



Bone ageing in practice

Kate Ward (PhD)

Associate Professor

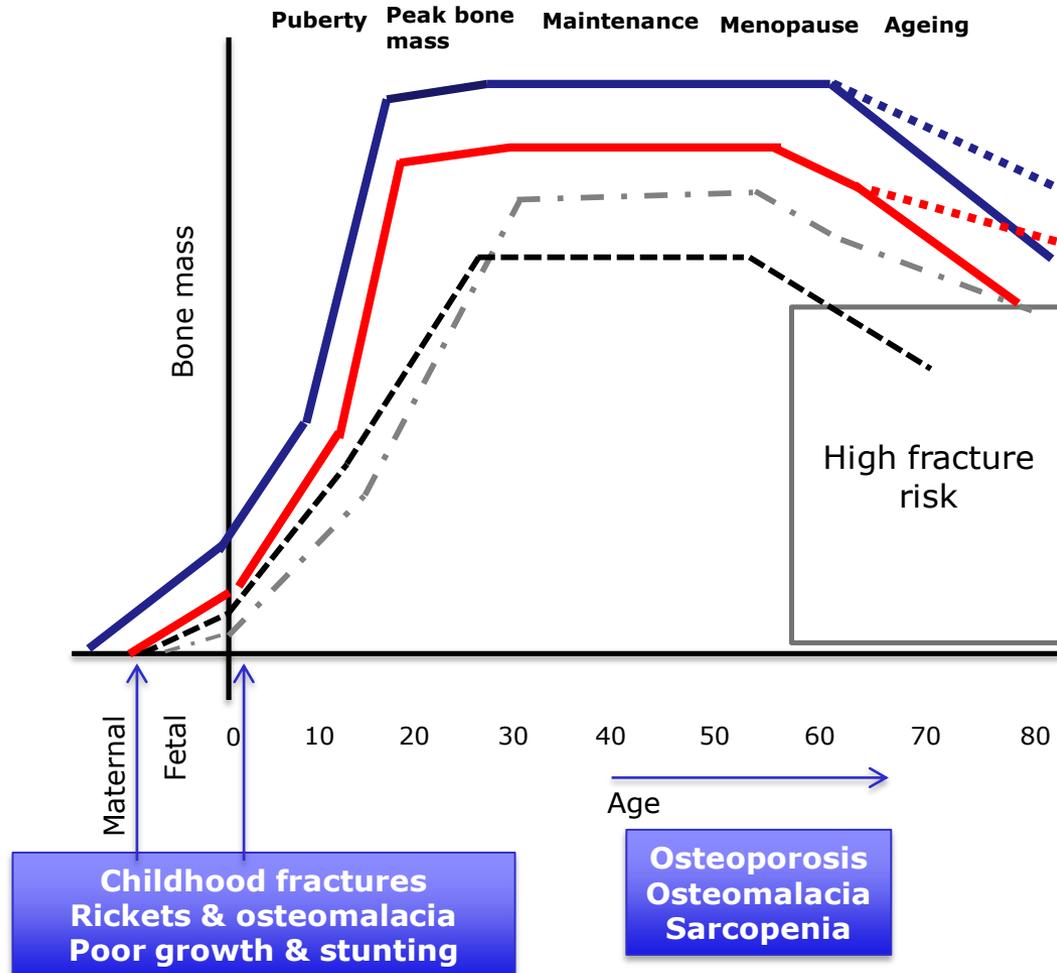
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Objectives

- Understand different methods of assessing bone in children and adults
- Optimise technique when performing pQCT
- Understand how to process and analyse the outputs generated by pQCT
- Understand and interpret assessments of bone age

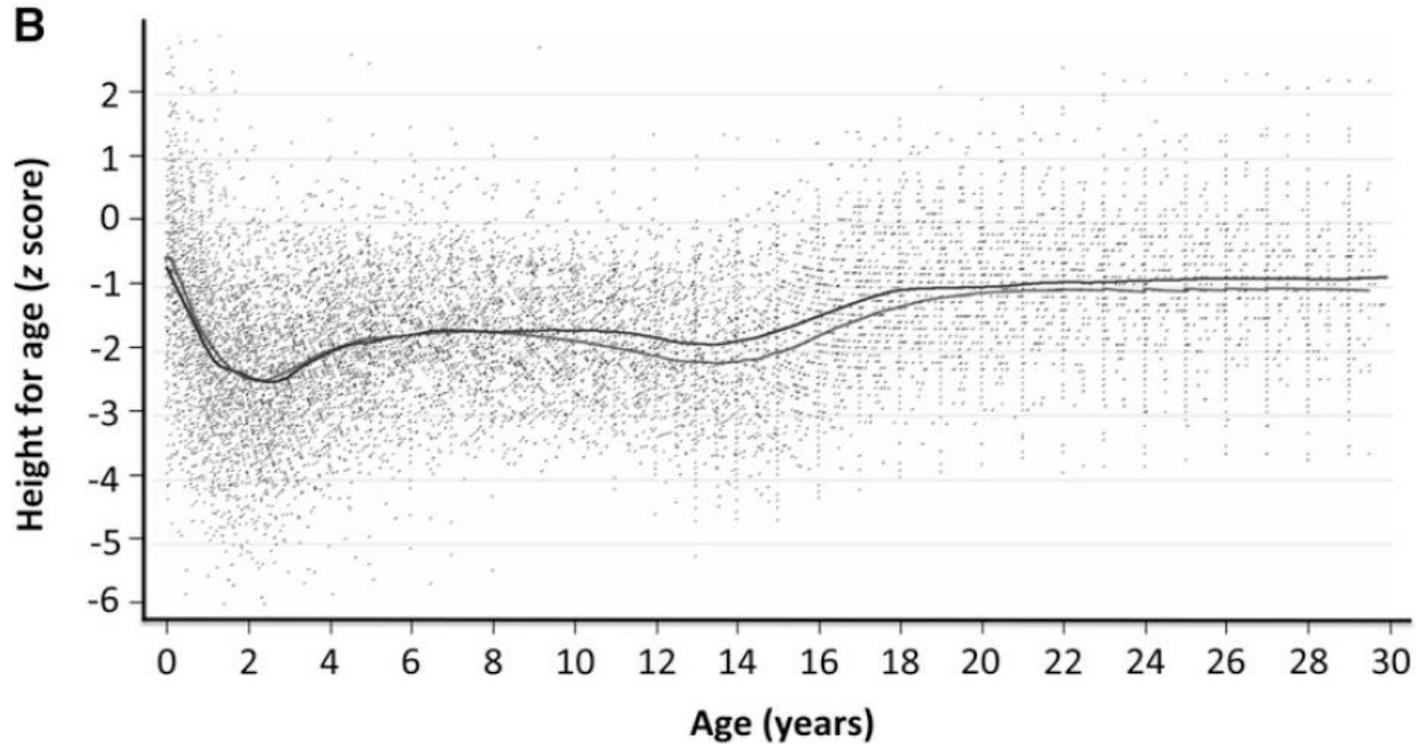


Musculoskeletal health through the lifecourse



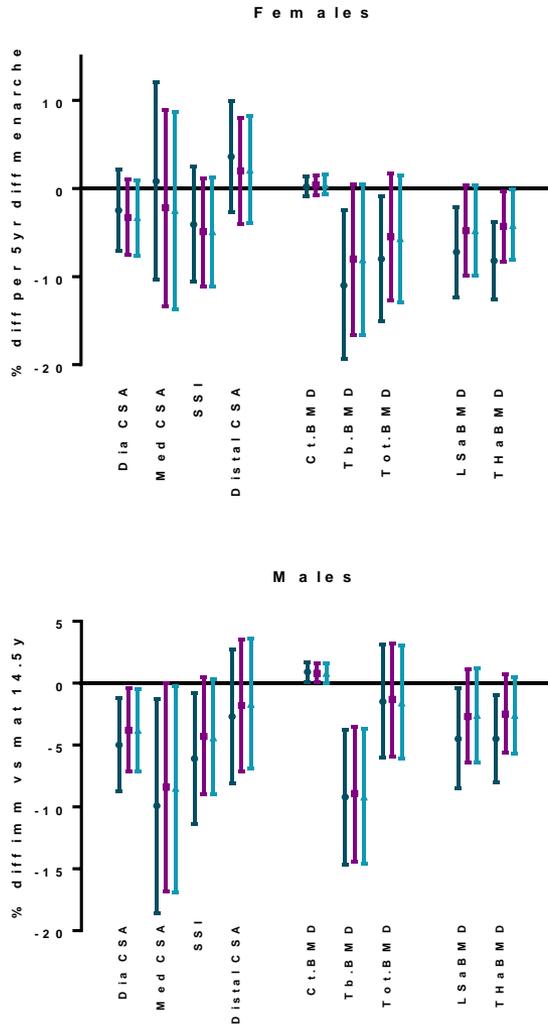
Ward, Proc Nutr Soc (2012), 71, 27-37
 Kuh, Ward et al JBMR 2014, IJE 2016
 Cole et al IJE 2016

Does everyone grow at the same rate?



National Survey of Health and Development

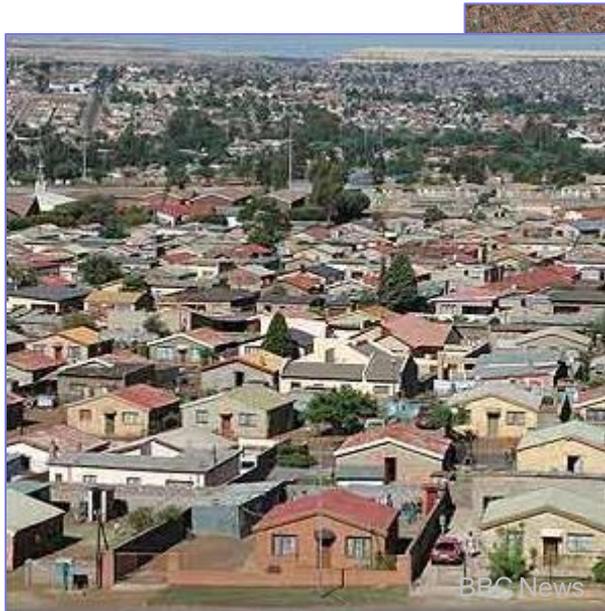
Childhood & adolescent growth, life course environment, adult bone phenotype, strength and fracture



- Associations between height and weight gain at different stages of growth and bone phenotype (using arbitrary growth periods 2-4, 7-15, 15-19)
- Importance of birth weight, childhood and adolescent growth in height and weight to bone size, shape, and strength, with fewer and weaker associations with vBMD and aBMD.
- Δ adult weight were also positively related to differences in vBMD at the radius and aBMD at the hip and lumbar spine.
- Later puberty was consistently associated with lower trab BMD and aBMD
- SITAR parameters strongly associated with vBMD, earlier puberty associated with 13% greater vBMD, and speed and amount of weight gain associated with bone size and strength

Birth to Twenty

- Soweto, Johannesburg
- Largest and longest-running longitudinal study in Africa: initial enrolment of 3200 black and white children, all born in 1991 (Bone Health sub-study, $n = 543$)





OPEN ACCESS

Ethnic and sex differences in skeletal maturation among the Birth to Twenty cohort in South Africa

Tim J Cole,¹ Emily K Rousham,² Nicola L Hawley,^{3,4} Noel Cameron,^{2,4}
Shane A Norris,⁴ John M Pettifor⁴

- Skeletal maturity is influenced by age, gender and ethnicity
- There is a paucity of data in LMIC's
- The timing tempo and rate at which growth proceeds determines the time at which skeletal maturity and so final height is reached
- 607 girls and boys measured annually from 9 to 20 years old
- Tanner Whitehouse III RUS scores; individual and mean growth curves
- Median #9 measurements

Paediatric left hand radiograph illustrating the groups of bones used in TW3 bone-ageing. The RUS group is shown in red and the CAR group is shown in black/white.

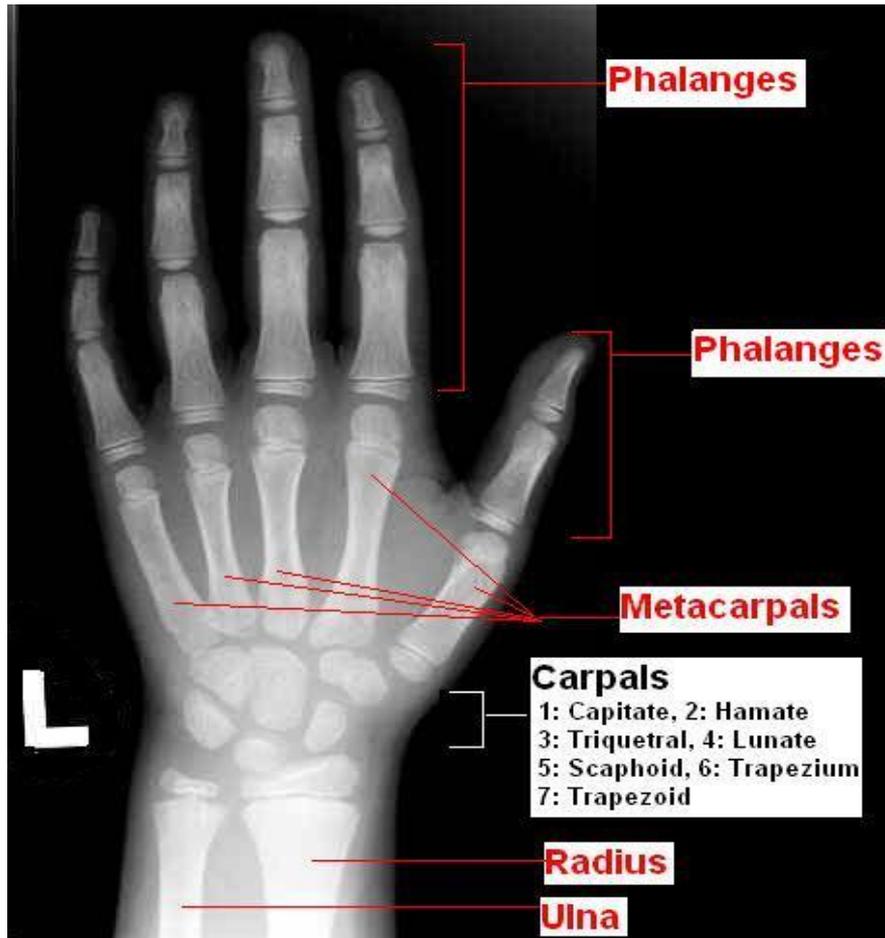
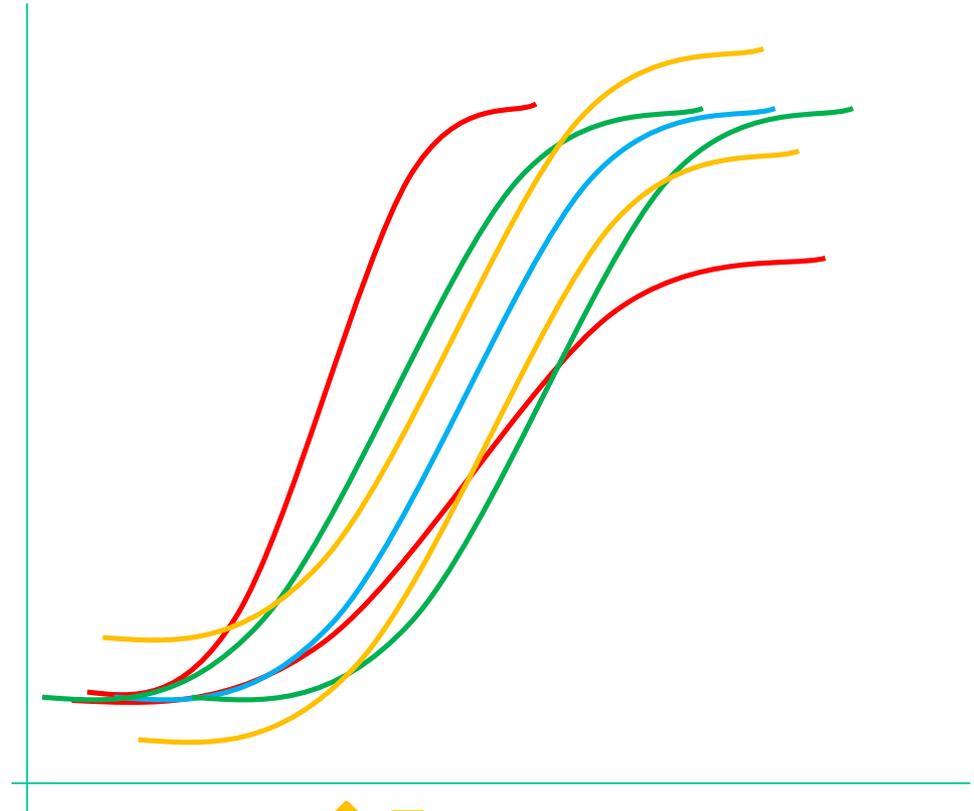
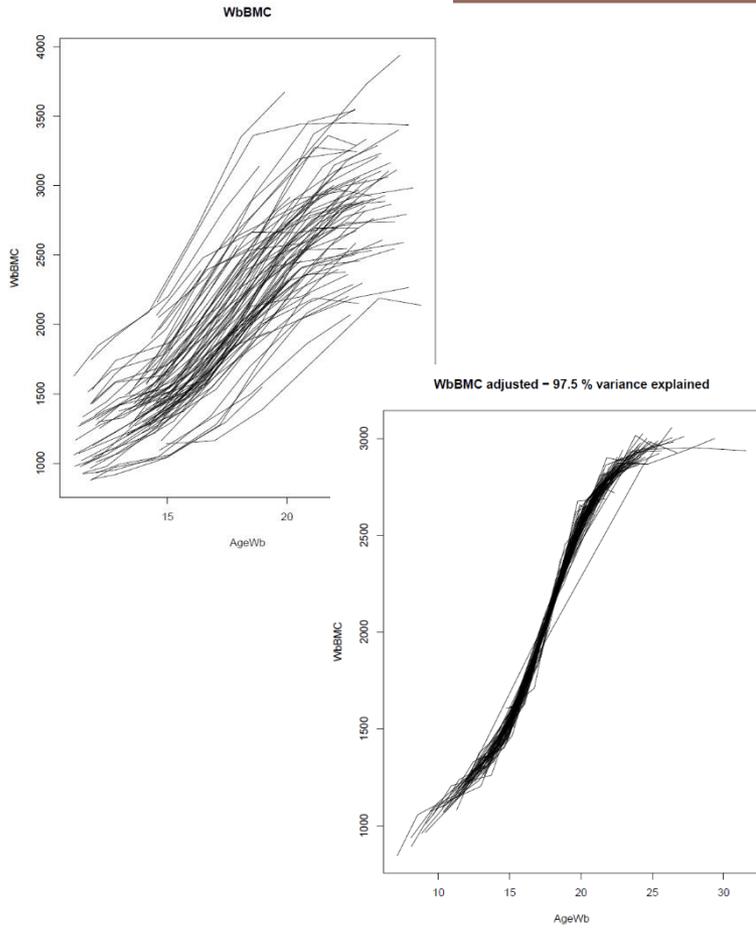


Table 2: Measurements	CV
GP Bone-ageing using hand radiographs (result from DXA hand study)	2.68
TW3 Bone-ageing using hand radiographs (RUS Scores)	1.61

SITAR

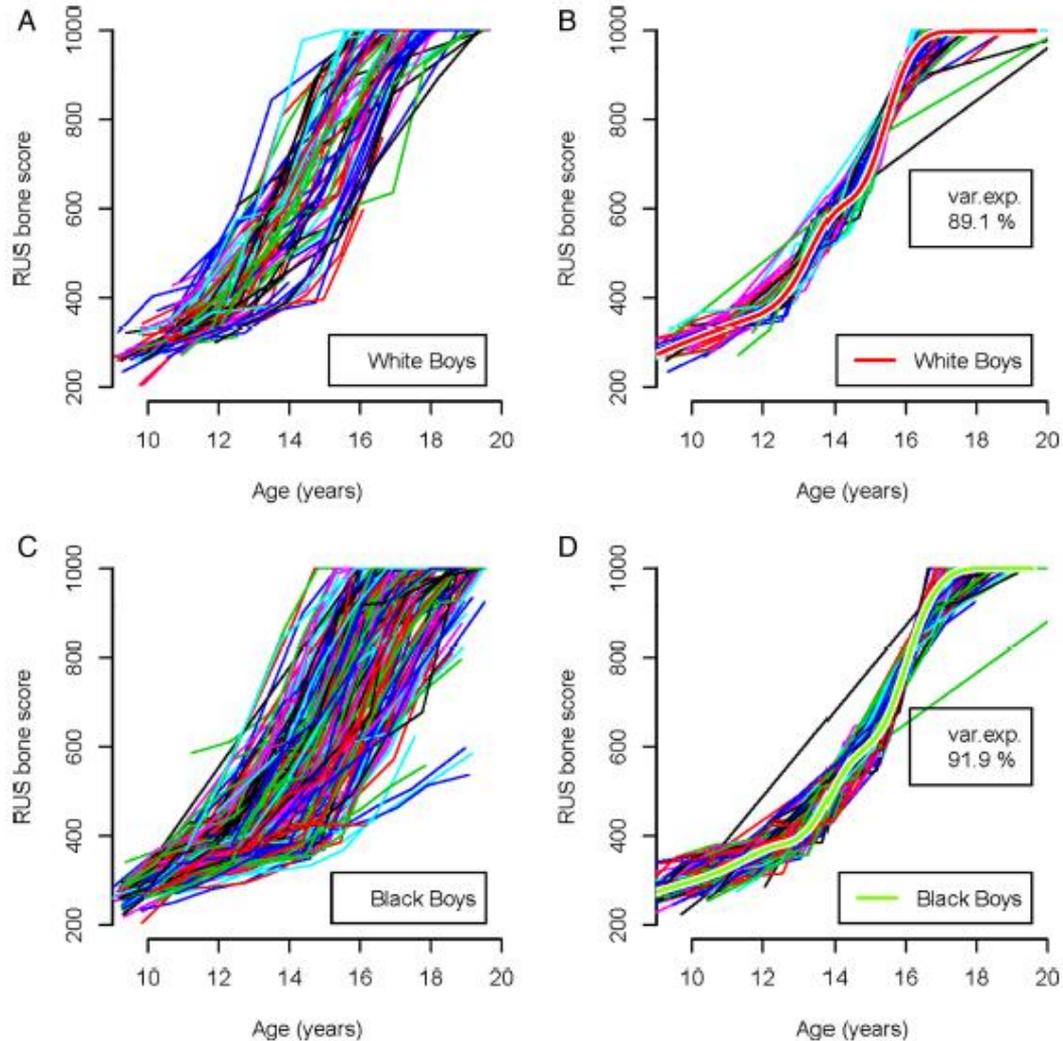


Tempo

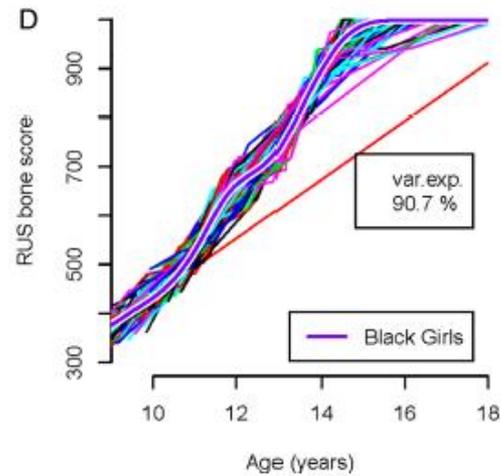
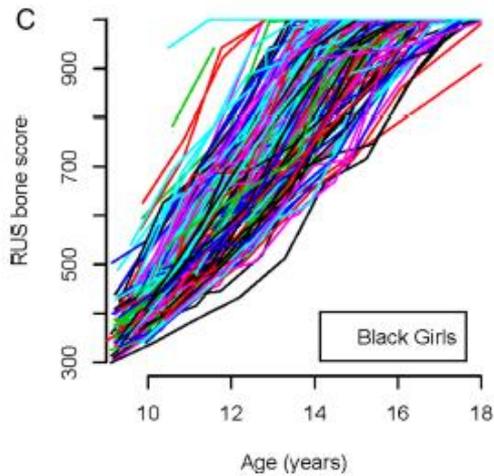
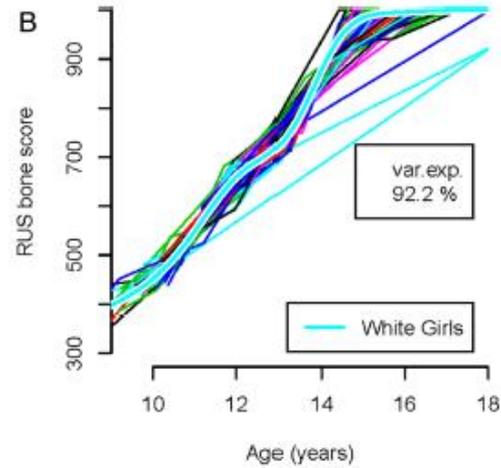
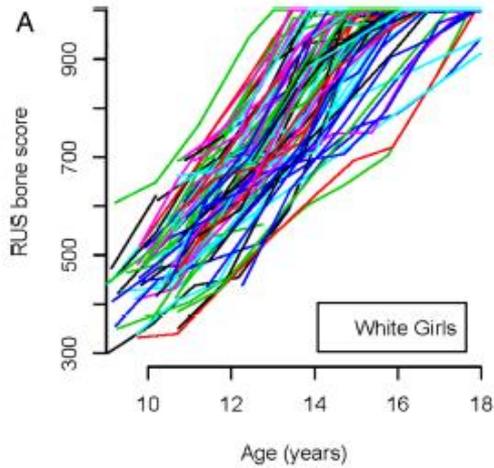
Size

Velocity

SITAR & skeletal maturity: Boys



SITAR & skeletal maturity: Girls



Results

Table 1 Median age at maturity, and summary of SITAR analyses of RUS bone score on age fitted to the four groups by sex and ethnicity

	White boys	Black boys	White girls	Black girls
N of subjects/measurements	106/575	214/1803	101/615	186/1572
Median age at maturity (years)	16.5	17.0	15.0	15.0
Spline degrees of freedom	5	7	7	6
Residual SD (bone score units)	29	30	22	23
SD of tempo random effect (%)	6.1	7.9	7.6	7.2
SD of velocity random effect (%)	20	20	22	15
Tempo–velocity correlation	0.2	0.2	–0.2	–0.2
Variance explained (%)	89	92	92	91

RUS, radius, ulna and short bones.

Summary

- First longitudinal data studying skeletal maturity in Sub-Saharan Africa, and one of a few across the globe.
- Black and white girls mature at a similar rate but black boys mature later than white boys.
- Girls mature earlier than boys
- Supports the hypothesis that boys may be more susceptible to unfavourable environments than girls
- Provides a standard reference for the region

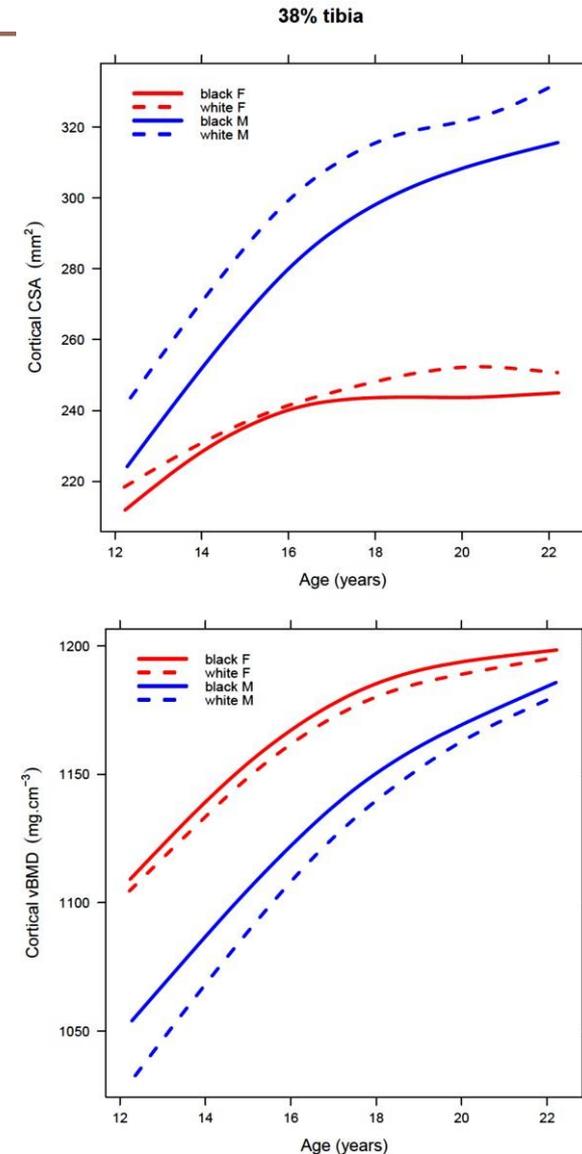
Aims and methods

- **To determine whether previously observed ethnic differences in pQCT outcomes are in part a result of differences in pubertal timing.**
 - Not comparing like with like?
- 543 subjects (255 male)
 - Birth to Twenty cohort: Bone Health sub-study
- Adjustment for maturational timing
 - 'Biological age' = years since peak height velocity (PHV), determined using SITAR
- 3,184 pQCT observations, ages 12.3 – 22.2 years
 - 5.8 observations per subject (mean interval 1.7 years)
 - Radius 65%; Tibia 38%

Unadjusted pQCT

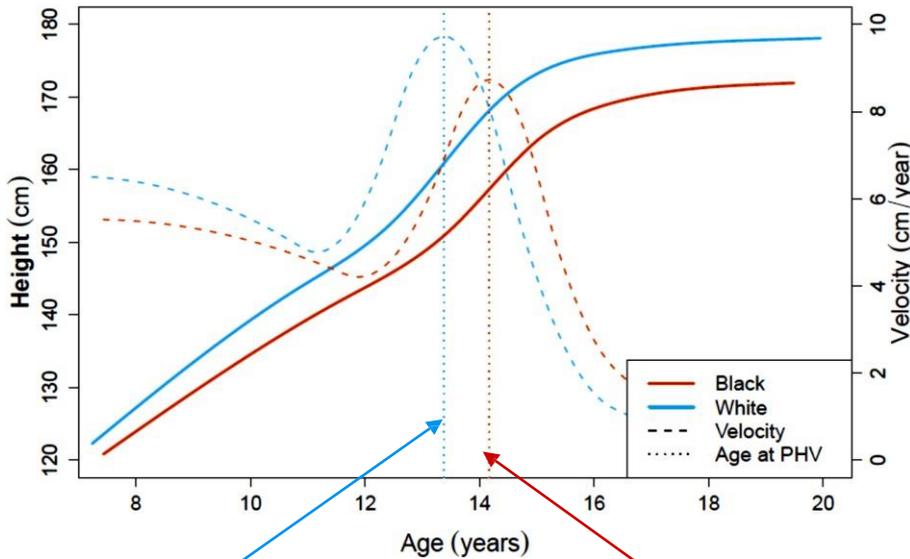
- Peripheral quantitative computed tomography (pQCT) vs *chronological age*
- Ethnic differences were age-, sex- and site-dependent
- Greater differences among boys than among girls
- Black adolescents tended to have narrower bones with a smaller cortical cross-section, but greater tibial density

(Schoenbuchner et al., OP10, *Bone Research Society Annual Meeting 2014, Sheffield, UK*)



Peak height velocity

Males: SITAR curves



White males 13.4 ± 0.7

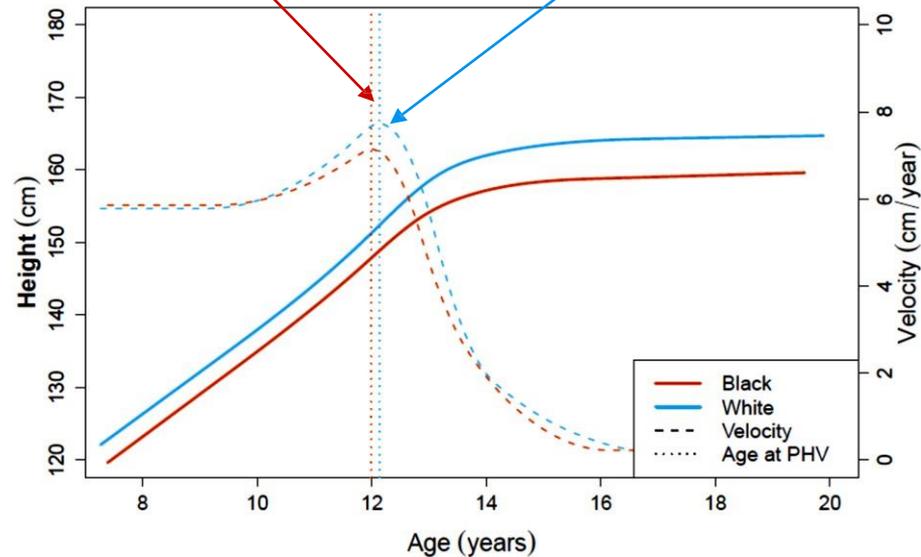
Black males 14.2 ± 1.0

- Height: 9 mo difference in APHV

White females 12.1 ± 0.9

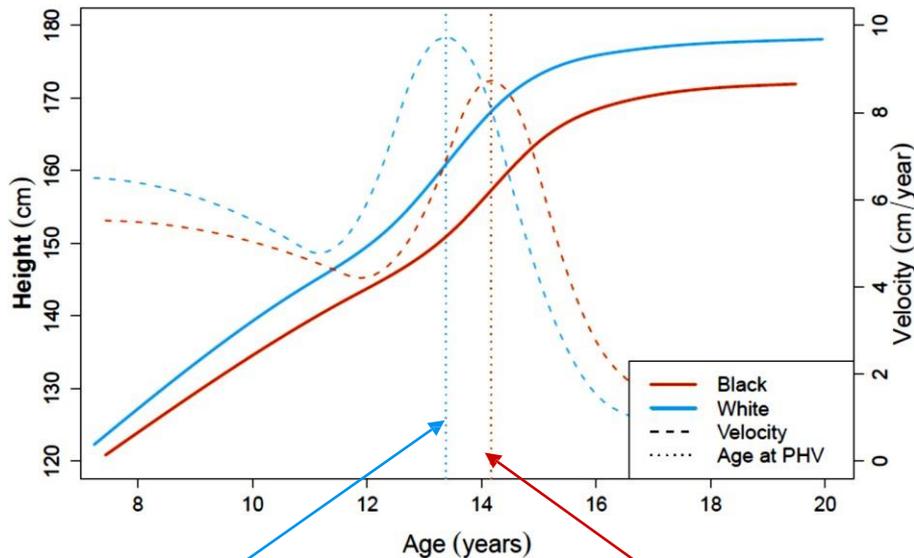
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Females: SITAR curves



Peak height velocity

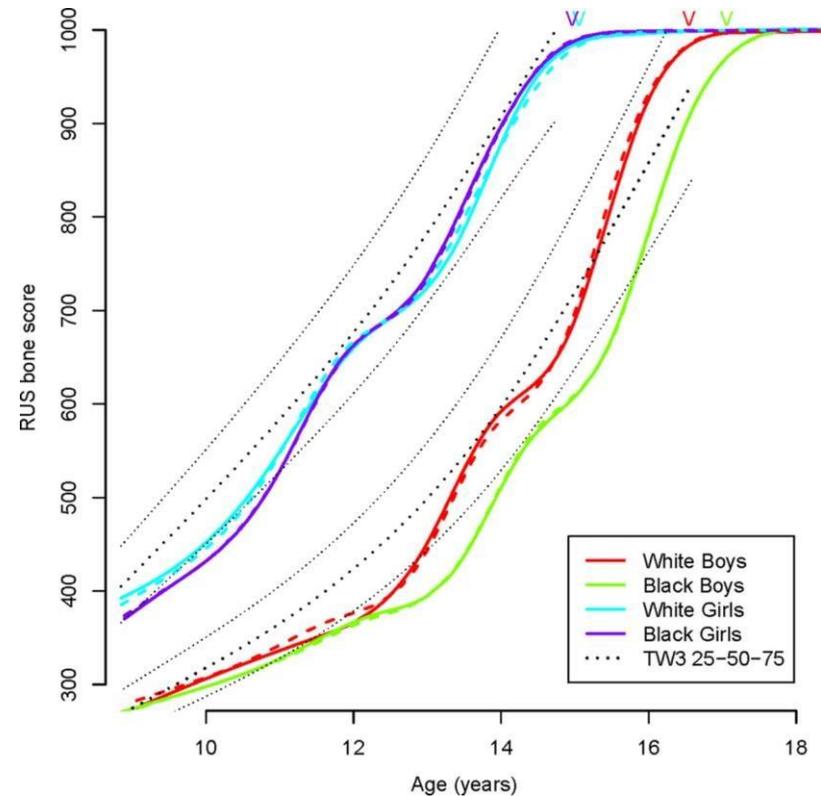
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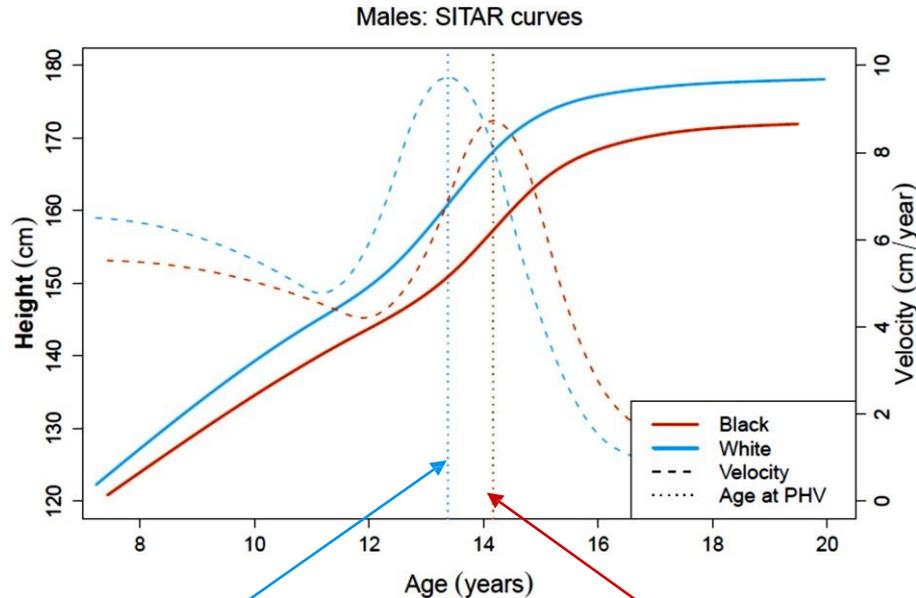
- Height: 9 mo difference in APHV



- Bone maturity (TW3):
7 mo difference in APHV

(Cole *et al.* 2014, *Arch Dis Child*)

Peak height velocity



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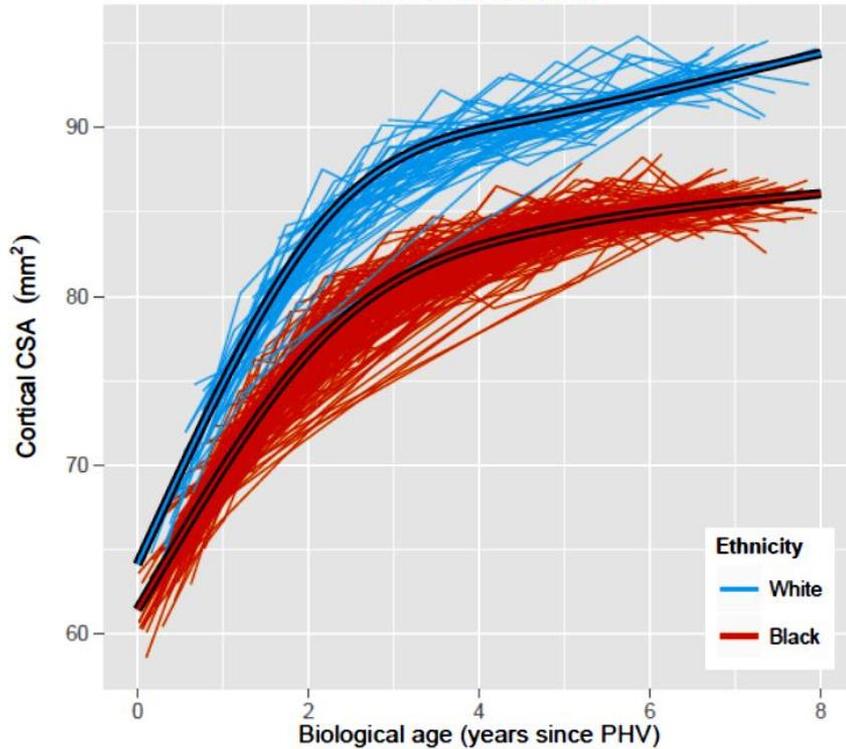
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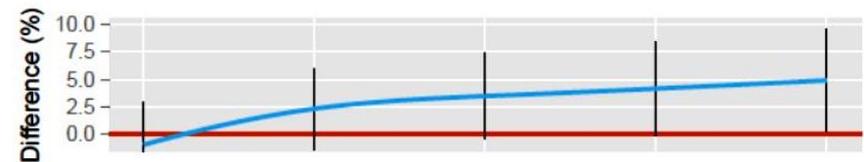
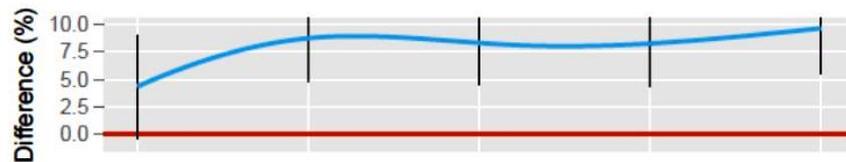
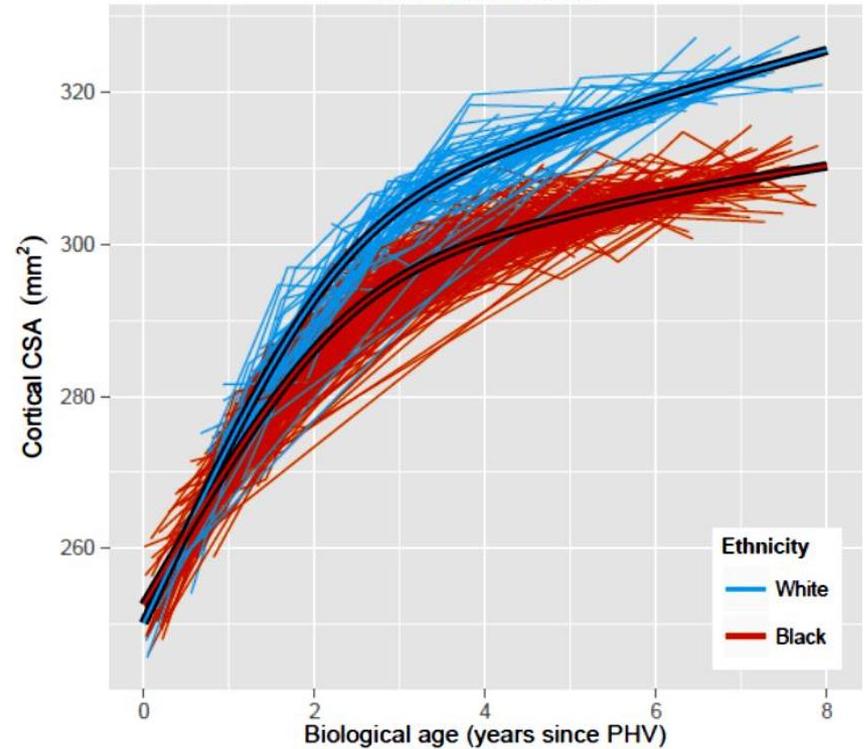
- Greater ethnic difference among males than among females: pQCT and age at PHV
- Differences in pubertal timing → not comparing like with like?
- 'Biological age' = years since PHV

Results

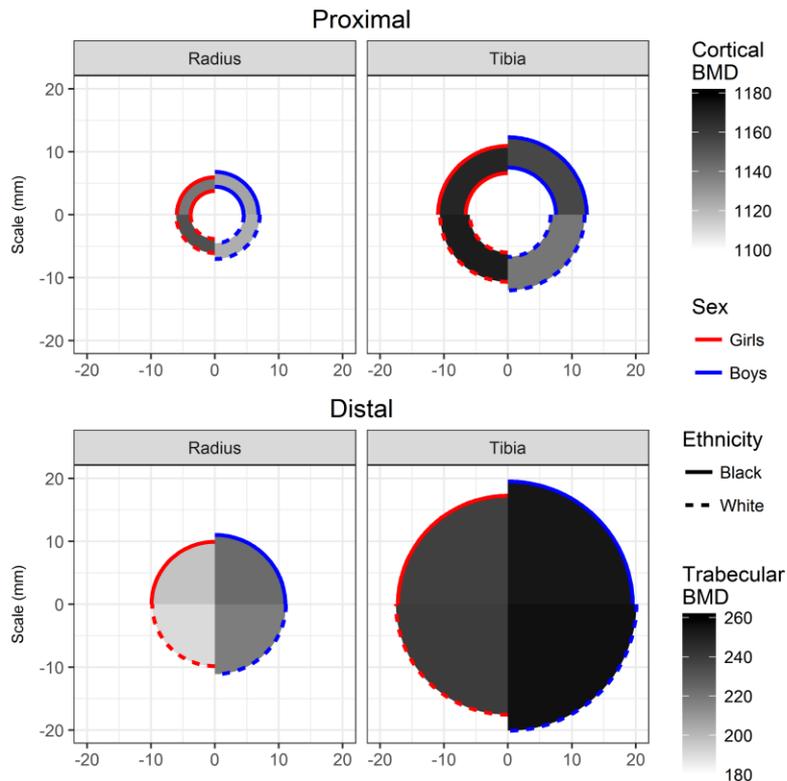
Males: 65% radius



Males: 38% tibia



Summary



Radius

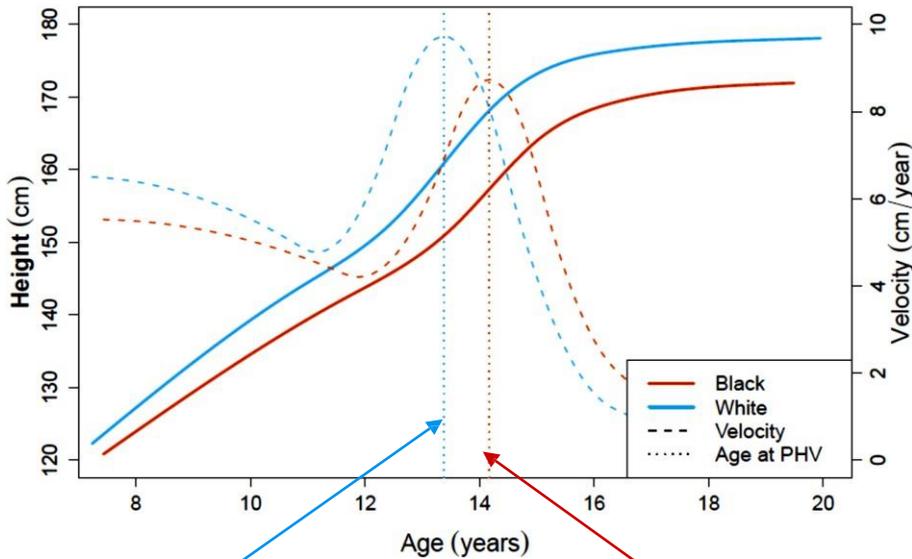
- White adolescents have larger cortical CSA & SSI than black
- Increasingly great trab BMD in black adolescents

Tibia

- White adolescents smaller bones wider medullary areas, lower SSI than black
- No ethnic differences in metaphyseal sites
- Fractures are greater in white adolescents than black (the same as in adults).

Peak height velocity

Males: SITAR curves

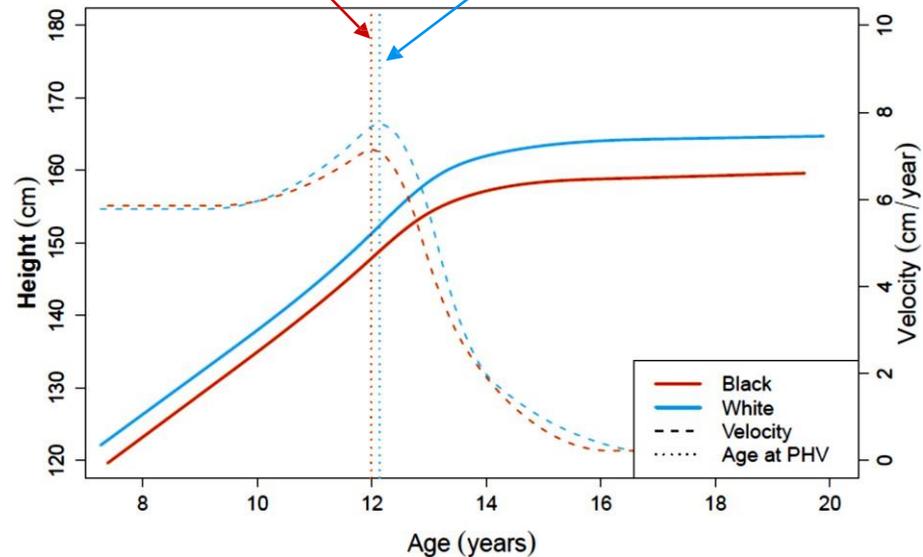


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Females: SITAR curves

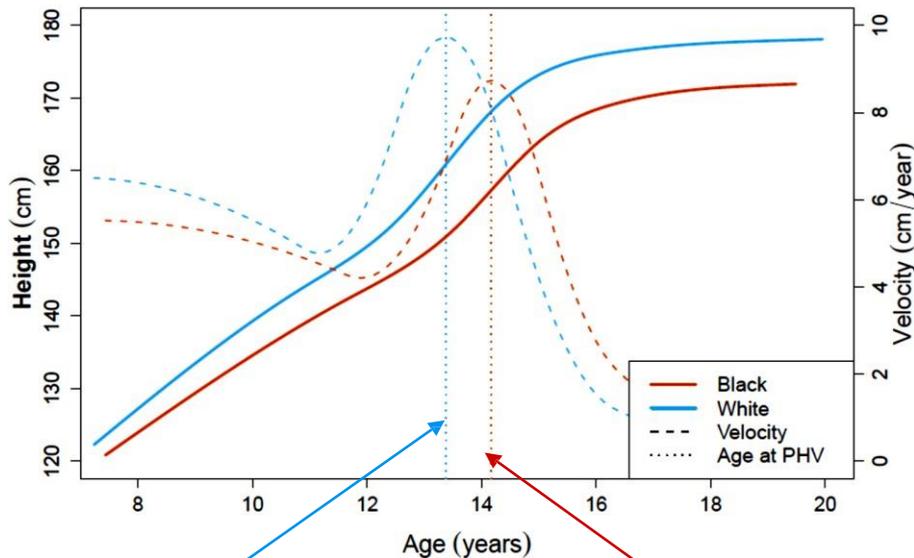


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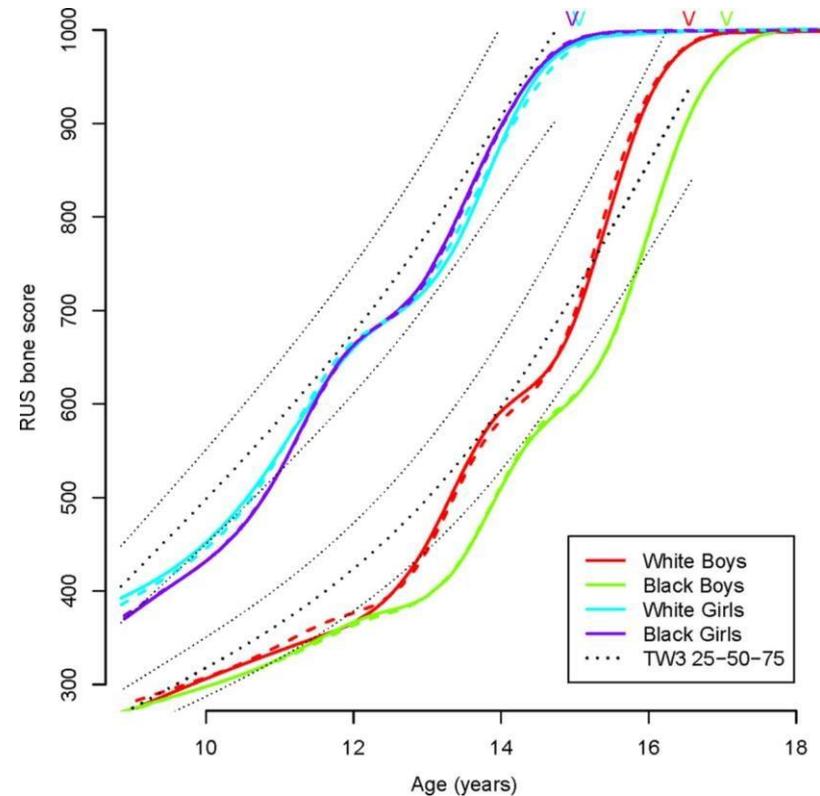
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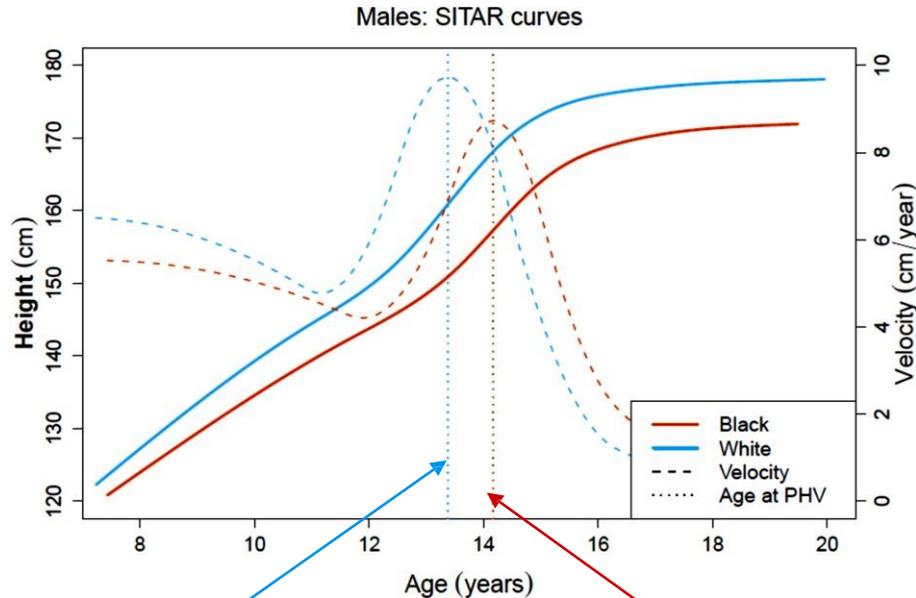
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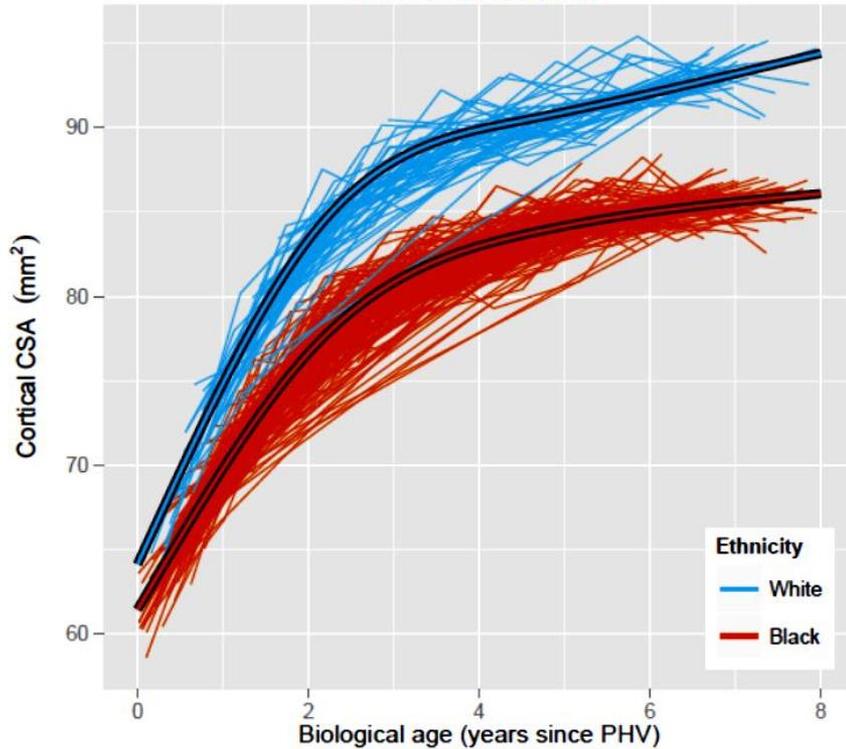
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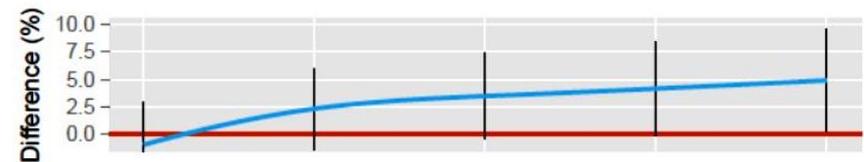
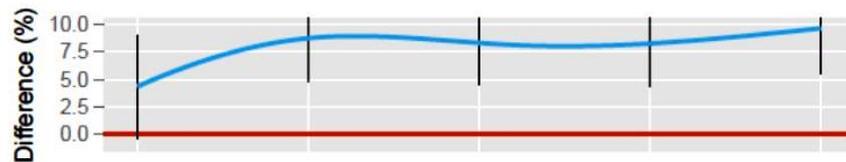
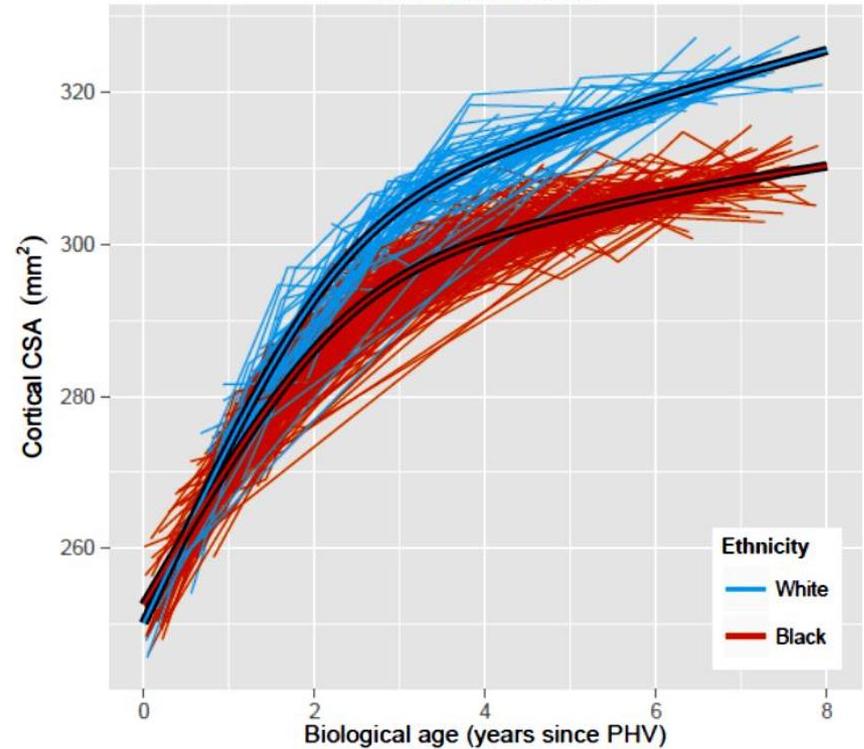
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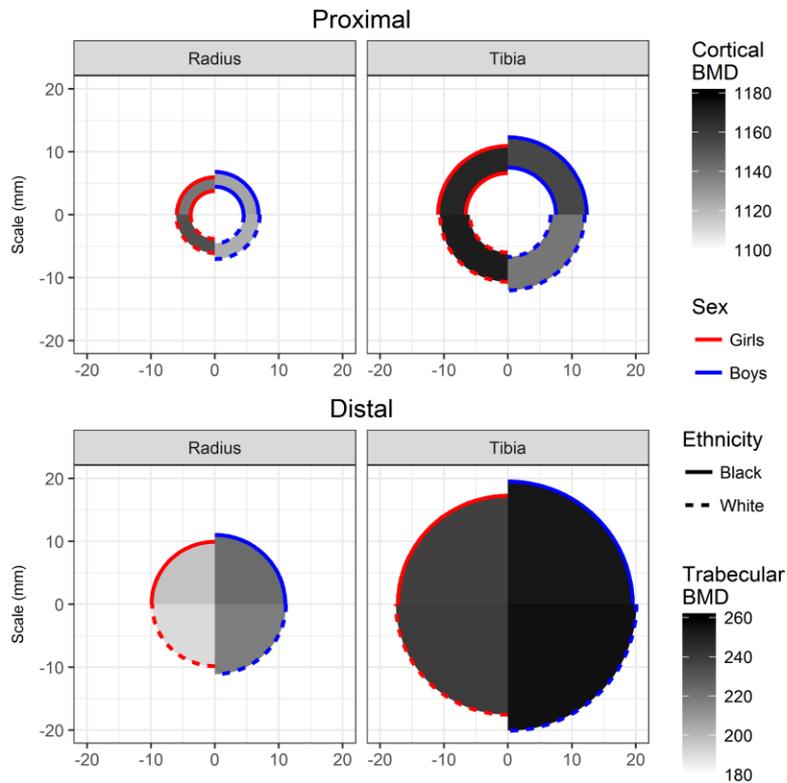
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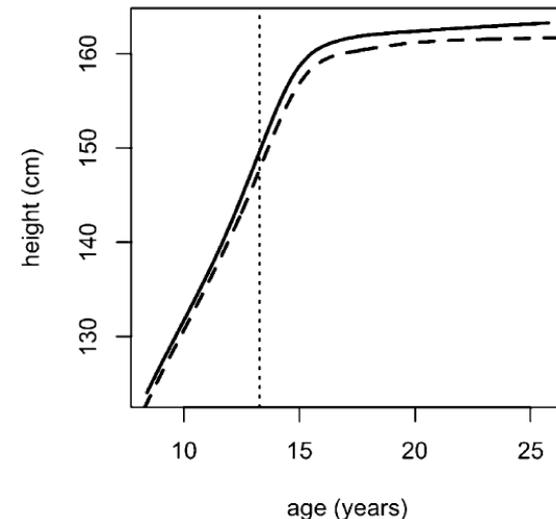
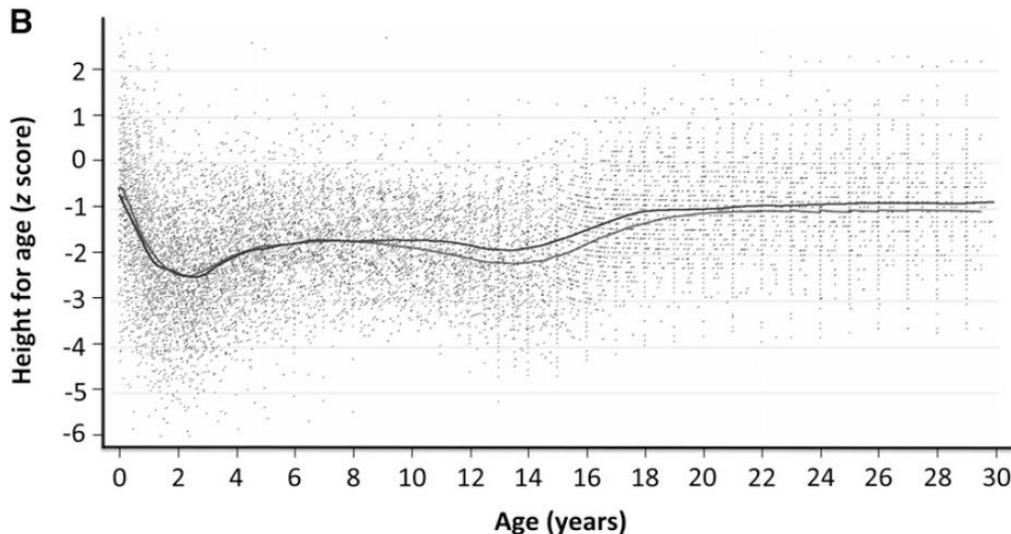
Discussion

- Differences remain site-specific:
 - May not generalise to others skeletal sites
- Associations with height remain to be tested:
 - Site-specificity of differences in bone implies that this is not just a matter of taller subjects having larger bones.
- Girls (not shown): after adjusting for maturational timing, patterns of the differences were similar, although absolute values were not

The Gambia



- High neonatal (29.9 per 1000) and maternal (706 per 1000) mortality ¹
- In 2010, 58.6% of girls were married before 18 years of age
- Rural, subsistence farming region
- Average life expectancy is 74.3 y (64.94 – 91.98) (The Gambia av. is 63y) ²
- Age at menarche ~14-15y ³ c.f. South Africa ~11-12y ⁴
- High rates of teenage pregnancy (191 per 1000 births) in rural regions ²



Gambia vs South Africa

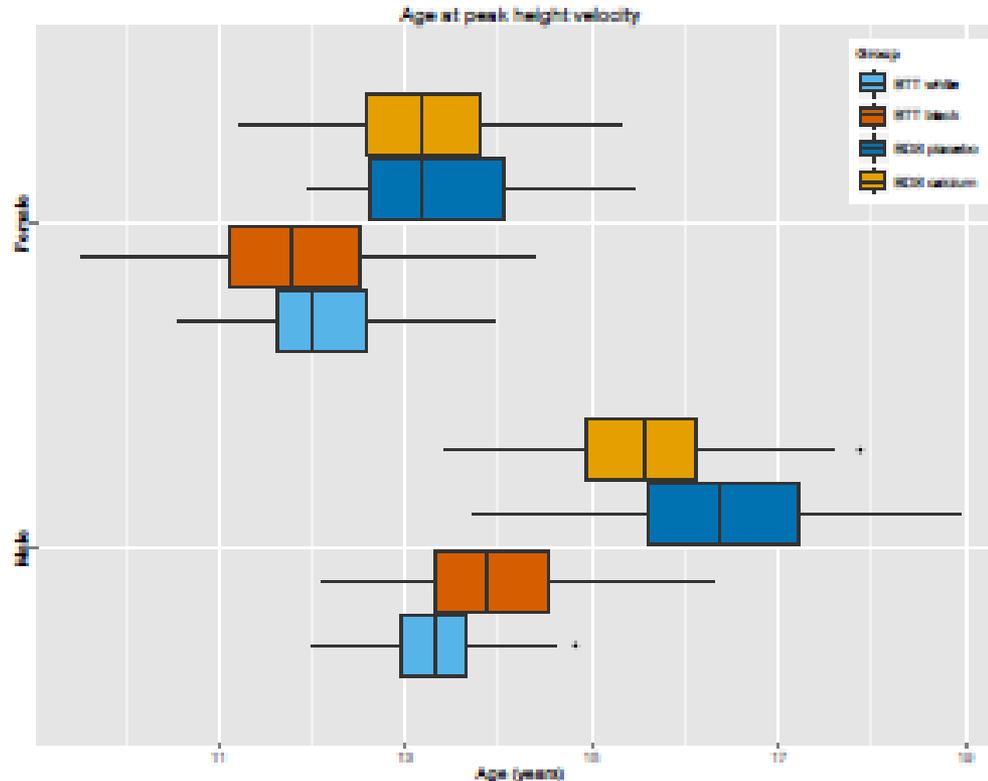


Figure 7.1: Age at PHV by sex and ethnicity or supplementation group. For the BTT cohort, only subjects from the Bone Health sub-study are shown.

Conclusions

- **Ethnic differences in long bone development are not only a result of variation in maturational timing**
- Comparisons of skeletal development between populations should take into account ethnic/individual differences in maturity
- Potential implications for adult skeletal health and fracture risk will require further investigation:

