



Decreased bone mass in perinatally HIV-infected school-aged South African children on ART

Childhood HAART Alterations in Normal Growth, Genes, and aGing Evaluation Study (CHANGES) Bone Study Team

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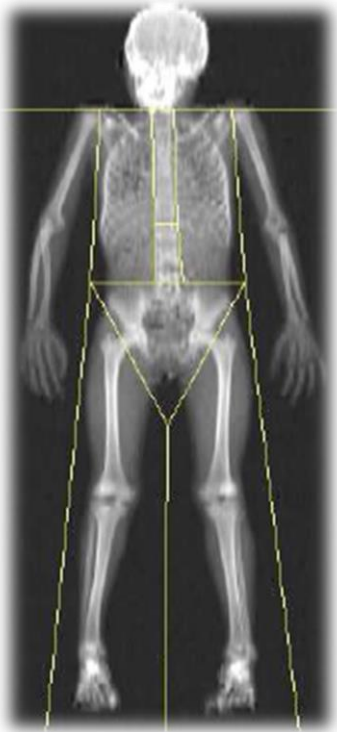


Background

- Increased risk of osteoporosis and fracture rates in HIV-infected adults
- Lower bone mineral content (BMC) and bone mineral density (BMD) also reported in HIV-infected children
 - Largest cumulative exposure to HIV and ART
 - Impaired bone accrual may compromise peak bone mass
- Little known about bone development among HIV infected children in resource-limited settings



Study Questions



Among South African pre-pubertal children:

1. Do HIV-infected children initiated on potent ART at an early age have lower bone mass compared to HIV-uninfected controls?
2. Is the lower bone mass solely due to the smaller size of the HIV-infected children?
3. Do HIV-infected children initiated and maintained on LPV/r-based ART have similar bone mass to children initiated on LPV/r-based ART and later switched to EFV?



Methods

- Analysis of baseline data from the **CHANGES** Bone Study
- Rahima Moosa Mother and Child Hospital, Johannesburg, South Africa
- Pre-pubertal children aged 5-9 years
 - **220** HIV-infected: initiated ART <2 years, enrolled from a prior clinical trial (NEVEREST 3)
 - **180** HIV-uninfected: siblings or household members of HIV-infected children as well as healthy children attending the site for preventive health services



Measurements

- Demographics
- Weight and height
- CD4 and HIV RNA levels (for HIV-infected children)
- Whole body bone mineral content (BMC) by dual-energy X-ray absorptiometry (DXA)



Hologic Discovery Wi bone densitometer



Statistical Approach

1. Compare BMC in grams between HIV+ and HIV-
2. Compare BMC-height Z-score between HIV+ and HIV- (to see if lower bone mass is due to smaller size)
 - BMC-height distribution of the uninfected children was used to generate a gender specific Z-score for each HIV-infected child
 - Generated using quantile regression
 - Used in studies of pediatric illnesses that adversely affect growth (cystic fibrosis¹, Crohn's disease², and sickle cell disease³)
 - Correlates well with volumetric cortical bone by QCT⁴
3. Compare BMC-height Z-score between children maintained on LPV/r and switched to EFV



¹Kelly J Clin Densitom 2008; ²Burnham JBMR 2004; ³Buison Pediatrics 2005; ⁴Leonard Bone 2004

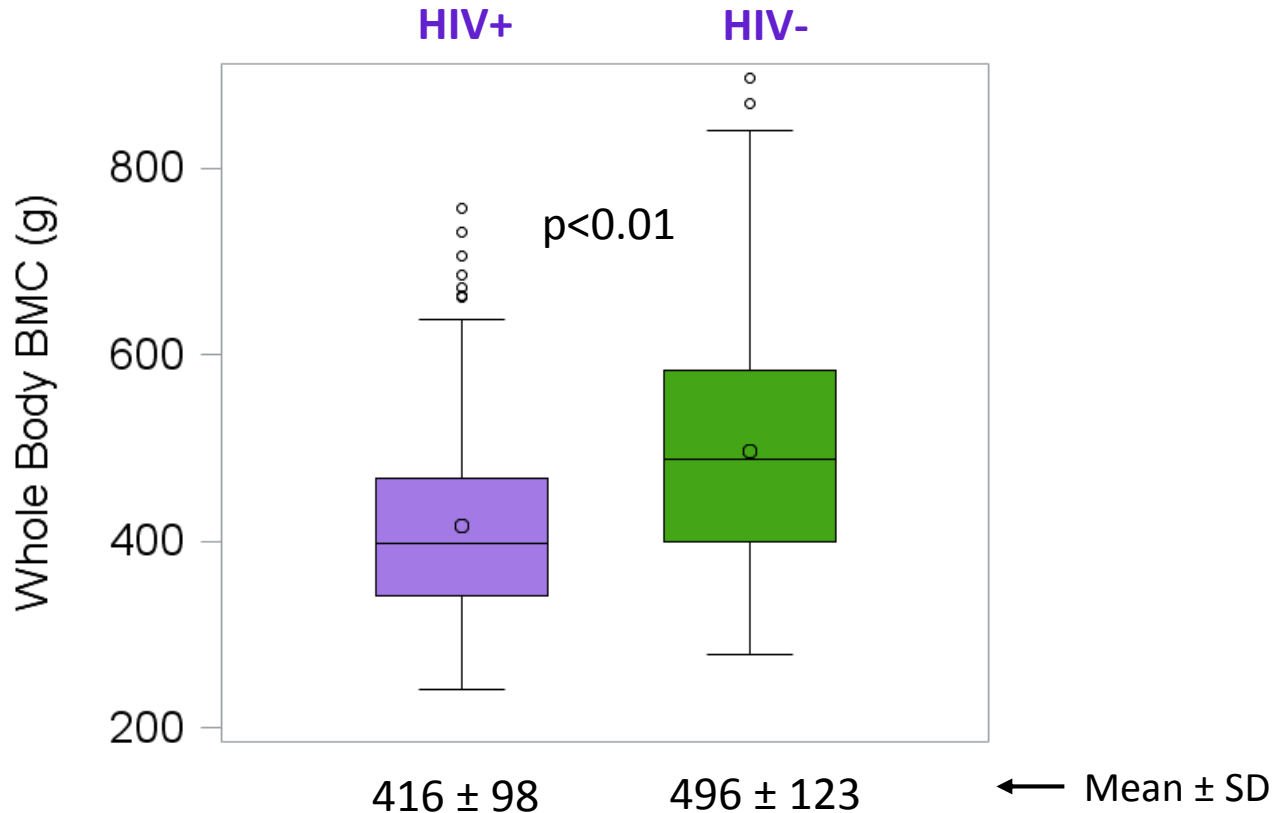
Characteristics of CHANGES Bone Study participants

Characteristic	HIV+ N=220	HIV- N=180	P
Male, %	49	55	0.24
Age in years, <i>Mean ± SD</i>	6.4 ± 1.3	7.1 ± 1.6	<0.01
WAZ, <i>Mean ± SD</i>	-0.8 ± 0.9	-0.6 ± 1.0	0.01
Underweight, %	11	5	0.03
HAZ, <i>Mean ± SD</i>	-1.4 ± 0.9	-1.2 ± 1.0	0.046
Stunted, %	26	19	0.08

WHO growth reference definitions: Underweight (WAZ < -2), Stunted (HAZ < -2)



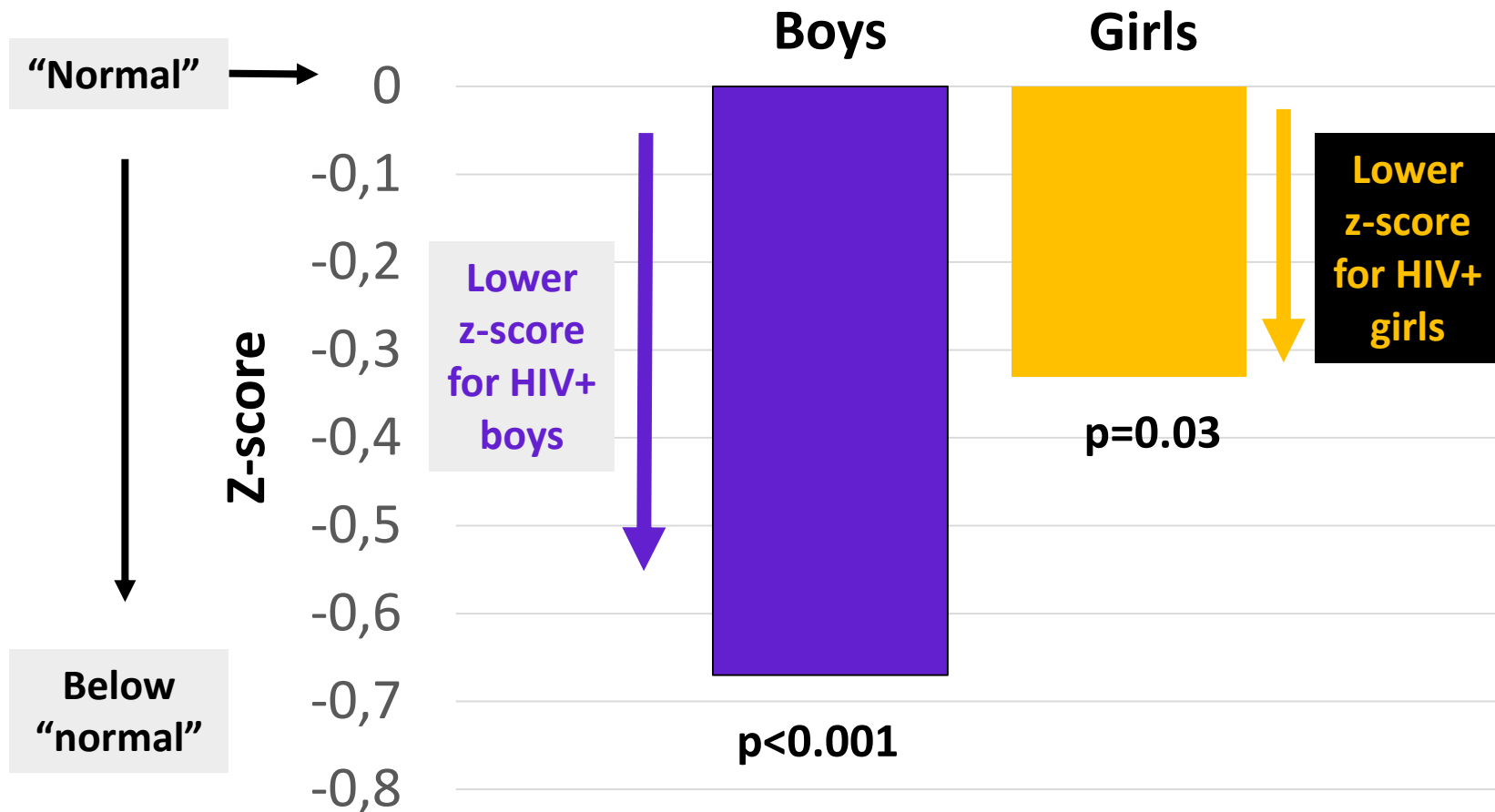
1. Bone mass is lower in HIV+ compared to HIV-



Is the lower bone mass due to smaller size of the HIV-infected children?



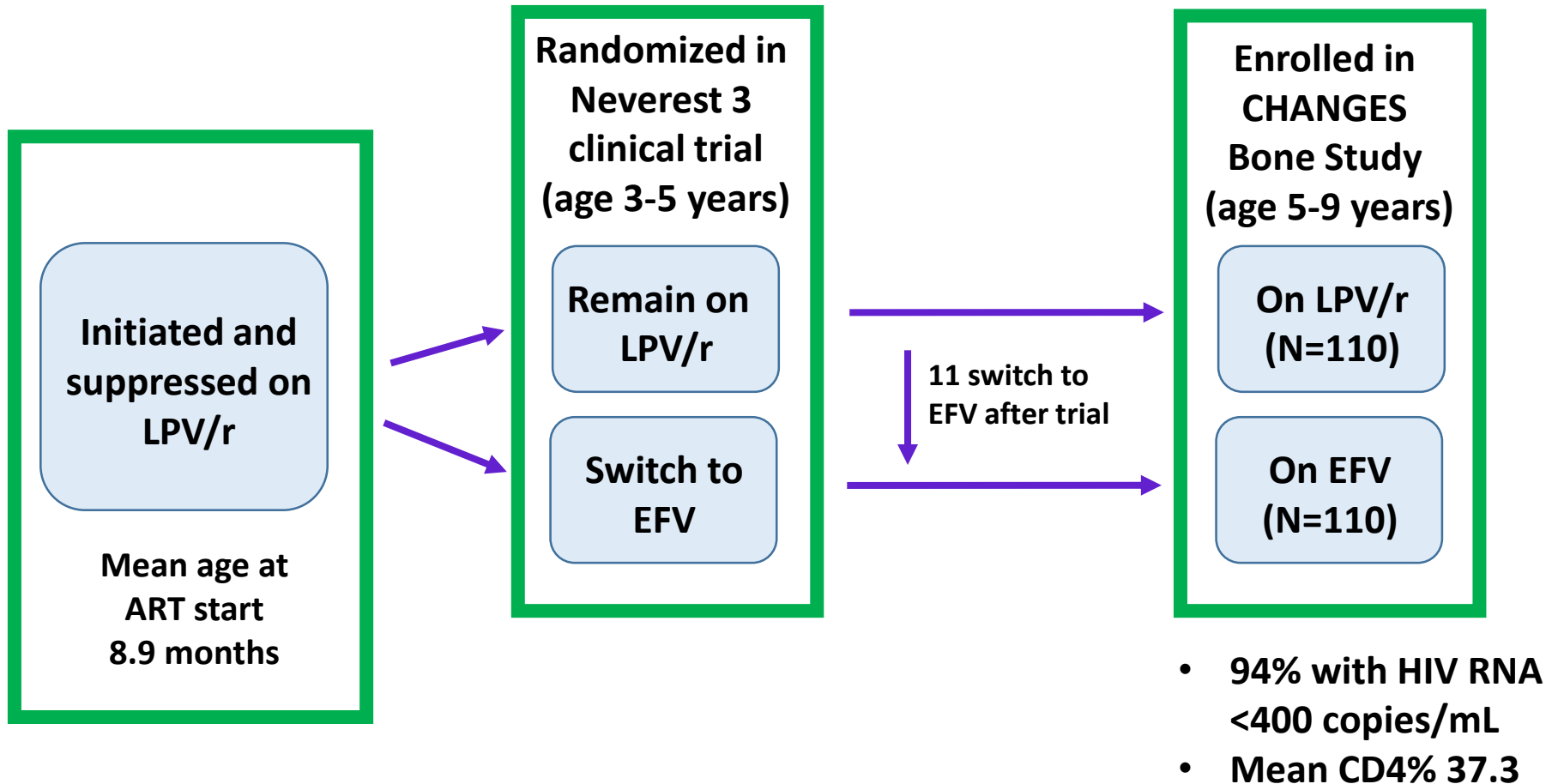
2. Difference in whole body BMC-height Z-score* between HIV+ and HIV-



*adjusted for age

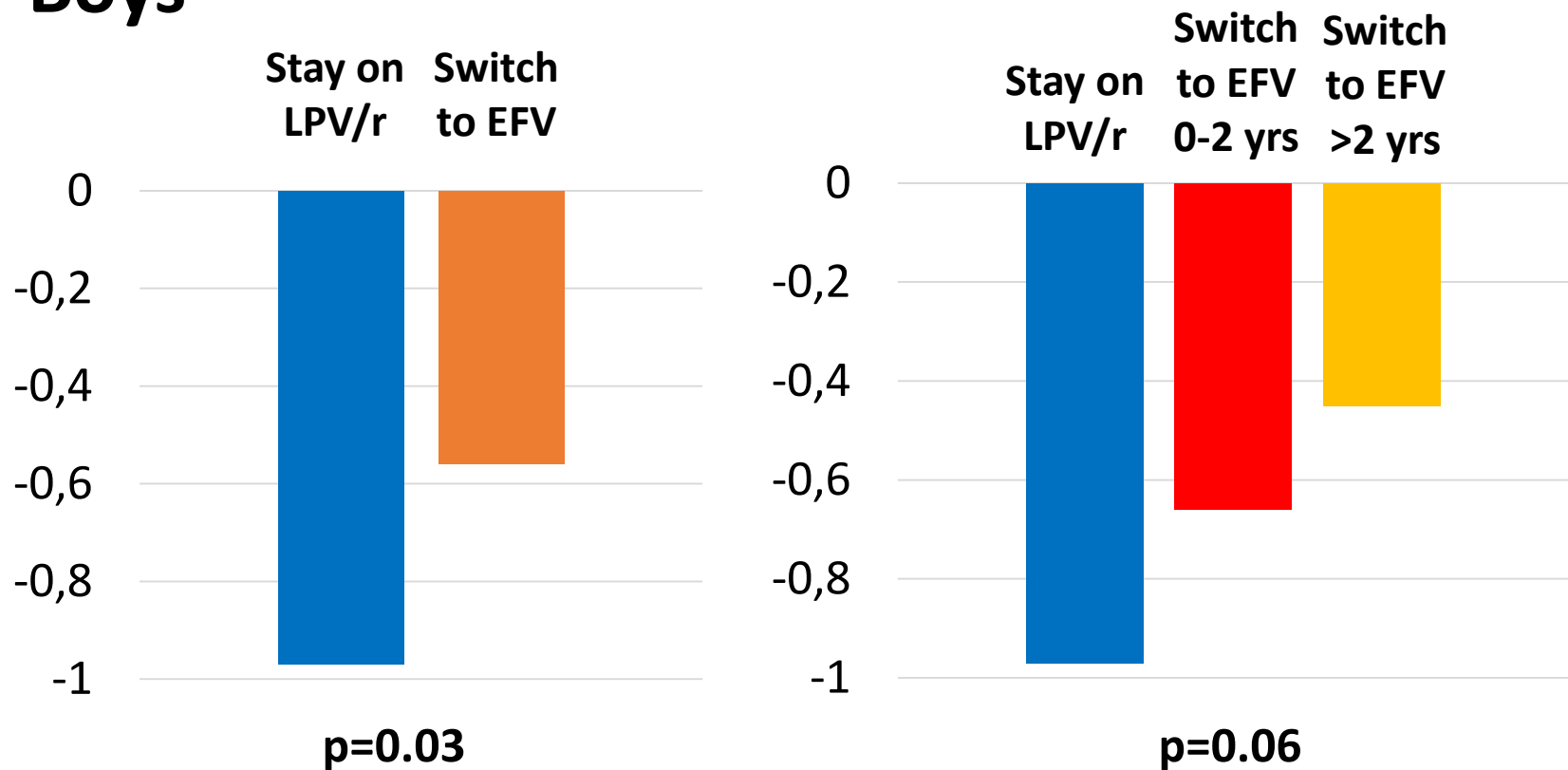
*also on two NRTIs including 3TC and ABC, d4T, or AZT but not TDF

Overview of treatment history



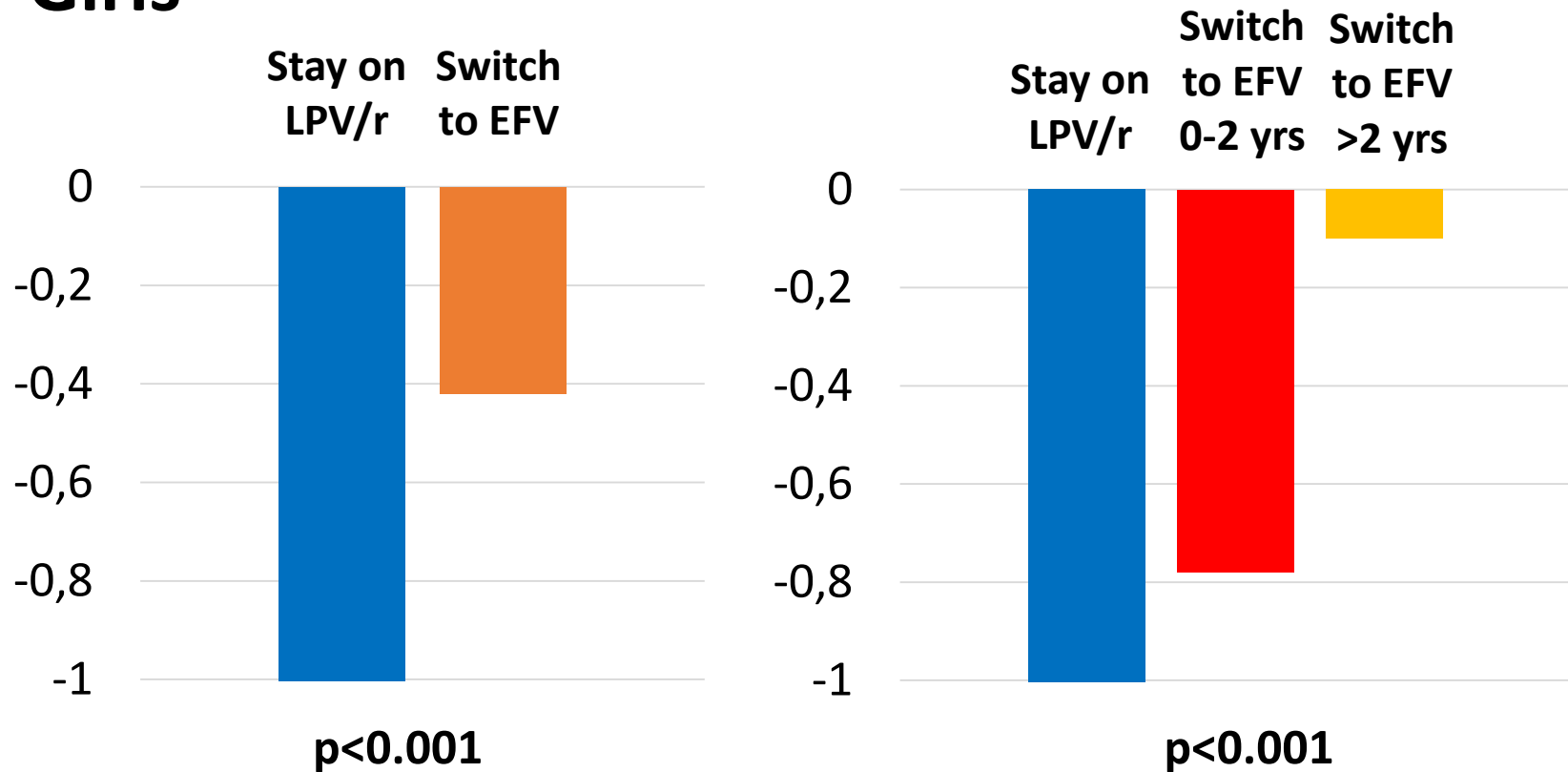
3. Mean whole body BMC-height Z-scores by treatment group

Boys



3. Mean whole body BMC-height Z-scores by treatment group

Girls



Conclusions

- Despite early initiation of ART and excellent virologic control, HIV-infected children receiving ART have decreased bone mass compared to HIV-uninfected controls
- Differences cannot entirely be accounted for by smaller body size
- Children switched to EFV have better bone mass compared to those maintained on LPV/r
- Use of bone-sparing regimens may enhance bone accrual during childhood





Acknowledgements

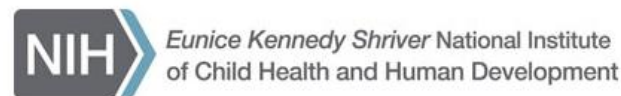
CHANGES Participants and Caregivers



CHANGES Bone Study Team



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Thank you!

