of bone mass, bone structure and bone strength. Eight studies showed positive association between adolescents' PA and high bone variables. The influence of PA may differ according to sex, skeletal sites and bone outcomes.

**Conclusion:** This study supported the importance of increase adolescents' regular PA in optimizing PBM thus preventing osteoporosis at later life.

**Keywords:** Adolescence, Exercise, Peak bone mass, Bone health, Osteoporosis

### **Introduction**

Osteoporosis is a progressive systemic skeletal disease marked by low bone mass and micro-architectural deterioration of bone tissue resulting in bone fragility with increased susceptibility to fracture (1, 2). Osteoporosis incidence increases significantly with advancing age (3) and is usually silent without any signs and symptoms of decreasing bone density. Bone fracture often occurs as the first presentation of osteoporosis (4). Significant morbidity, cost and reduced quality of life have been attributed to osteoporosis (5). Preventive strategies are a crucial first step to over-

coming this global problem. Prevention of osteoporosis undertake by maximizing bone tissue accretion during growing yr, maintaining bone tissue acquisition during adulthood and reducing bone loss in elderly (6, 7).

During adolescence, peak bone mineral accrual occurs and continues to accumulate until PBM is achieved. PBM is the maximum accretion of bone mass and strength deposited in one's life at the end of the growth period (8). The time frame differs, either during the first two decades (9), early third decade (10), or late third decade (7) of

life or even as early as 16 yr old (11). After PBM was achieved, bone is lost at a rate of about 0.5%-1.0% per yr at most skeletal site (12). PBM together with subsequent bone loss are important determinants associated with risks of osteoporosis (13, 7).

Interestingly, adolescence offers a window of opportunity within the critical two-yr surrounding the age of peak bone mineral accrual (7). About 26% of adult peak total body bones mineral were accrued during this key time (14-16). Thus, adolescent years could be the final opportunity to maximize PBM. High PBM is an important determinant in preventing osteoporosis and risk of osteoporotic fracture (7, 17- 20).

Early detection and prevention to improve bone health will only be possible by identification of modifiable lifestyle factors that may augment bone mineral accrual. During this critical window, early detection could identify adolescents 'at-risk of low bone mass' followed by modifying lifestyle factors through lifestyle modification such as exercise.

Several modifiable lifestyle factors may contribute to adolescent bone health. These include Physical activity (PA), medications, body weight, healthy nutrition and other lifestyle factors such as smoking that can deteriorate bone health (10, 21). Exercise during the early stage of life plays an important role for the prevention of osteoporosis (22).

Exercise is often used interchangeably with PA because both share some common elements. Exercise is a sub-category of PA planned, structured, repetitive and purposive with an intention to improve or maintain physical fitness (23). On the other hand, PA is a parental term that covers all activities. By definition, PA is described as any bodily movement produced by skeletal muscles that require energy expenditure beyond resting expenditure. (23). There are four area of PA includes frequency, intensity (dose), time (duration), and type (load) or also known as (FITT). PA may involve some form of loading (weight-bearing) or free of loading (non-weight-bearing). Weight-bearing (WB) is defined as movement or type of exercise forces the body (muscle and

bones) to work against the force of gravity while carrying body weight such as walking, jogging or dancing (24).

Results from the high-quality reviews of controlled trials during the growing years had provided us with a better understanding on bone adaptation to weight bearing. However, interventional studies do not represent general population activities. Observational studies allow for comparison between different kinds of the same exposure to evaluate in the same population. Therefore, the purpose of this review was to examine relevant observational studies and to provide a systematic literature review over the influence of adolescents' PA in optimizing's bone health. High PBM and improve bone structure are two important determinant of bone strength. Strong bone mirrors healthy bone. Building healthy bone is thus the first step to overcome osteoporosis.

## Methods

A computerized literature search was conducted to identify relevant studies on the influence of adolescents' physical activities and weight-bearing activities towards bone health. To conduct a comprehensive search, two databases were used. Medline via Ovid Medline and SCOPUS published between 1946 to Feb 2016. The search strategy involved a combination of four sets of the following keywords:

1. bone density or bone strength or bone mass or bone health
2. exercise\* or physical activity\*
3. weight bearing or load bearing
4. adolescent\* or teenager\*

### *Selection of research articles*

Results generated by the two databases, were retrieved with the following inclusion and exclusion criteria. All relevant articles included in this study were limited to English language due to limited funding and resources for translation services. Multiple translators would need to be involved from the initial screening of title, abstract and to the complete article.

The following were the selection criteria for the present study: [1] observational studies [2] Healthy participants representing general adolescent population [3] exposure of PA should be measured in adolescents with age range from 8 to 20 yr.

While, study that focus on [1] Unhealthy subjects, postmenopausal women, adults, minority groups [2] intervention or controlled trial, organized activities, comparative study, specific exercise, [3] specific population: athletes (junior or elite), dancer or gymnast and [4] review articles, letter to editorial were excluded from the review.

### ***Data Extraction and management***

All articles generated by databases underwent three phases of screening. Three reviewers independently assessed all articles for inclusion in this review. Any articles not relevant to this study based solely upon the title were excluded in the first phase. In the second phase, duplicates from the two databases were removed and abstracts of the remaining titles were obtained. Remaining articles abstract were screened to further exclude articles that did not match the inclusion criteria and removed if fulfill exclusion criteria.

In the final phase, full articles from the remaining studies were retrieved, read entirely and assessed to ensure fulfillment of all the inclusion and exclusion criteria as well as quality assessment were performed. Papers extracted were from established journals with good impact factors. All three reviewers must agree that the full articles should be included in the review. Any differences in opinions were resolved in the discussion among the reviewers.

The following data were extracted from each study article: [1] study design; [2] sample population; [3] brief description of the study methods to measure exposure of interest and bone parameter; [4] brief description of the study results.

## **Results**

Computerized literature searches identified sixty-five potentially relevant articles. Fifty-six articles

were not included in the study. The reasons for exclusion were that studies failed to fulfill inclusion criteria number 1: children or mixed population of children and adolescent (n=6). Studies that match the exclusion criteria were as follow: studies that conducted among young adult (n=5), postmenopausal women (n=1), comparative studies between different types of sports and/or focused on athletes (n=16), and secondary studies (n=24) were also excluded from this review. Nine articles were retrieved for further assessment and data extraction. All nine articles retrieved fulfill the inclusion and exclusion criteria and therefore were included for the purpose of this study. A flow chart of study selection shows in Fig. 1.

### ***Study characteristics***

The description of the selected studies is shown in Table 1. Six were longitudinal studies (6, 25-29) and three were cross-sectional studies (30-32). Only one study was published before the year 1999 (25), whereas, the other eight were published in the year 2000 to 2015. Five studies were carried out in Europe (6, 25, 27, 29, 31) and the other four studies were conducted in Northern America (26, 28, 30, 32).

Two out of nine studies had sample size of fewer than 100 participants (28, 27) with only four studies (29- 32) had more than 400 participants. With three out of four studies were cross-sectional. Most of the studies had low sample size (n<200) due to high drop-out rates during the final measurements of longitudinal cohort studies (6, 25, 28).

From the nine studies selected, only one study was performed on males (6), three studies were carried out on the females (26, 27, 32), whereas, five studies included both gender (25, 28- 31).

The final nine articles include two types of bone densitometry. Five studies used Dual Energy X-Ray Absorptiometry (DEXA) as the method to evaluate Bone Mineral Density (BMD) (6, 25-27) and bone structural strength (28). Four studies used peripheral Quantitative Computed Tomography (pQCT) (29-32).

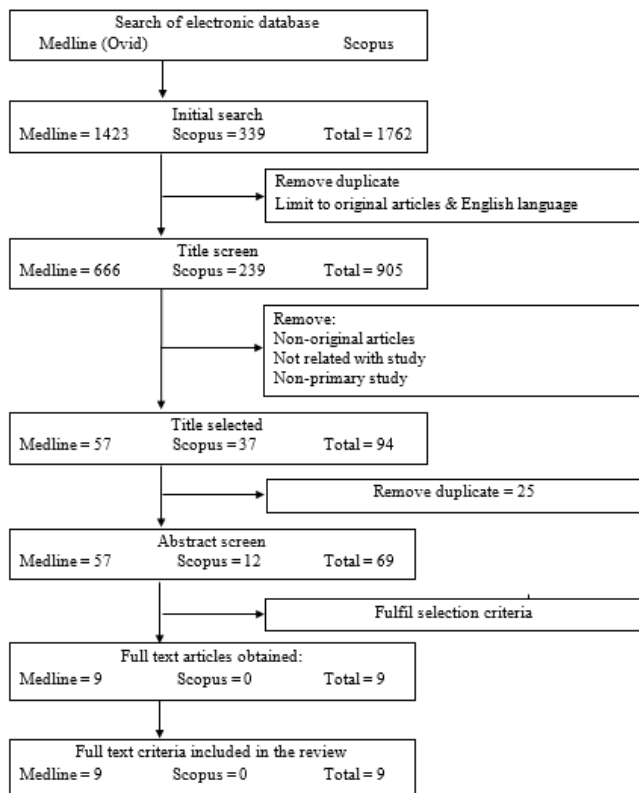


Fig. 1: Flow Chart showing selection process of the articles in this review

Different anatomical sites for evaluation were identified in this present review. Five different skeletal sites were found in five articles with DEXA as the method of bone evaluation. Total body (TB) (6, 26, 27), lumbar spine (LS) (6, 25, 27) and hip (26-28) were the skeletal sites evaluated in most studies, followed by arms and legs (27). Tibia (29-31) and combination of tibia and femur (32) were the skeletal sites assessed by pQCT in four of the studies.

Different methods were used to measure PA. Eight studies used questionnaire (including interview and report) while one study (31) used accelerometer to objectively measure PA. Most studies used questionnaire self-designed by the researcher, with three studies using the known-validated questionnaire such as Physical Activity questionnaire (PAQ) (28, 30) and Past Year PA Questionnaire (PYPAQ) (32). Several ways were used to classify PA, which we had briefly

Table 1: Study Description

Study design			
Cross-sectional study			3
Longitudinal study			6
Year of publication			
Up to year 1999			1
Year 2000 and upward			8
Continents			
Europe			5
North America			4
Sample size			
<100			2
>101-199			3
>200			4
Gender			
Male only			1
Female only			3
Both gender			5
Bone densitometry instruments			
DXA			5
pQCT			4
Anatomical site			
Total body			3
Vertebra			3
Hip	Proximal Femur	1/3	3
	Femoral Neck	2/3	
	Trochanter	1/3	
Leg	Tibia	4/4	4
	Femur	1/4	
Arm			1
Physical Activity instruments			
Questionnaire			8
Motion sensor (Accelerometer)			1

summarized them accordingly under the methodology column of Table 2. We implemented exact description for PA as used by the researcher in their original papers. The summary of the characteristics of all studies is displayed in Table 2.

### Findings based on method of bone measurement and bone variables

All five longitudinal studies, except (29) used DEXA as the measurement tool for bone evaluation. Regular WB (25), cumulative sport-exercises (26) and participation in a sports club (27) during adolescence was associated with a significant increase in high adult BMD. In addition, adolescents' PA was found to provide greater geometric bone strength as compared to their physically inactive peers (28). Conversely, one study showed negative association between sport participation during adolescence and adult BMD (6).

Table 2: Summary of the characteristic of studies included in the present review

Reference	Subjects	Methodology	Results	Remark	
Welten et al. (1994) (25)	182 (84 ♂ & 98 ♀)	<u>PA Measurement</u>	<u>Bone Measurement</u>		
Longitudinal	Age at baseline: 13 yr	Cross-check interview was used. Activities were limited to a minimal of 4 METs with minimum of 5 min. The average of weekly time spent in 3 categories: light (4-7 METs), medium heavy (7-10 METs), and heavy (>10 METs) were collected. The total activity score per week was the summation of the time spent per level of intensity (light:1, medium:2, heavy:3). Only WB activities were selected. The mean for adolescence period age 13-17 were calculated.	BMD of the LS (L2-L4) was determined at age 27 by DEXA (DXA; Norland XR-26).	In ♂, WB activity was a significant predictor of LS BMD. In ♀, WB activity was not a significant predictor of LS BMD.	Regular WB activity in adolescence is importance in reaching the highest lumbar PBM in ♂ but not in ♀.
Amsterdam Growth and Health Longitudinal Study (AGAHLIS).	Follow-up: 14 yr Country: Netherlands				
Reference	Subjects	Methodology	Results	Remark	
Lloyd et al. (2000) (26)	81 ♀	<u>PA Measurement</u>	<u>Bone Measurement</u>		
Longitudinal	Age at baseline: 11.9± 0.5 yr	Sport-exercise questionnaire was used. Cumulative sport-exercise score is the arithmetic sum of scores using different ranges of values (ages 12-18 yr) were obtained from questionnaire which listed 28 activities: school based activities, outside of school organized activities and individual activities.	TB BMD gain (TB bone gain during ages 12-18 yr). BMD of the PF (hip) at age 18 yr was measured by using DEXA (Hologic Corporation, Waltham, MA)	The cumulative sport-exercise score was positively associated with the Hip BMD at age 18 yr but not with TB bone mineral gain between ages 12-18 yr. The cumulative Sport-exercise was a significant predictor for hip BMD at ages of 18 yr.	♀ who participate in sport-exercise during adolescence is related to a significant increase in peak hip BMD but not with TB bone mineral gain.
Penn State Young Women's Health Study	Follow up: 6 yr Country: USA				
Reference	Subjects	Methodology	Results	Remark	
Van Langendonck et al. (2003) (6)	154 ♂	<u>PA measurement</u>	<u>Bone Measurement</u>		
Longitudinal	Age at baseline: 13 yr Follow up: 6yr	Sports participation inventory was used: Types of sports and time spent per week were obtained. The mean score for 6 yr (ages 13-18 yr) was calculated to obtain: Time spent in sports activities during adolescence and impact score. PS scores (0-3) for all activities according to GRF were summed.	BMD of the LS and TB was measured by using DEXA (Hologic QDR-4500A; Hologic, Inc., Bedford, Massachusetts)	Time spent in sports activities during adolescence and Impact scores during adolescence were not predictors of adult TB BMD and LS BMD.	Sports participation during adolescence did not result in a better bone status (BMD) in adulthood.
Leuven Longitudinal Study of Lifestyle, Fitness and Health (LLSLFH)	Country: Belgium				
Reference	Subjects	Methodology	Results	Remark	
Barnekow-Bergkvist et al. (2006) (27)	36 ♀	<u>PA measurement</u>	<u>Bone Measurement</u>		
Longitudinal	Age: 15-17 yr. Follow-up: 20yr Country: Sweden	Standardized questionnaire on participation in PA was used: (1) leisure-time sports activity (yes/no), (2) membership of a sports club (yes/no; MSC16), (3) kind of activity/ies	BMD of the TB, arms, legs, LS, right FN and TR was measured by using DEXA (Lunar Co., Madison, Wisconsin, USA).	♀ who were members of a sports club (MSC16) at baseline had significantly higher adult BMD values at all skeletal sites except for the arms compared with those women who were not physically active at baseline.	Membership in a sport club during adolescence contributes to higher adult BMD.
Reference	Subjects	Methodology	Results	Remark	
McKay et al. (2011) (30)	278 (146 ♂ and 132 ♀)	<u>PA measurement</u>	<u>Bone measurement</u>		
Cross-sectional	Age: 15-20 yr.	PAQ-A was used to assessed Moderate to vigorous PA. The outcomes were Impact-loading PA time (ImpactPA, min/wk) and non-impact loading PA time (NoimpactPa, min/wk). e.g. of impact loading PA: all activities that involve running. Non- impact loading PA: cycling and swimming.	Bone density (Tt.Dn, Ct.Dn, Tb.Dn), Bone architecture (Tt.Ar = BA, Ct.Th, Tb.N, Tb.Th), Bone strength (Imin & Imax) of the non-dominant tibia were measured using HR-pQCT (XtremeCT; Scanco Medical AG, Switzerland).	Impact PA had significantly positive relation with Imin & Imax in ♂ only. Impact PA had significantly association with Bone density variables in ♀ except Ct.Dn and ♂.	Impact PA was associated with Bone strength and Bone Area in ♂. Impact PA was associated with Bone density and Bone Architecture in ♀.
Healthy Bones (HBS) III study	Country: Canada				
Reference	Subjects	Methodology	Results	Remark	
Sayers et al. (2011) (31)	1748 (778 ♂, 970 ♀)	<u>PA Measurement</u>	<u>Bone Measurement</u>		
Cross-sectional analysis based on the Avon Longitudinal Study of Parents	Age: 15.5 yr. Country: UK	MTI Actigraph accelerometer was worn for 7 consecutive d. Individual Accumulated PA was categorized into different intensities (cpm) by using cut-point (sedentary:0-199 cpm, light:200-3599 cpm, moderate:3600-6199 cpm)	Cortical BMC (BMCc), cortical BMD (BMDc), cortical BA (BAc), PC, EC and SSI of the mid (50%) right tibia were obtained using pQCT (Stratec XCT 2000L, Stratec, Pforz-	Vigorous PA had the highest association with BMCc and BAc Only light and vigorous PA showed positive association with PC.	Vigorous day-to-day PA was associated with cortical BMC, BA and PC as well as SSI.

and children (ALSPAC).	and vigorous and (6200+ cpm). These cut-points are associated with METs (validated).	heim, Germany).	All intensities of PA showed negative association with BMDc and endosteal circumference adjusted for periosteal circumference.		
<b>Reference</b>	<b>Subjects</b>	<b>Methodology</b>	<b>Results</b>	<b>Remark</b>	
Farr et al. (2011) (32)	465 ♀ Age: 8–13yr Country: USA	<u>PA Measurement</u> PYPAQ was used. A list of 41 activities in the past year outside of PE class. Duration and frequency were obtained. PYPAQ score = $\sum 1-n$ (duration (average min/session) × frequency (months/12) × d/wk) × load (=PS score). Load (PS score) values were assigned to each activity based on GRF. Jumping PA (3), involve changing directions quickly and sprinting PA (2), Low-impact PA (1.5), Non-WB (0.5). PYPAQ score were divided into groups: low, moderate and high.	<u>Bone Measurement</u> vBMD, bone structure (Ct.Ar, EC, PC, Ct.Th) and bone strength (BSI &SSI) at the distal metaphyseal (4% femur, tibia) and diaphyseal (20% femur, 66% tibia) sites of the non-dominant leg were assessed using pQCT (XCT 3000; stratec Medizintechnik GmbH, Pforzheim, Germany, Division of Orthometrix; White Plains, NY).	High PA ♀ had higher bone geometric and bone strength than low PA ♀, except for 4% femur BSI, diaphyseal Ct.Ar and diaphyseal Ct.Th,  High PA had similar bone parameters with moderate PA except for 66% tibia EC.  Moderate PA had higher bone parameters compared with inactive ♀, except for 4% femur BSI, diaphyseal Ct.Ar, diaphyseal Ct.Th, and 66% tibia EC.	Active ♀ had higher values on bone geometry (EC, PC) and bone strength (BSI, SSI) at metaphyseal and diaphyseal sites of the femur and tibia compared with less active girls.
<b>Reference</b>	<b>Subjects</b>	<b>Methodology</b>	<b>Results</b>	<b>Remark</b>	
Jackowski et al. (2014) (28)	104 (55 ♂, 49 ♀) Age at baseline: 8–15 yr Follow-up: more than 7 yr. Country: Canada	<u>PA Measurement</u> PAQ-C and A were used. Nine items scored on a five-point Likert-type scale. Final PA scores range from: lowest (1) to highest (5). An age and sex-specific Z score was determined and individuals were ranked into three quartiles: Highest (active), middle three (average), and lowest (inactive).	<u>Bone Measurement</u> Bone geometric strength: CSA and Z at the NN, IT, and S sites of the PF were assessed from FN using DXA (Hologic QDR-2000; Hologic, Bedford, MA).	PA during adolescence was positively related with adolescent bone CSA and Z of the PF.  Active adolescents had significantly greater adjusted adult bone geometric measures at the PF than participants who were classified as inactive during adolescence.	Being active during adolescence provides greater adolescent geometric strength at the PF.
<b>Reference</b>	<b>Subjects</b>	<b>Methodology</b>	<b>Results</b>	<b>Remark</b>	
Tolonen et al. (2015) (29)	1884 (1135 ♂, 1174 ♀) Age:9-18 yr old Follow-up: 28yr. Country: Finland	<u>PA Measurement</u> Total PA sum indices based on PA index (PAI). PAI includes intensity (breathlessness and sweating during exercise), leisure-time PA (at least half an hour/session), participation in sport club, competitions (yes/no), and common leisure-time activity coded as 1=inactivity, 2=intermediate and 3=frequent or vigorous PA. The PA sum indices were divided into: very low, low, intermediate and frequent according to the cut-off values: <8, <9 and <10 in ♀ and <9, <10 and <11 in ♂.	<u>Bone Measurement</u> BMC, Tt.Ar, Tb.Dn and BSI at the distal tibia (5%) and Tt.Ar, Cortical CSA, Ct.Dn, BMC, SSI and CSI at the tibial shaft (30%) of the left leg were obtained using pQCT (Stratec XCT 2000R, Stratec, Medizintechnik GmbH, Pforzheim, Germany).	In ♀, frequent PA was associated with higher adult BSI at the distal tibia, Tt.Ar and Cortical CSA, BMC, CSI and SSI at the tibial shaft.  In ♂, frequent PA was associated with higher adult Tt.Ar at distal tibia, and Cortical CSA and CSI at the tibial shaft.  No association between frequent PA and tibial bone density in both gender.	Frequent habitual PA in adolescence was associated with greater bone size, mineral content and strength at the weight-bearing tibia in adulthood.

♀ = (female), ♂ = (male)

Bone Indices: Bone Mineral Density (BMD), Bone Mineral Content (BMC), volumetric Bone Mineral Density (vBMD), Total Bone Density (Tt.Dn), Cortical Density (Ct.Dn), Trabecular Density (Tb.Dn), Bone Area (BA), Cortical Area (Ct.Ar), Total Bone Area (Tt.Ar), Periosteal Circumference (PC), Endosteal Circumference (EC), Cross-Sectional Area (CSA), Cortical Thickness (Ct.Th), Trabecular No. (Tb.N), Trabecular Thickness (Tb.Th), Minimum & Maximum Cross-Sectional Of Inertia (Imin & Imax), Bone Strength Index (BSI), Strength-Strain Index (SSI), Section Modulus (Z), Cortical Strength Index (CSI)

Skeletal Site: Total Body (TB), Lumbar Spine (LS), Proximal Femur (PF), Femoral Neck (FN), Trochanter (TR), Narrow Neck (NN), Intertrochanter (IT), Femoral Shaft (S)

Bone Densitometry: Dual Energy X-Ray Absorptiometry (DEXA), Peripheral Quantitative Computed Tomography (pQCT)

PBM, Peak Strain (PS), Physical Activity (PA), Physical Education (PE), Ground Reaction Force (GRF),

PA Questionnaire for adolescents (PAQ-A), PA Questionnaire for children (PAQ-C), Past Year PA Questionnaire (PYPAQ)

Four out of five studies demonstrated significant contribution of adolescents' regular PA with improved BMD (25- 27) and bone geometrical strength (28) regardless of gender and skeletal sites of interest. The three studies used pQCT to evaluate bone outcomes were all cross-sectional study, except Tolonen et al. (29).

Concerning bone mass, three studies demonstrated positive association between frequent PA (29), vigorous PA (31), and Impact PA (30) and with at least one of the bone mass variables. Conversely, one study showed negative association between PA and vBMD (32). Nevertheless, all four studies reported a significant association

between increased PA and bone strength and bone structure (29- 32).

**Findings based on Gender and anatomical sites**

Referring to Table 3, eleven analyses were extracted from the five studies that implemented DEXA. The first four analyses were females LS

BMD (25, 27) and male LS BMD (6, 25). In females, one study found significant association (27) while the other study showed no association (25). This one-to-one result was found similar in male's LS BMD (25, 6). In brief, two over four analyses demonstrated positive association with equal contribution from each gender (25, 27).

**Table 3:** Bone Mass, Bone Structure and Bone strength Outcomes

Tools	Study	Skeletal sites	Bone Mass			Bone architecture			Bone area			Bone geometry			Total proportion		
			♀	♀♂	♂	♀	♀♂	♂	♀	♀♂	♂	♀	♀♂	♂			
DEXA	Welten et al. (1994) (25)	LS	0	-	1	-	-	-	-	-	-	-	-	-	-	-	
	Barnekow-Bergkvist et al. (2006) (27)	LS	1	-	-	-	-	-	-	-	-	-	-	-	-	-	
	Van Langendonck et al. (2003) (6)	LS	-	-	0	-	-	-	-	-	-	-	-	-	-	-	2/4
	Lloyd et al. (2000) (26)	TB	0	-	-	-	-	-	-	-	-	-	-	-	-	-	
	Barnekow-Bergkvist et al. (2006) (27)	TB	1	-	-	-	-	-	-	-	-	-	-	-	-	-	
	Van Langendonck et al. (2003) (6)	TB	-	-	0	-	-	-	-	-	-	-	-	-	-	-	1/3
	Barnekow-Bergkvist et al. (2006) (27)	Arms	0	-	-	-	-	-	-	-	-	-	-	-	-	-	0/1
	Lloyd et al. (2000) (26)	Hip	1	-	-	-	-	-	-	-	-	-	-	-	-	-	
	Barnekow-Bergkvist et al. (2006) (27)	Hip	1	-	-	-	-	-	-	-	-	-	-	-	-	-	2/2
pQCT	Jackowski et al. (2014) (28)	Hip	-	-	-	-	-	-	-	-	-	1	-	-	1	-	2/2
DEXA	Barnekow-Bergkvist et al. (2006) (27)	Legs	1	-	-	-	-	-	-	-	-	-	-	-	-	-	1/1
pQCT	McKay et al. (2011) (30)	Legs	1*	-	0	1*	-	0	0	-	1	-	-	-	0	-	1
	Sayers et al. (2011) (31)	Legs	-	1*	-	-	-	-	-	1	-	-	1*	-	-	1	-
	Farr et al. (2011) (32)	Legs	0	-	-	0	-	-	0	-	-	1	-	-	1	-	-
	Tolonen et al. (2015) (29)	Legs	1*	-	0	-	-	-	1	-	1	1	-	1	1	-	1
	Proportion according to gender		7/11	1/1	1/5	1/2	-	0/1	1/3	1/1	2/2	2/2	2/2	1/1	2/3	2/2	2/2
	Total proportion			9/17			1/3		4/6			5/5		6/7			25/38
	Grand proportion			9/17					10/14					6/7			

1=significant association, 0 =no significant, - =not assessed  
 \*Significant with at least one of the indices under its group.

Regarding TB, three analyses were extracted for TB with only one out of three analyses showed positive association. In females, one analysis showed positive association (27) while one analysis showed reverse association (26). In male, only one study was evaluated but the result failed to reach significant (6).

Two analyses were extracted from one study evaluates female peripheral BMD; one analysis at the arms and one analysis at the leg (27). However, only legs BMD presented significant association with participation in PA.

At the hip skeletal site, four analyses were extracted from three studies (26- 28). Both analyses carried out in females showed that PA was significantly associated with hip BMD as measured by DEXA (26, 27). As for pQCT, combined gender analyses showed positive association with both hip geometric and strength (28). Thus, all four analyses evaluated at the hip site reported positive association between increase PA and bone variables.

Twenty-five analyses were extracted from pQCT study at the leg site. Three out of six analyses of bone mass outcomes exhibited positive association with high PA level, with no positive association in male bone density (29, 30). Regarding bone strength outcomes, five over six analyses demonstrated positive outcomes. Three studies measured influence of PA on bone geometry (29, 31, 32). All studies demonstrated a positive relationship. As for the bone area, only one analysis (29) found positive relationship between female bone area and PA, while another two analyses did not find any relationship (30, 32). The reverse association was found for males (29, 30). Regarding bone architecture, one study comparing the gender effect found positive association only in females (30) but different study focusing in female showed no significant association (32).

#### ***Key findings according to gender, anatomical site and bone outcomes***

Regular WB activity is importance in reaching the highest LS BMD in male (25) but not in female.

Conversely, PA analyzed by PS score did not result in increased male's LS or TB BMD (6).

Membership in a sports club had significantly higher female TB, LS, hip and legs BMD compared with inactive females (27). Similarly, female who participate in sport-exercise during adolescence is related to a significant increase in peak hip BMD (26). In addition, being active during adolescence was related to greater bone geometric strength at the hip as measured by pQCT (28).

Regarding pQCT, a study that combined gender analyses showed everyday vigorous PA during adolescence was associated with cortical bone mass (BMC), bone area, bone geometry (PC) and bone strength (SSI) (31). Gender wise, Impact PA was associated with tibia bone strength and area in male while bone density and architecture in female (30). Conversely, active girls (analyzed by PS score) also had higher bone geometry (EC, PC) and bone strength (BSI, SSI) at metaphyseal and diaphyseal sites of the femur and tibia compared with less active girls (32). In addition, frequent PA was associated with greater adult tibial bone strength, bone geometry and bone area in both genders than inactive adolescents. No similar association was found for male bone mass (29).

All studies exhibited significant contribution between adolescents' PA and greater bone mass and/or bone structural and strength variables (at least one of the indices showed significant result) (6).

## **Discussion**

This review was systematically done to investigate the influence of regular PA during the 'window of opportunity' toward positive bone outcomes among the healthy adolescent population. Research papers were carefully selected to highlight the influence of day-to-day PA in maximizing bone health.

Regarding the age of adolescence, none of the studies included in this review indicated the rea-



son over the selected age range. According to the WHO, adolescence is defined as the period of development between the ages of 10 and 19 yr old, or begins with the onset of physiologically normal puberty (a mature reproductive system is attained) and ends when an adult identity and behavior are accepted (33).

Concerning bone densitometry and its outcome measures, all studies defined their reason over the choice of bone densitometry devices. All studies either focused on assessment of bone mass only (6, 25- 27), or bone structural strength (28) or combination of both bone properties (29- 32). We include all bone measurement reported as; Bone Mineral Density (BMD), Bone Mineral Content (BMC), volumetric Bone Mineral Density (vBMD), bone density [Total Bone Density (Tt.Dn), Cortical Density (Ct.Dn), Trabecular Density (Tb.Dn)] as the outcomes for bone mass. As for the bone structure, we include the following reported variables; (1) bone architecture [Cortical Thickness (Ct.Th), Trabecular No. (Tb.N), Trabecular Thickness (Tb.Th)], (2) bone area (BA) or total area (Tt.Ar) [Cortical Area (Ct.Ar) or cortical BA (Bac)] and (3) bone geometry [Periosteal Circumference (PC), Endosteal Circumference (EC), Cross-Sectional Area (CSA)] to represent the bone structure outcomes.

In general, bone mass and bone structure are two important determinants govern the bone strength (34-36). A combination of both measurements has been acknowledged to improve fracture prediction (28). In this review, all bone strength measurements included were reported as surrogates of bone strength. Bone strength is represented by Minimum & Maximum Cross-Sectional of Inertia (Imin & Imax), Strength-Strain Index (SSI), Bone Strength Index (BSI), Section Modulus (Z) and Cortical Strength Index (CSI).

In adult, bone mass is determined by PBM, rate and amount of bone loss (37). Bone mass is expressed as BMD, which is the core clinical assessment to evaluate bone mass and forms the basic measurement for detecting osteoporosis (38). DEXA uses absolute BMD values as the common outcome measure. Furthermore, BMD

results measured by DEXA at the hip and spine can be interpreted using the WHO T-score definition of osteoporosis and osteopenia (39). Consequently, the gold standard for diagnosis of osteoporosis is by using the DEXA machine (40).

There is an increasing interest to look for alternative devices other than DEXA in many epidemiologic studies. Consequently, the inclusion of another bone densitometry in this review is mainly due to the limitation of DEXA in measuring bone structure (35) and bone geometry (41). These bone parameters are important determinants in the developing skeleton and thus the preferred choice of densitometry techniques, especially in pediatric population (21).

In this present review, three studies had employed pQCT. The Quantitative Computed Tomography (QCT) is one of the established tools for bone densitometry measurement. As an alternative to DEXA, QCT measures BMD at the vertebra and peripheral skeleton of the forearm or tibia. Besides, its ability to measure bone mass, there are several advantages of pQCT, include its ability to measure different types of bone tissue and provide three-dimensional data on bone biomechanical properties (42). All these were done non-invasively, making it an interesting alternative to the standard DEXA densitometry technique (43).

Questionnaire is the most feasible instruments for assessment of exposure of interest (44). Previous validation study had suggested that objective measurement is a better method for assessment of PA among school children compared to administration of questionnaire (44). Objective measurement from a motion sensor such as pedometer and accelerometer is used to assess PA due to its ability to provide frequency, intensity, duration and the total amount of PA in daily life (45). However, administration of motion sensor for large population studies is challenging. This could be one for the reasons why the majority of studies (eight out of nine) used questionnaire or self-administered instruments over objective measurement to assess PA.

From the nine studies included, we identified nine different ways of classifying General PA.

General or regular PA reflects all activities in everyday living. Fundamentally, PA introduces force/stress on the bone. Stress/strain acting on the bone will stimulate the osteogenic response that influence bone outcomes (46). Loaded PA above a physiological threshold or higher than usual forces would elicit osteogenesis response (17, 46). The relationship between loading magnitude and bone could be explained by increased bone mass via modeling and the added bone retained by remodeling (47). In addition, bone respond to stress and undergo modification with a subsequent increase in bone mass, external shape and internal structure and thus bone strength (34, 48).

Pertaining to the bone outcome as measured by the pQCT, combining both genders, Sayers and colleagues found positive relationship between vigorous PA and bone mass and bone structural strength (31). High impact PA was significantly associated with bone density in females (29, 30) or bone area in males (30, 32). This general trend was proposed that boys have bigger bones while girls have denser bones (49).

This current review also supports the positive relationship between adolescents' PA and structural bone strength (29-32). As aforementioned, bone structure and mass are the important components of bone strength. The relationship between bone mass and PA can be explained by a relationship between PA and bone area with contribution from increased PC (bone geometry) (31). Thus, relationship between PA and PC reflects the bone strength indices. Therefore, reverse relationship in females may adversely affect bone strength (50). However, Farr and colleagues support the finding that PA is related to PC but at the same time do not support a significant association with vBMD (32). We postulate that either exercise at late puberty promotes PC only in males (51) or the estrogen levels attenuate the relationship between PA and bone density in females (32).

From the five anatomical sites included, the most consistent positive association was seen at the hip followed by leg. Bone responsiveness to mechanical load might be specific to load bearing

regions (52, 53). Hip is the skeletal site that benefited the most from the force of loading activities (24). Alternatively, the peak hip bone mass was achieved earlier than the peak LS and TB skeletal mass (54-57). At the leg site, WB activities such as walking and running were the most common PA practiced by many people (58). Thus, it is easier to detect significant differences in the load bearing region of the leg. In contrast, the lack of association at the vertebrae could be explained by the influence of endocrine factors (59).

It is impossible to recommend the adequate amount of PA needed to promote bone health since different instruments to classify PA were used. However, adolescents with the highest PA have high bone status as compared to their inactive peers and PA is one of the most important determinants of good bone status in later life.

## Limitation

There are barriers in comparing and interpreting results because different approaches were used such as different skeletal sites, various bone outcomes and method of classifying PA. We acknowledge the differences across the studies because different tools and approaches were adapted to meet the study objective. Importantly, we excluded studies that evaluated mediators between PA and bone outcomes since it was not the primary interest of this study. However, the role of mediators such as muscle and maturity level should be included in future studies.

## Conclusion

We suggested several possible explanations that could affect the achievement of PBM. First, differences between genders are observed where the influence of PA and bone area seems to be dichotomous; boys have greater bone area while girls have higher bone density. Second, bone responsiveness to mechanical load is limited to load bearing regions. The timing of PBM achievement is also region-specific. Fourth, the convergence of bone mass and bone structure is a better re-

flection of bone strength. Bone strength in addition to bone mass has been acknowledged to improved fracture prediction. Increased regular PA during the age of peak bone mineral accrual appeared to be beneficial in fostering bone acquisition (bone mass, bone geometry, bone architecture and bone strength) as a whole. Thus, implementation of regular PA started at early life particularly during adolescence is the key towards achieving healthy bone and a practical way to overcome the increasing incidence of osteoporosis and future risk of fracture

## Ethical Considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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