Learnings from the Birth to Twenty (Bt20) study

Lisa Micklesfield, PhD

MRC/Wits Developmental Pathways for Health Research Unit

University of the Witwatersrand, Johannesburg, South Africa

Sub-Saharan **A**frican **M**u**S**cul**O**skeletal **N**etwork (SAMSON)

Musculoskeletal Research Training Workshop, Harare, Zimbabwe

Monday 19 - Thursday 22 March 2018

BTT – broadly surveyed children's health and development

birth to ten

1990

3273 children born to women resident in the Greater Johannesburg metropolitan area

Bt20 – targeted towards answering specific questions related to risk associated with lifestyle, including sexual and reproductive disorders, CV disease, diabetes

2000

2300 (70%) Average attrition rate <3%/annum, most attrition in first 2 years of study)

2010

DPHRU
MRC/Wits Developmental Pathways for Health Research Unit

MRC SOUTH AFRICA

DPHRU
MRC/Wits Developmental Pathways for Health Research Unit

Birth to Twenty PLUS

Prospective birth cohort (Johannesburg-Soweto; South Africa)

Recruited 3273 mothers and babies (households) in 1990 to understand growth and development in a transitioning urban setting

birth to ten

~70% (67%) still in contact with the study

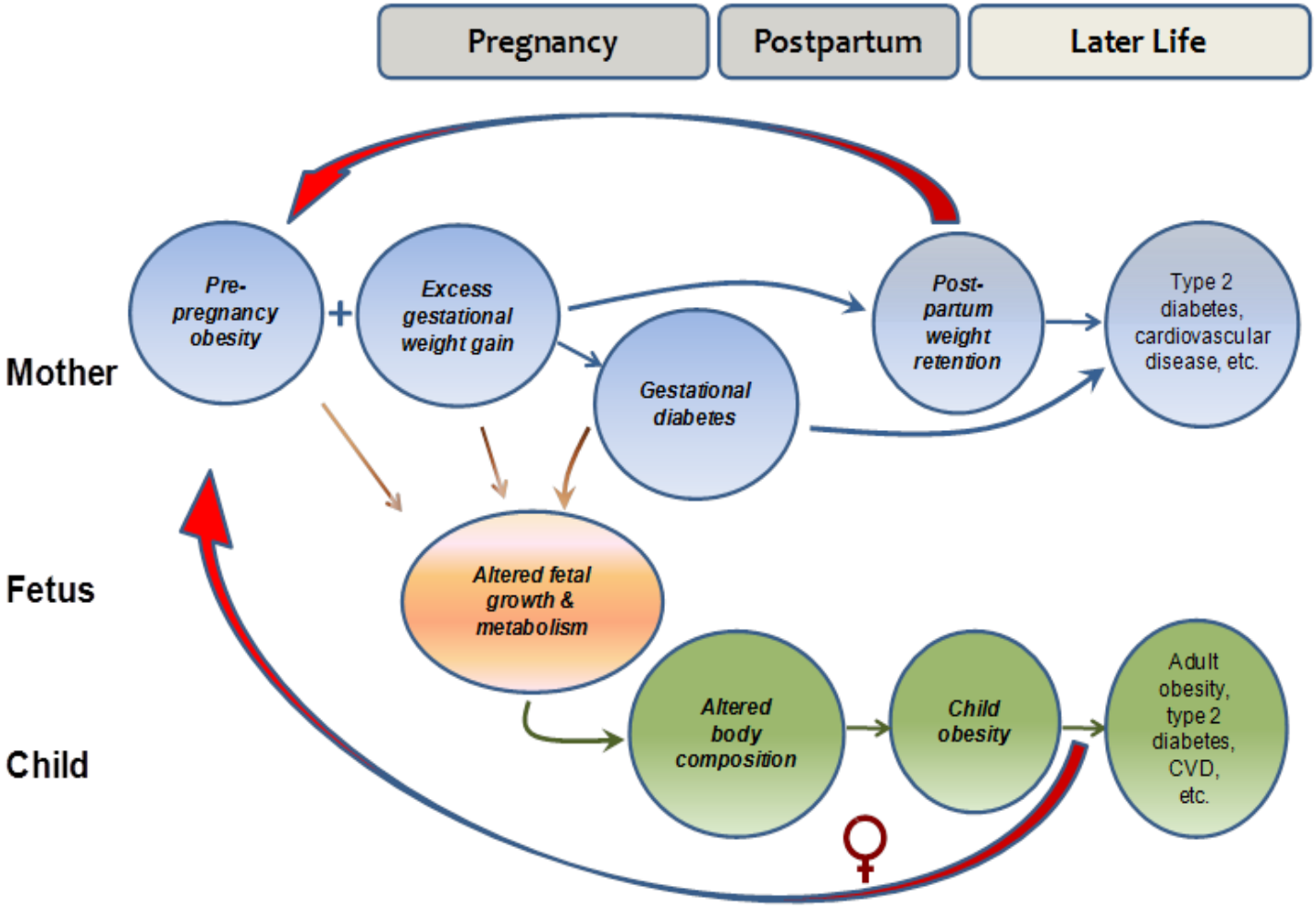
21 data collection waves completed

most recently completed the age 22-24 year survey

3 generations

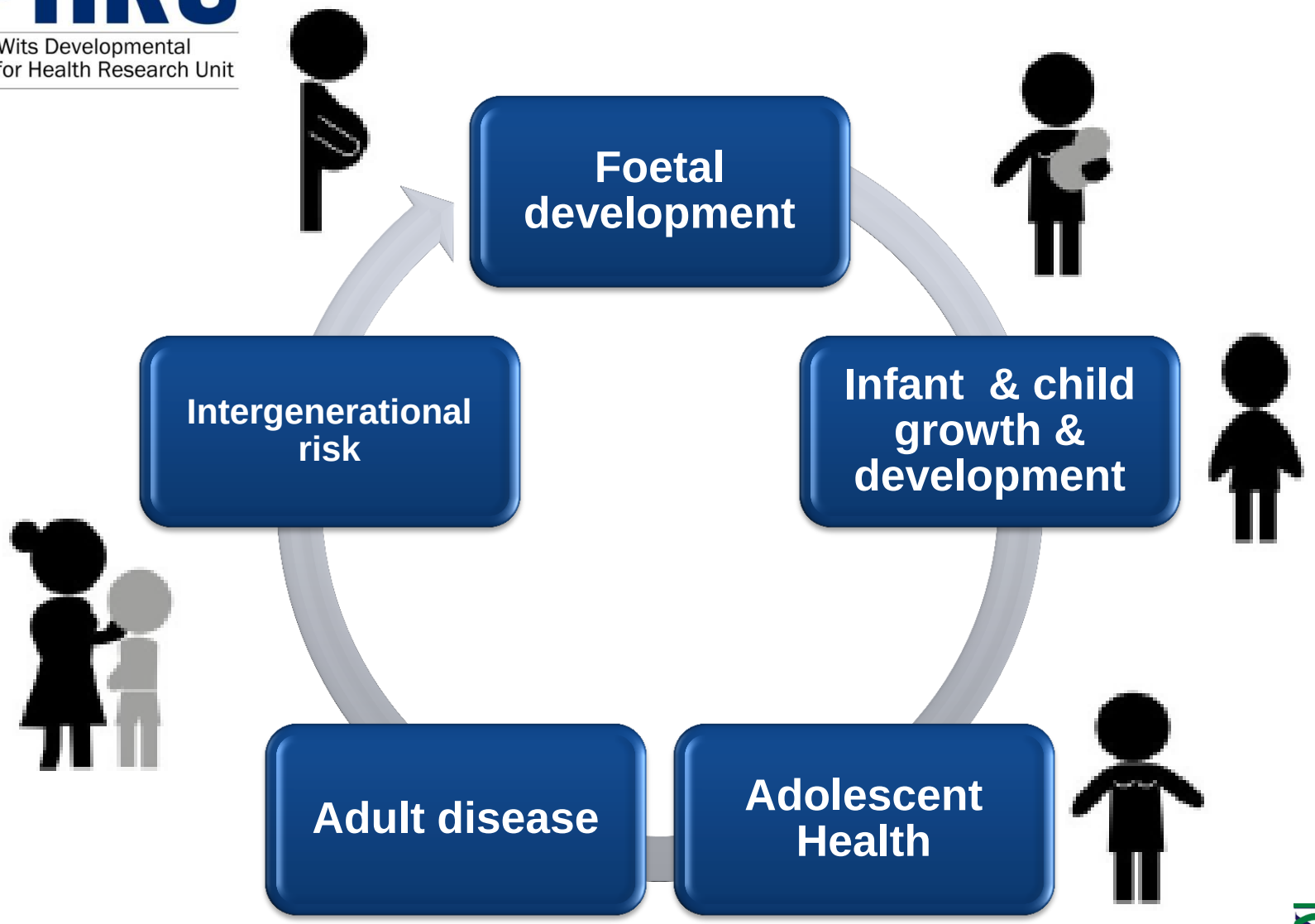
approx 720+ 3G babies

Impact on the next generation



DPHRU
MRC/Wits Developmental Pathways for Health Research Unit

Life-course framework



MRC SOUTH AFRICA

SOWETO

- 2008 Census put its population at 1.3 million or about one-third of the city's total population.
- Soweto's population is predominantly black.
- All eleven of the country's official languages are spoken and the main linguistic groups are Zulu, Sotho, Tswana, Venda and Tsonga.

Area: 200.03 km^2
1,776.42 households/km^2

DPHRU
MRC/Wits Developmental Pathways for Health Research Unit

MRC SOUTH AFRICA

Research highlights

DPHRU
MRC/Wits Developmental Pathways for Health Research Unit

MRC
SOUTH AFRICA

BTT – broadly surveyed children's health and development

birth to ten

1990 — 3273 children born to women resident in the Greater Johannesburg metropolitan area

Yr 9 — BONE HEALTH COHORT (n=475)

Bt20 – targeted towards answering specific questions related to risk associated with lifestyle, including sexual and reproductive disorders, CV disease, diabetes

2000 — 2300 (70%) Average attrition rate <3%/annum, most attrition in first 2 years of study)

2010

DPHRU
MRC/Wits Developmental Pathways for Health Research Unit

MRC SOUTH AFRICA

DPHRU
MRC/Wits Developmental Pathways for Health Research Unit

Bone Health Cohort

Measurements

Anthropometry: height, weight, circumferences, skinfolds, limb lengths

DXA: whole-body, radius, lumbar spine, hip, vertebral morphometry

pQCT (from age 12 years)

Hand x-ray: bone age & metacarpal indices

Dietary intake & physical activity

Blood & urine & DNA

Pubertal assessment

Hand grip assessment

Blood pressure

Questionnaires (Fracture history)

MRC SOUTH AFRICA

A snapshot of some Bt20 MSK findings….

J Bone Miner Metab (2011) 29:257–267
DOI 10.1007/s00774-011-0269-5

INVITED REVIEW

Ethnicity and bone: a South African perspective

Lisa K. Micklesfield · Shane A. Norris ·
John M. Pettifor

DPHRU
MRC/Wits Developmental Pathways for Health Research Unit

MRC SOUTH AFRICA

J Bone Miner Metab (2011) 29:257–267
DOI 10.1007/s00774-011-0269-5

INVITED REVIEW

Growth and DXA measures

Ethnicity and bone: a South African perspective

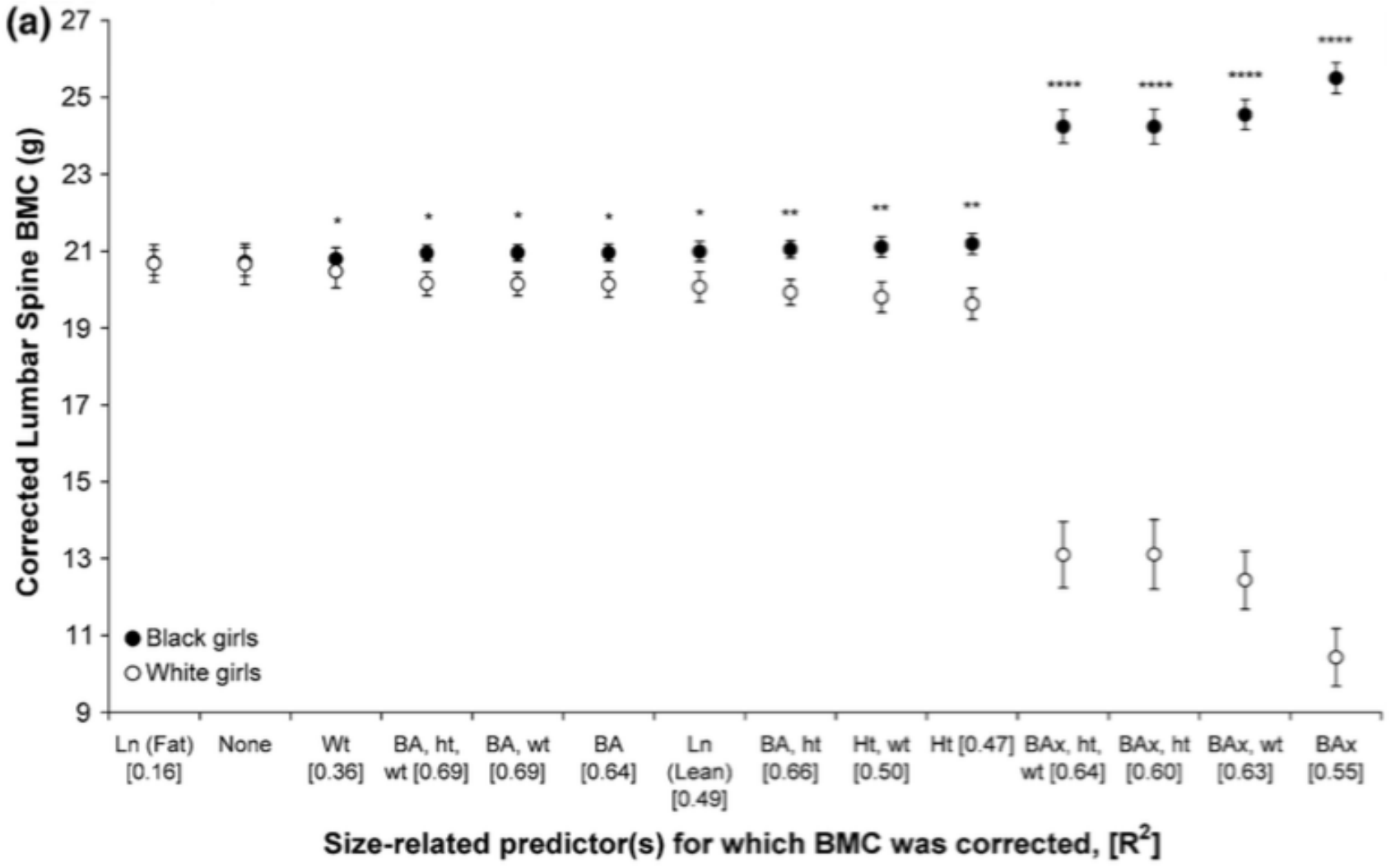
Lisa K. Micklesfield · Shane A. Norris · John M. Pettifor

	SA
Growth	
Weight	*B<W (boys only)*
Height	*B<W*
Sitting height	*B<W (boys only)*
Body composition	
Fat mass	
Lean mass	*B<W*
DXA measures	
Whole body BMC	B>W; B=W
Lumbar spine BMC	B>W (girls only); B=W
Femoral neck BMC	B>W
Mid-radius BMC	B>W

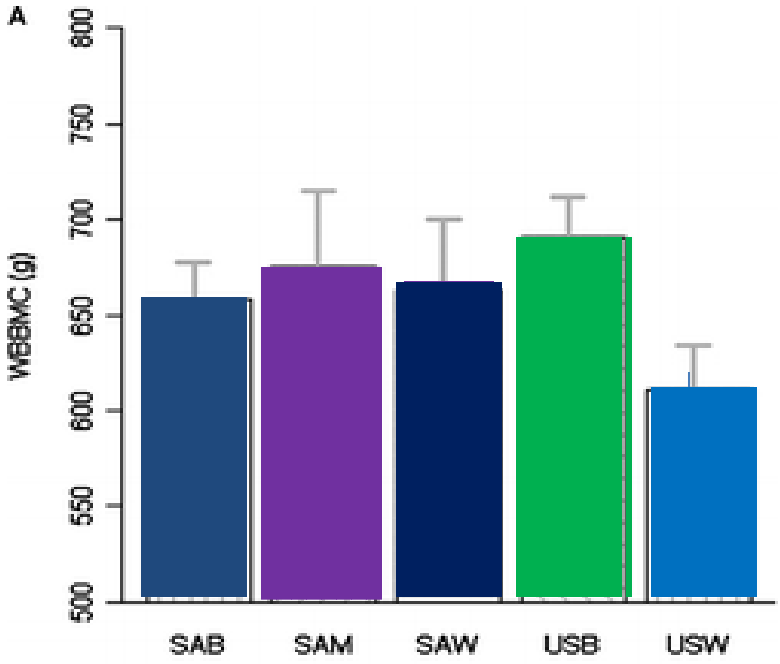
McVeigh et al., 2004
Nyati et al., 2006
Vidulich et al., 2006
Micklesfield et al., 2007, 2009, 2011

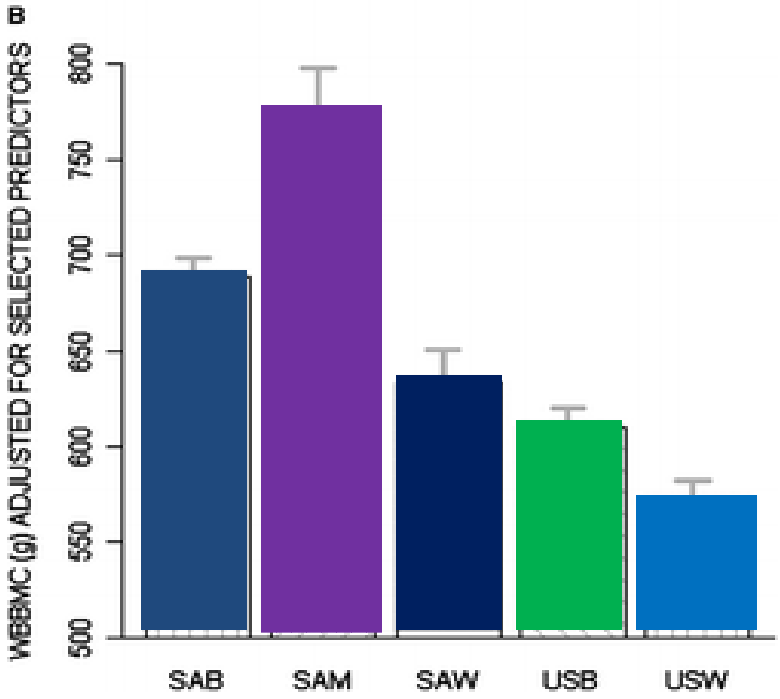
DPHRU MRC/Wits Developmental Pathways for Health Research Unit
MRC SOUTH AFRICA

Size-related adjustments



Vidulich et al., CTI 2011





- **whole body** BMC is lower in children of European ancestry compared with African ancestry, irrespective of geographical location.

- whole body BMC is higher in South African children compared to their US counterparts

- highlights the need to investigate the bone status of the mixed ancestral group more closely.

Micklesfield et al., JBMR 2007;22:1869-1877

pQCT measures – 4% (metaphyseal sites) radius and tibia

	White girls ($n=67$)	Black girls ($n=165$)	White boys ($n=59$)	Black boys ($n=179$)	p value ethnicity
4% Radius					
TotD (mg/cm^3)	279.4 (26.0)	287.1 (35.8)	303.2 (27.2)	310.5 (36.7)	B: NS G: NS
TrbD (mg/cm^3)	222.7 (34.2)	239.5 (49.5)	262.6 (38.9)	273.0 (45.5)	B:NS G: <0.05
TotA (mm^2)*	372.5 (360–386)	371.4 (363–380)	425.3 (409–442)	405.5 (397–414)	B: <0.05 G: NS
BSI (mg^2/mm^4)	2948.5 (718.6)	3073.1 (749.4)	4151.2 (1147.5)	3893.7 (1109.1)	B: NS G: NS
4% Tibia					
TotD (mg/cm^3)	287.4 (28.8)	292.8 (35.6)	296.1 (27.3)	301.3 (36.1)	B: NS G: NS
TrbD (mg/cm^3)	233.2 (30.3)	232.0 (36.0)	259.9 (29.4)	255.4 (44.4)	B: NS G:NS
TotA (mm^2)*	961.4 (930–993)	951.6 (933–971)	1146.2 (1102–1190)	1113.6 (1091–1136)	B: NS G:NS
BSI (mg^2/mm^4)	8006.1 (1974.6)	8209.4 (1988.8)	10562.1 (2933.6)	10129.9 (2600.1)	B: NS G:NS

Micklesfield et al., Bone, 2011

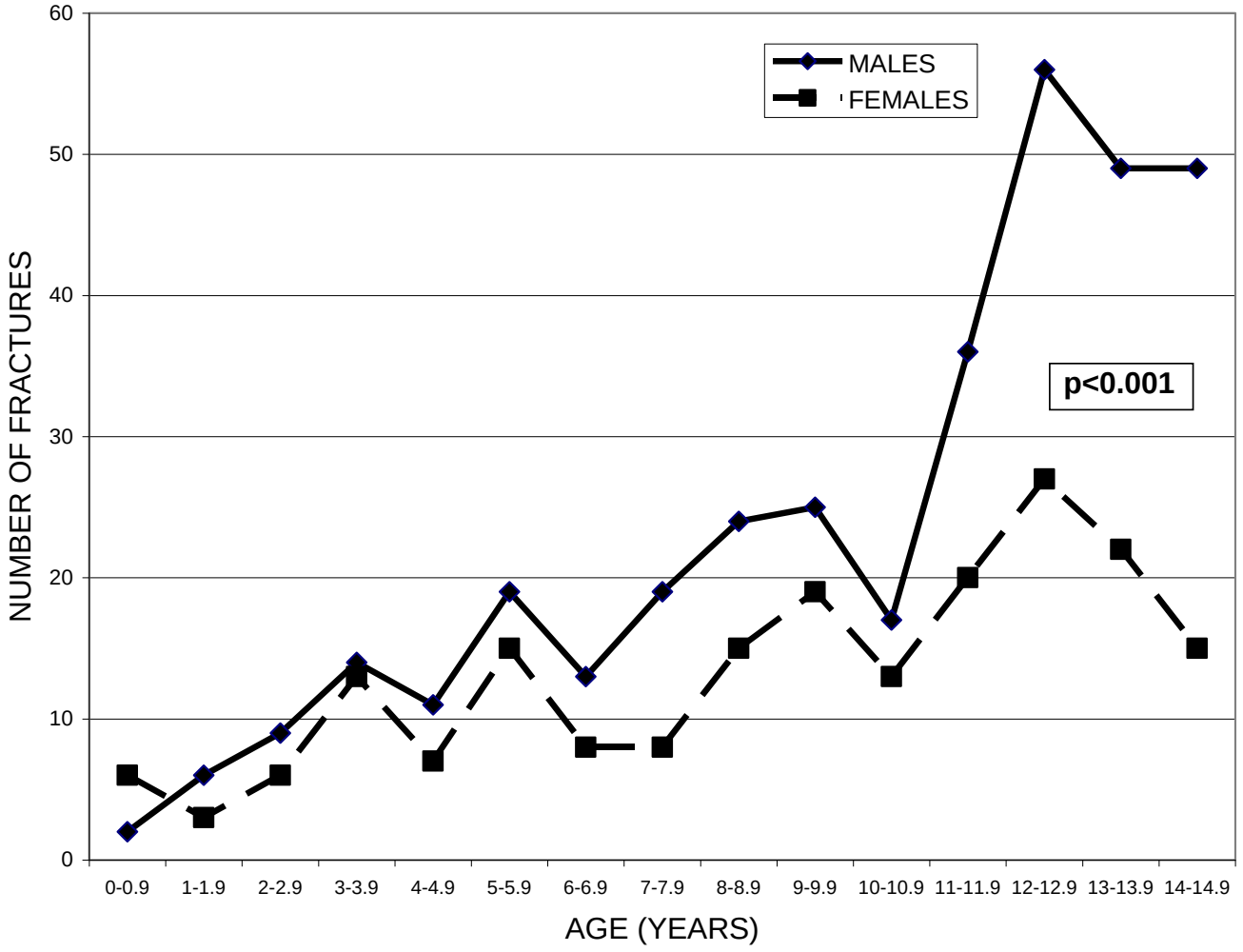
pQCT measures – 38% (diaphyseal site) tibia

	White girls ($n=67$)	Black girls ($n=165$)	White boys ($n=51$)	Black boys ($n=173$)	p value ethnicity
TotA (mm^2)*	339.3 (327–352)	366.2 (359–374)	357.6 (339–376)	417.3 (408–427)	B: <0.001 G: <0.001
CoA (mm^2)*	226.9 (219-235)	226.2 (222–231)	242.1 (232–252)	246.9 (242–252)	B: NS G: NS
CoD (mg/mm^3)	1126.8 (28.3)	1129.3 (33.7)	1058.7 (34.5)	1079.0 (39.4)	B: <0.001 G: NS
CT (mm)*	4.4 (4.3–4.5)	4.1 (4.1–4.2)	4.6 (4.4–4.7)	4.2 (4.1–4.3)	B: <0.001 G: <0.001
EDiam (mm)*	11.9 (11.5–12.3)	13.3 (13.0–13.5)	12.1 (11.5–12.7)	14.6 (14.2–14.9)	B: <0.001 G: <0.001
TDiam (mm)*	20.7 (20.4–21.1)	21.5 (21.3–21.8)	21.2 (20.7–21.8)	23.0 (22.7–23.2)	B: <0.001 G: <0.001
PC (mm)*	65.1 (64.0–66.3)	67.7 (67.0–68.4)	66.7 (65.1–68.4)	72.2 (71.3–73.0)	B: <0.001 G: <0.001
SSIp (mm^3)*	1186.7 (1127–1247)	1304.9 (1268–1341)	1218.6 (1138–1299)	1485.1 (1444–1526)	B: <0.001 G: <0.01

South African black children have wider diaphyseal regions of appendicular bones with greater measures of bone strength.

Micklesfield et al., Bone, 2011

Fractures per year by age and sex distribution



DPHRU MRC/Wits Developmental Pathways for Health Research Unit

MRC SOUTH AFRICA

Thandrayen et al., Osteoporos Int, 2008

The number of children who sustained fractures over 15 years according to ethnicity

Ethnicity	Number of children with fractures		All children
	n	%	N
White	78	**41.5***	188
Mixed ancestry	44	21	213
Black	310	19	1600
Total	432	22	2001

DPHRU
MRC/Wits Developmental Pathways for Health Research Unit

* p< 0.001

Thandrayen et al., Osteoporos Int, 2008

Anthropometric and body composition measurements of white males and females at age 15 years

	White males		White females	
	Without fractures (n=25) Mean (SD)	With fractures (n=20) Mean (SD)	Without fractures (n=37) Mean (SD)	With fractures (n=15) Mean (SD)
Height Z Score	-0.13 (0.94)	0.19 (0.99)	0.01 (0.98)	-0.17 (1.11)
Weight Z Score	-0.22 (1.05)	0.29 (0.94)	-0.09 (0.82)	0.35 (1.09)
Lean mass Z score	**-0.27 (0.99)**	**0.35‡ (0.85)**	-0.13 (0.89)	0.33 (1.14)
Fat mass Z score	-0.04 (1.09)	0.17 (1.04)	-0.08 (0.81)	0.21 (1.03)
BMI Z score	-0.20 (1.07)	0.25 (1.03)	**-0.11 (0.86)**	**0.50** ** **(1.12)**

‡ p=0.02 between white males with and without fractures

** p=0.04 between white females with and without fractures

There were no significant differences in Black males or females

DPHRU
MRC/Wits Developmental Pathways for Health Research Unit

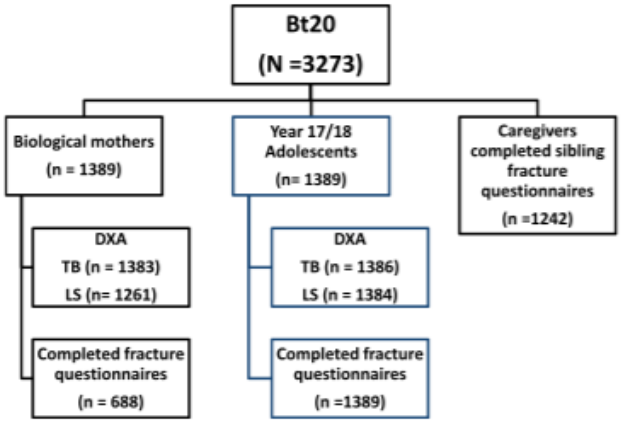
Thandrayen et al., JBMR, 2011

Osteoporos Int (2014) 25:693–700
DOI 10.1007/s00198-013-2477-4

ORIGINAL ARTICLE

Fracture patterns and bone mass in South African adolescent–mother pairs: the Birth to Twenty cohort

K. Thandrayen · S. A. Norris · L. K. Micklesfield · J. M. Pettifor



Odds ratios for fractures in 17/18-year-old adolescents

Fractures (n=1,099)	Adjusted odds ratio	95 % Confidence interval
Whites	3.16*	1.89–5.32
Males	1.94**	1.25–2.99
Sibling history of fracture	1.50***	1.02–2.21
Maternal LS BMC (Z-score)	0.76**	0.63–0.91

24 % reduction in fracture risk for every SD increase in maternal LS BMC

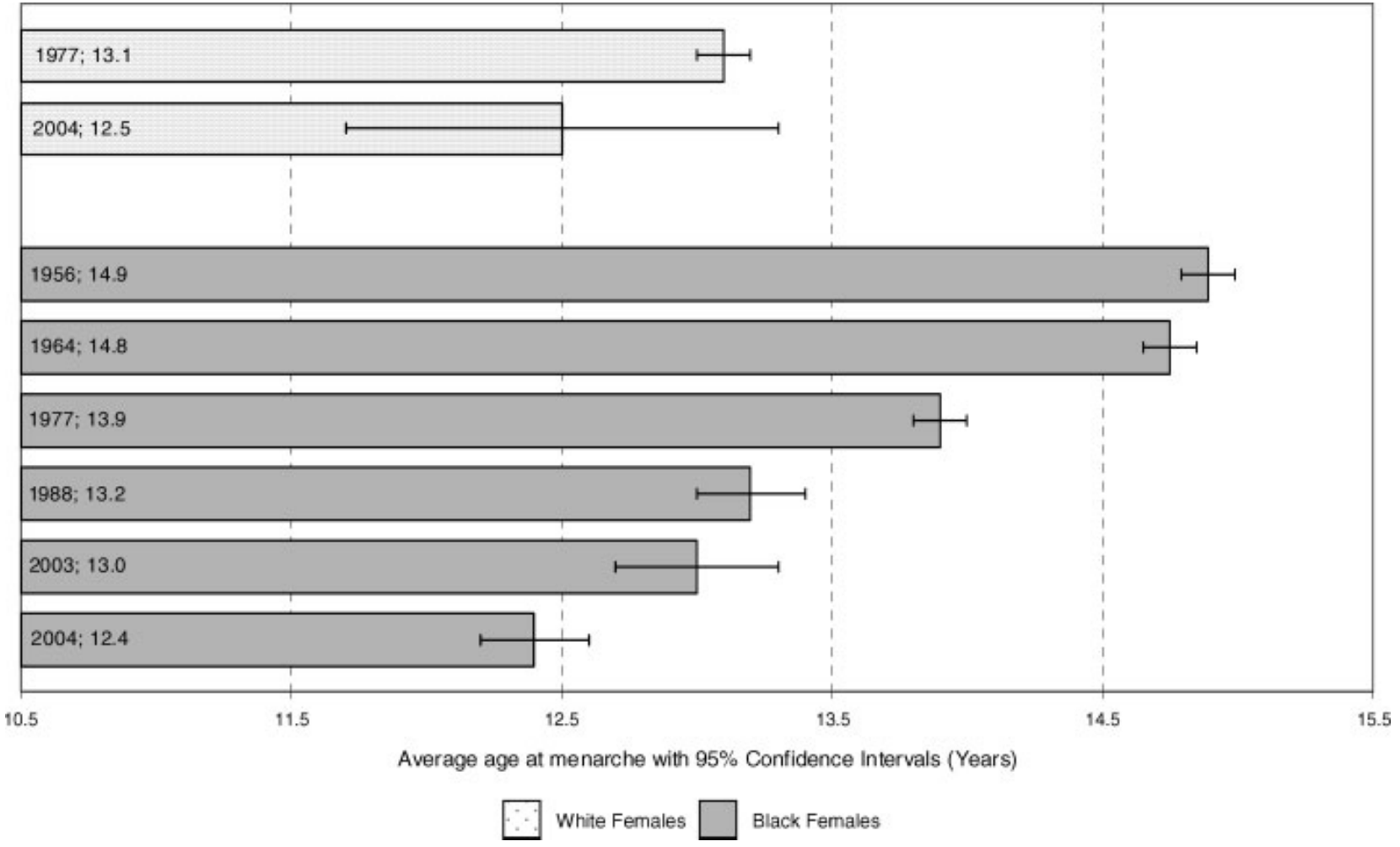
Bone Health children at age 15 years

Age 15.3 yrs
Tanner 5
BA 16.4 yrs

Age 15.2 yrs
Tanner 2
BA 13.8 yrs

Age 15.3 yrs
Tanner 4
BA 15.7 yrs

Age of menarche in South African girls

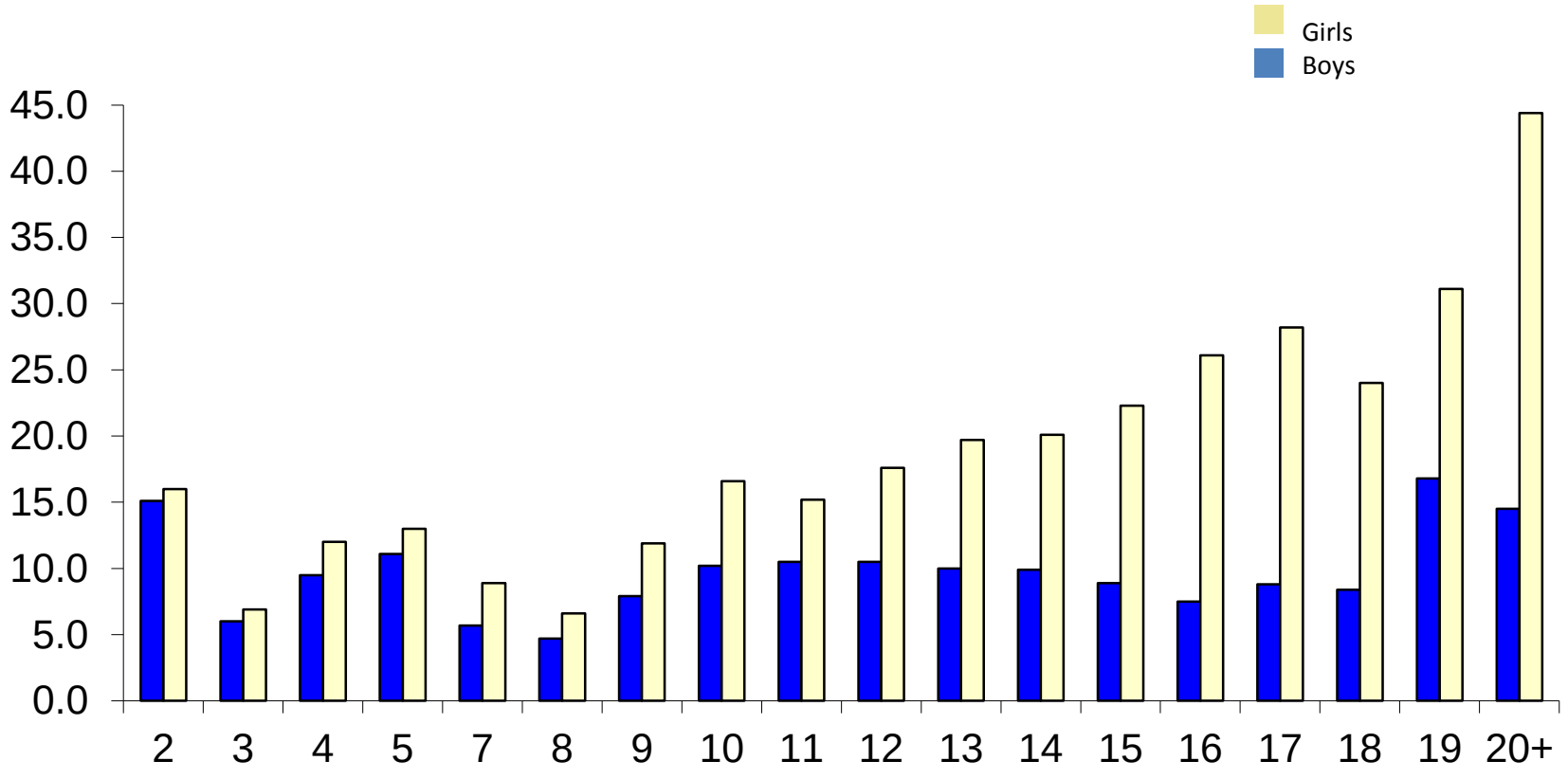


Jones LL et al Am J Hum Biol 2009; 21: 130

DPHRU
MRC/Wits Developmental Pathways for Health Research Unit

DPHRU
MRC/Wits Developmental Pathways for Health Research Unit

Overweight & obesity prevalence (%)



DPHRU
MRC/Wits Developmental Pathways for Health Research Unit

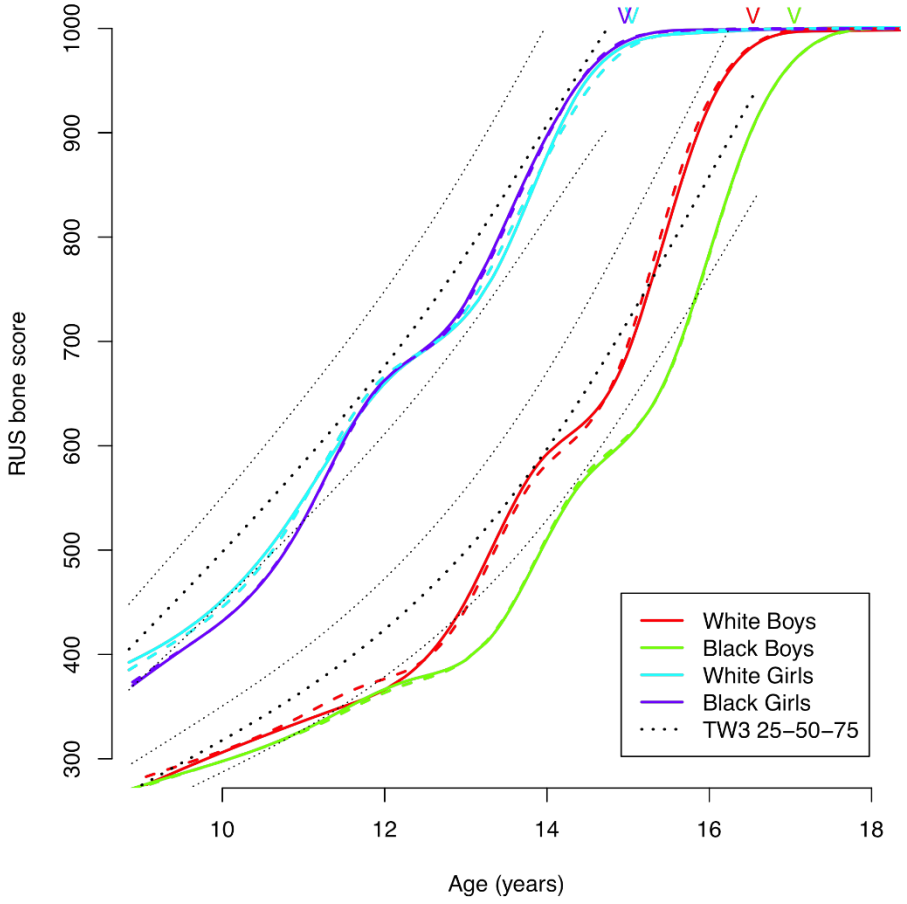
Risk of obesity at 16-18 years of age based on status at the infant/toddler or early childhood periods

	Odds Ratio	95% confidence interval
Girls		
Infancy/toddlerhood (1–2 years)		
Overweight	3.6***	1.8, 7.2
Obese	8.0***	3.7, 17.6
Early childhood (4–8 years)		
Overweight	6.8***	3.3, 13.9
Obese	42.3***	15.0, 118.8
Boys		
Infancy/toddlerhood (1–2 years)		
Overweight	5.6**	1.7, 18.0
Obese	3.4	0.6, 17.8
Early childhood (4–8 years)		
Overweight	2.1	0.5, 8.4
Obese	19.7***	5.1, 75.9

Girls who were obese in early childhood had 42.3 times greater odds of being obese at 16-18 yrs

Lundeen et al., Paediatric Obesity, 2015

Skeletal age development (Birth to 20 cohort)



- Skeletal maturity was reached 1.9 years earlier in girls than boys;
- Skeletal maturity was delayed by 7 months in black boys compared to white boys

DPHRU
MRC/Wits Developmental Pathways for Health Research Unit

Cole TJ et al. Arch Dis Child 2015; 100:138-43

ORIGINAL ARTICLE

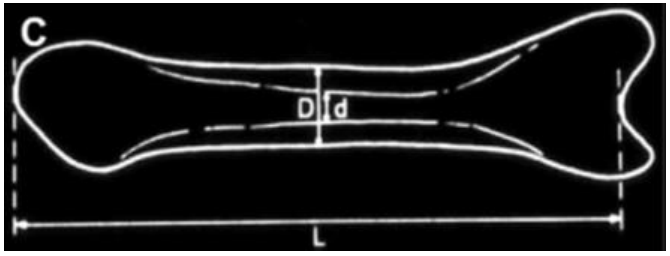
JBMR®

Metacarpal Growth During Adolescence in a Longitudinal South African Cohort

Ansuyah Magan, Lukhanyo H Nyati, Lisa K Micklesfield, Shane A Norris, and John M Pettifor

South African Medical Research Council/Wits Developmental Pathways for Health Research Unit, Department of Paediatrics, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

To monitor the drift of the periosteal and endocortical surfaces during metacarpal growth longitudinally, radiogrammetry was carried out on hand-wrist X-rays of 572 children from the Birth to Twenty Bone Health Cohort annually from ages 9 to 21 years. This is the largest collection of longitudinal X-rays in African children.



DPHRU
MRC/Wits Developmental Pathways for Health Research Unit

HIGHLIGHTS

ORIGINAL ARTICLE

JBMR®

Metacarpal Growth During Adolescence in a Longitudinal South African Cohort

Ansuyah Magan, Lukhanyo H Nyati, Lisa K Micklesfield, Shane A Norris, and John M Pettifor

South African Medical Research Council/Wits Developmental Pathways for Health Research Unit, Department of Paediatrics, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

- Black adolescents had wider bones with relatively thinner cortices and wider medullary cavities than their white peers.
- In black males, medullary width contraction commenced approximately 3 years later than in black females, whereas in white males this occurred a year later than in white females.
- The ethnic and sex differences in bone acquisition reported in this study may differentially affect bone mass in later life.

Conclusions

- Largest longitudinal cohort in Africa
- Provides longitudinal data throughout childhood and adolescence, and into young adulthood
- 3 generations – intergenerational transfer of risk

DPHRU
MRC/Wits Developmental Pathways for Health Research Unit

DPHRU
MRC/Wits Developmental Pathways for Health Research Unit