Southern African HIV Clinicians Society

3rd Biennial Conference

13 - 16 April 2016
Sandton Convention Centre
Johannesburg

Our Issues, Our Drugs, Our Patients

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Long-term Pulse-Wave Velocity changes in children receiving very early ART

Evidence from the CHER Trial Cohort

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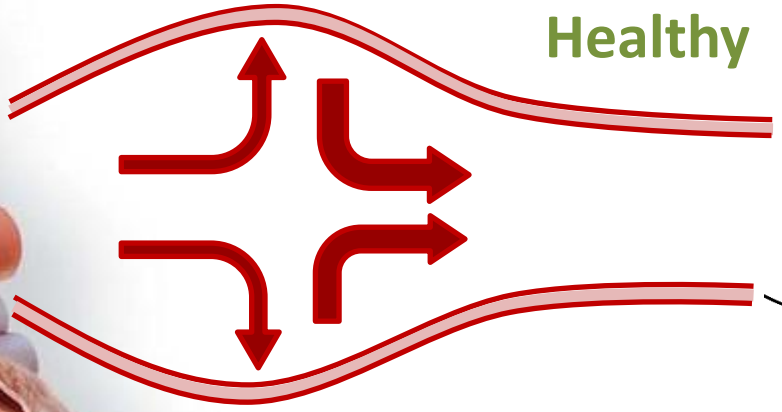
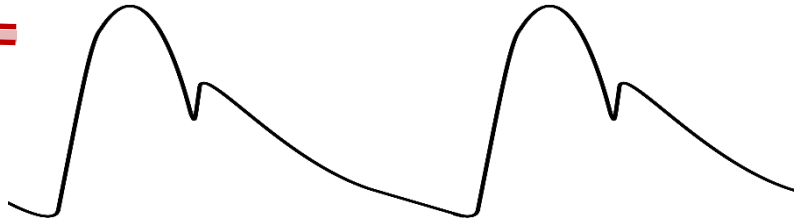
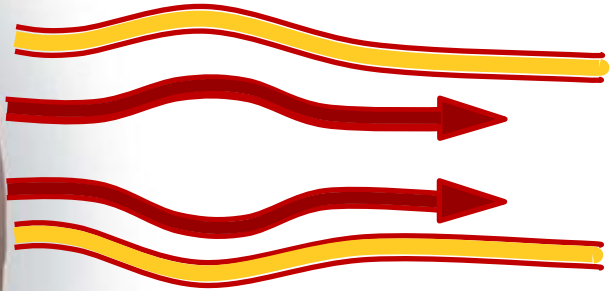
2016

Pulse Wave Velocity (PWV)

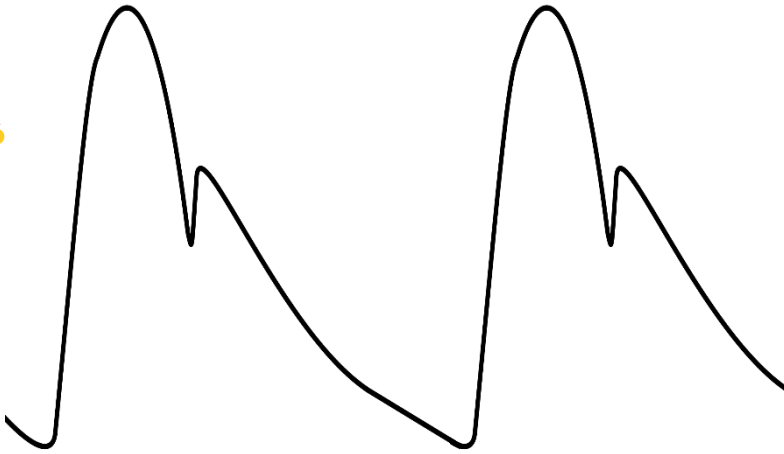


Healthy





Diseased



Background

- Vascular disease is accelerated in HIV+ children on ART [1-5]
- Whether initiating ART very early in life modifies vascular disease risk is unknown

Method

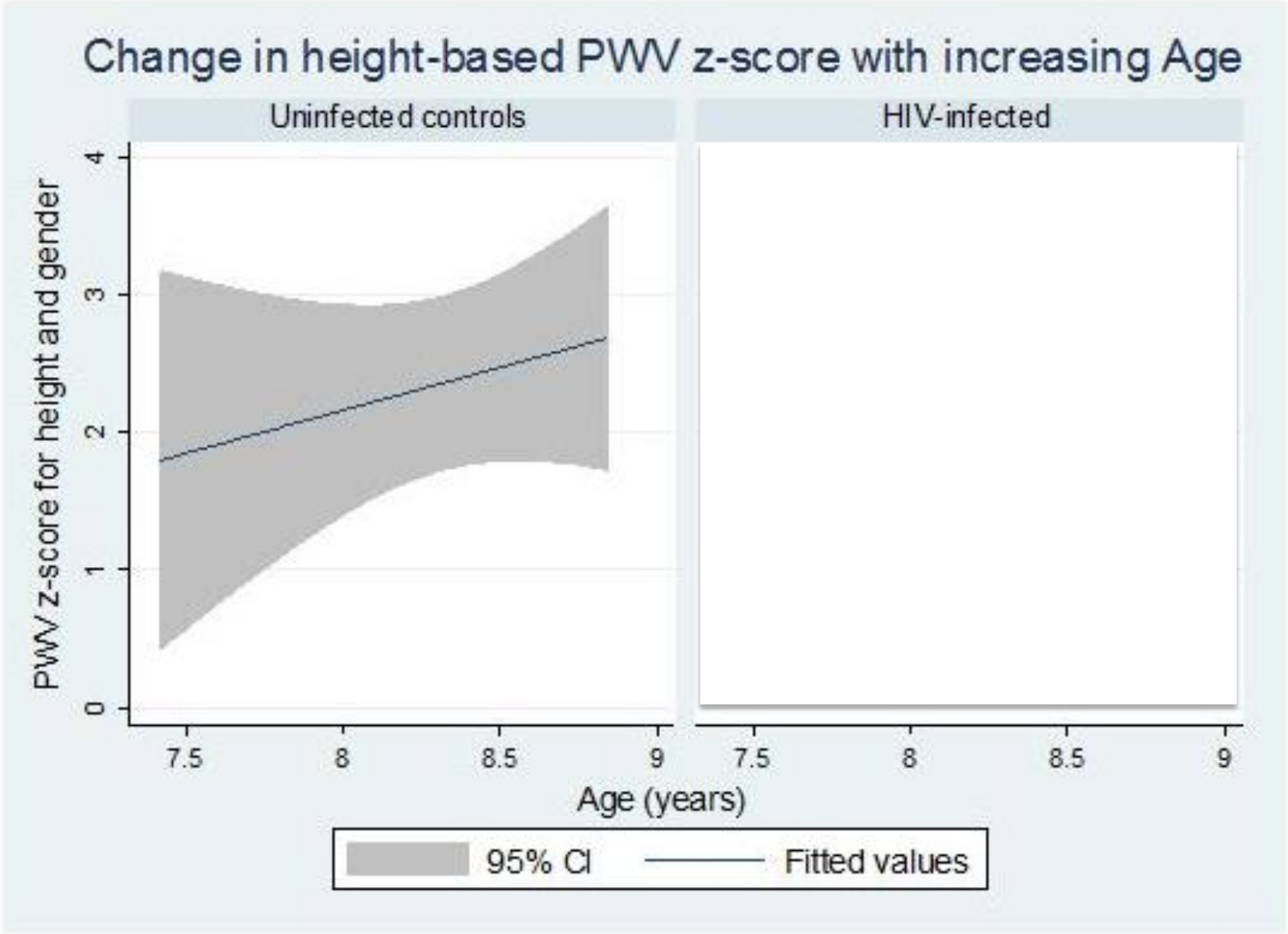
- **Following Cape Town participants in CHER trial [7,8]**

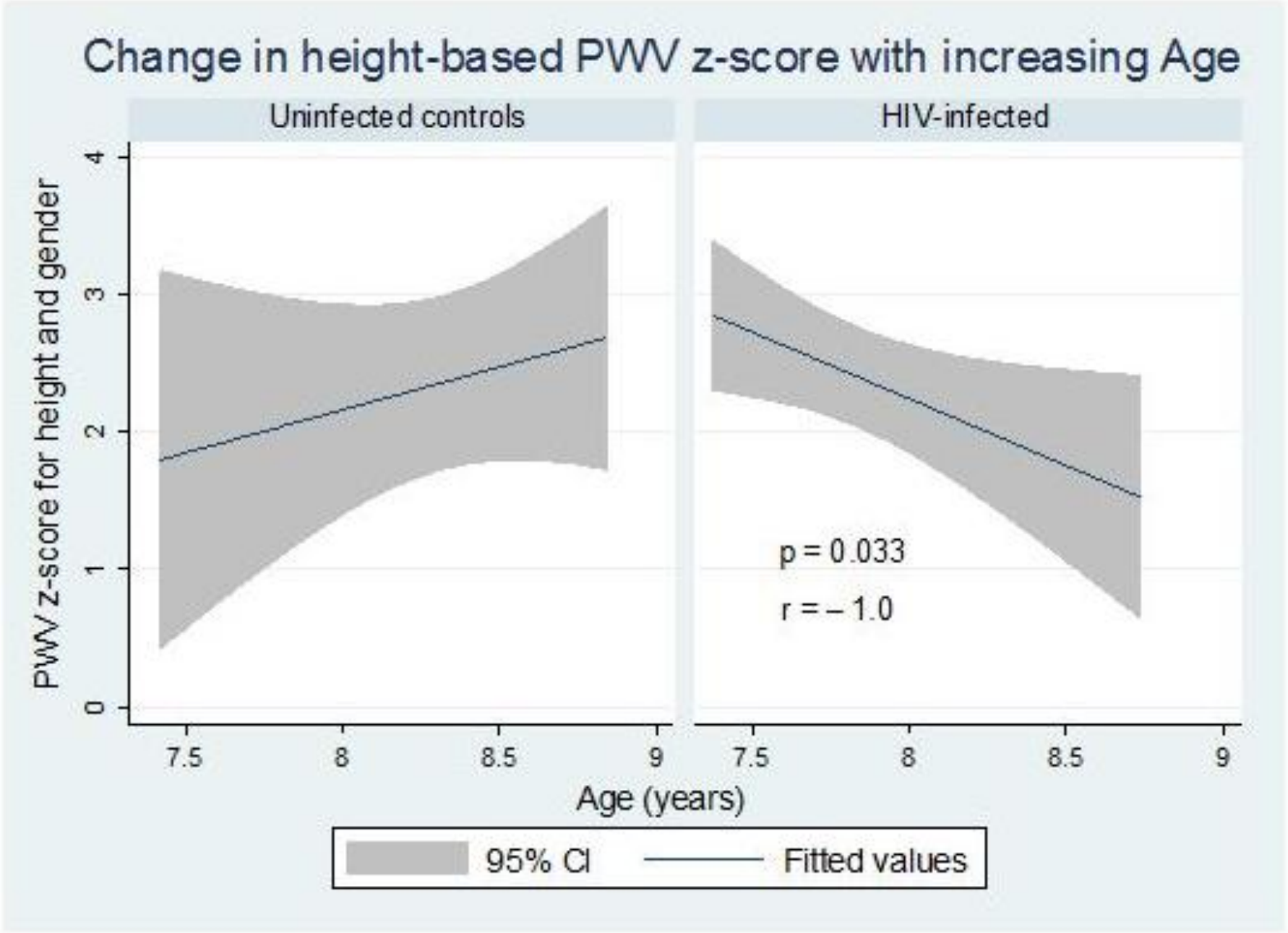
  (initiated ZDV+3TC+LPVr at median 9 [IQR: 7–12] weeks of age)

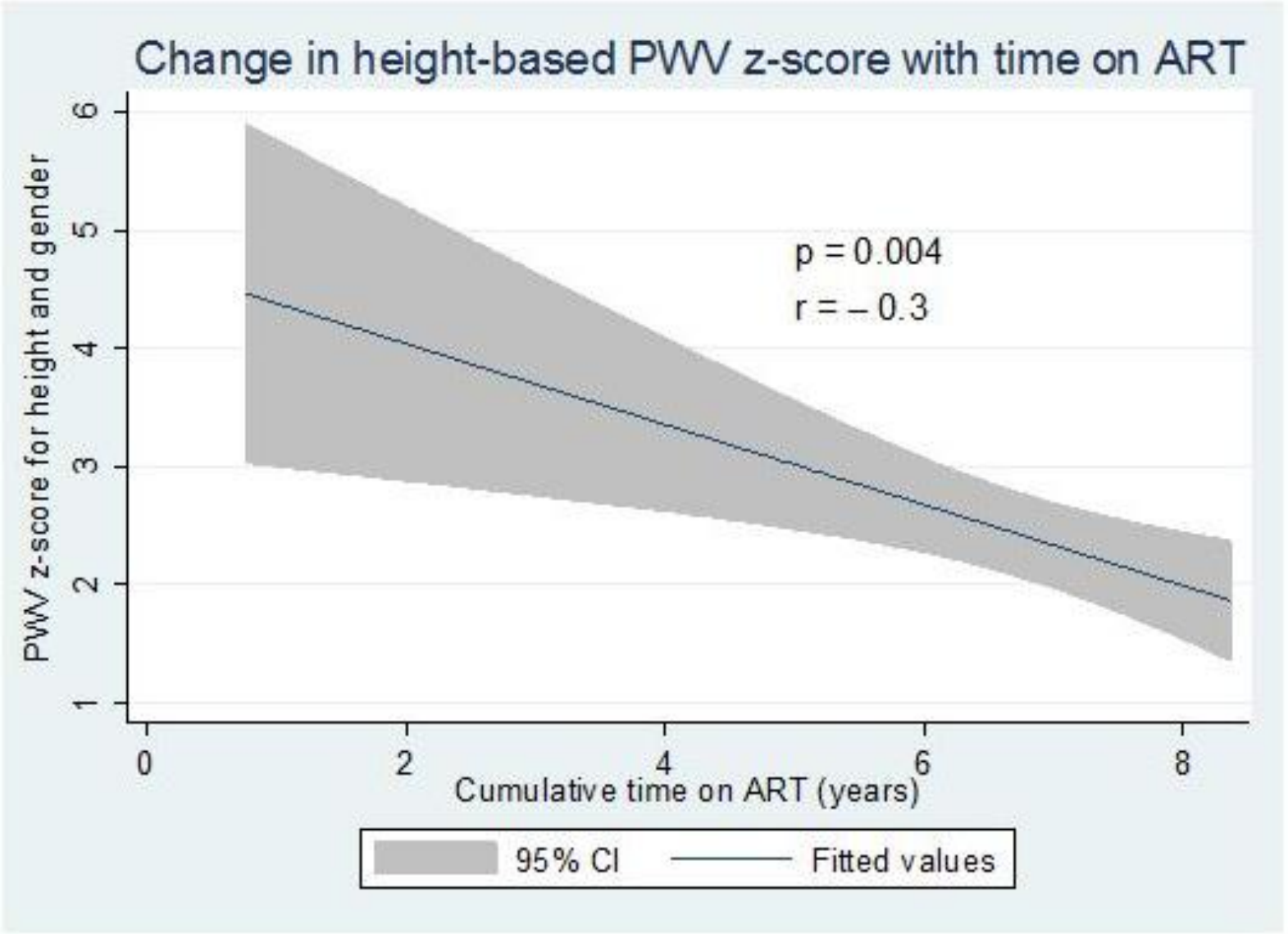
- **HIV-uninfected control group from the same communities and socio-economic background**

Method

- Pulse Wave Velocity (PWV) is sophisticated and sensitive measure of arterial wall stiffness (atherosclerosis)
- Reduced elasticity leads to faster propagation of the arterial pulse wave
- In asymptomatic adults, PWV elevations strongly predict subsequent incident cardiovascular events [6]


Change in height-based PWV z-score with increasing Age
Uninfected controls
HIV-infected
PWV z-score for height and gender
0
1
2
3
4
7.5
8
8.5
9
Age (years)
95% CI
Fitted values


Change in height-based PWV z-score with increasing Age
Uninfected controls
HIV-infected
PWV z-score for height and gender
0
1
2
3
4
7.5
8
8.5
9
p = 0.033
r = – 1.0
Age (years)
95% CI
Fitted values


Change in height-based PWV z-score with time on ART
PWV z-score for height and gender
1
2
3
4
5
6
p = 0.004
r = – 0.3
0
2
4
6
8
Cumulative time on ART (years)
95% CI
Fitted values

Conclusion

In children initiating ART very early in infancy in a high-care trial setting, pulse-wave velocity (a measure of arterial wall stiffness, atherosclerosis) *improved* with increasing time on effective ART

Acknowledgements

- Trial participants and their families
- Prof Mark Cotton
- Extensive support staff in FAM-CRU

- My ever-patient funders :

CFAR CENTER FOR AIDS RESEARCH University of California San Diego

CIPHER Paediatric HIV Matters

FOGARTY INTERNATIONAL CENTER

NIH Eunice Kennedy Shriver National Institute of Child Health and Human Development

ViiV Healthcare

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Results

Demographics and clinical characteristics presented as median (interquartile range)

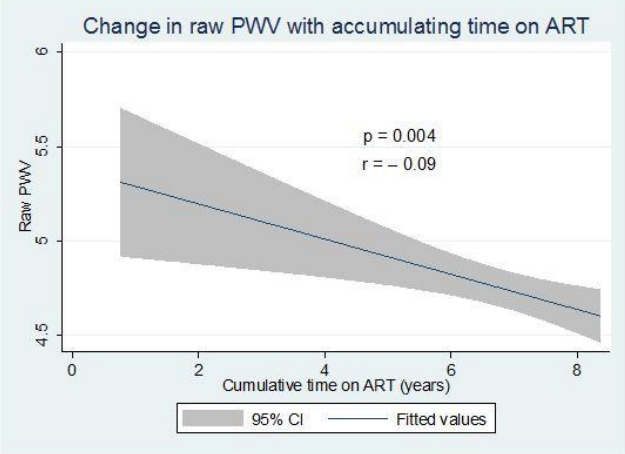
	HIV-infected n = 89	Uninfected controls n = 53	Unadjusted p-value (2-tailed)
Age at study visit (years)	7.7 (7.6 – 7.8)	8.5 (7.8 – 8.7)	<0.0001
Gender (male/female)	46% / 54%	60% / 40%	0.10
Cumulative time on ART (years)	7.1 (6.7 – 7.5)	---	---
% with undetectable HIV RNA PCR (<150 c/ml)	91%	---	---
Nadir CD4%	21% (16 – 26%)	---	---
Nadir CD4 (cells/mm^3)	694 (521 – 871)	---	---
Cumulative months with low CD4 or CD4% §	3 (0 – 14)	---	---
Current CD4 (cells/mm^3)	1115 (861 – 1434)	---	---
Maximum WHO clinical stage (1 or 2 / 3 / 4)	10% / 42% / 48%	---	---
Nadir weight-for-age Z-score	-1.7 (-2.5 – -0.8)	-0.8 (-1.5 – 0.1)	0.0007
Nadir height-for-age Z-score	-1.9 (-2.6 – -1.5)	-1.5 (-2.2 – -0.9)	0.11
Nadir weight-for-height Z-score	-0.8 (-2.0 – 0.0)	-0.5 (-1.4 – 0.4)	0.06
Nadir body mass index-for-age Z-score	-0.6 (-1.8 – -0.1)	-0.6 (-1.3 – -0.1)	0.21

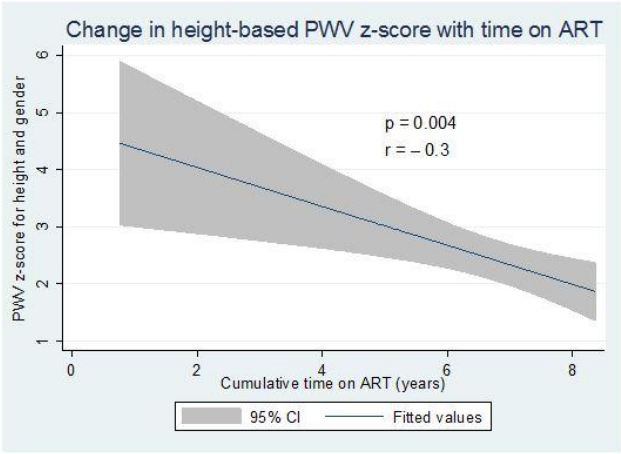
§ Low CD4 or CD4% was defined as CD4<1000 or CD4%<25% for <12 months of age; CD4 <750 or CD4% <20% for 12-35months of age; CD4 <500 or CD4% <20% for >36months of age

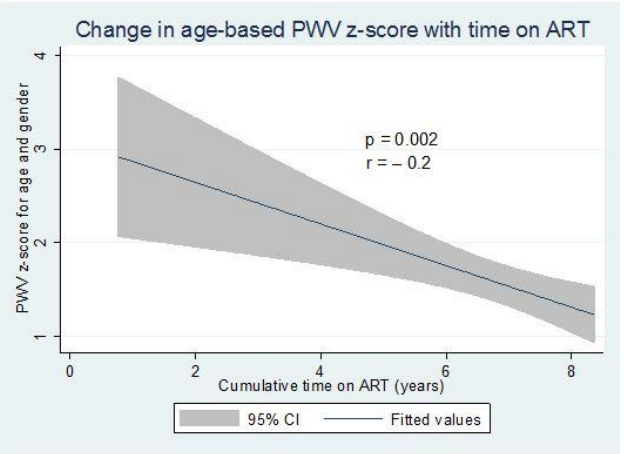
Results continued

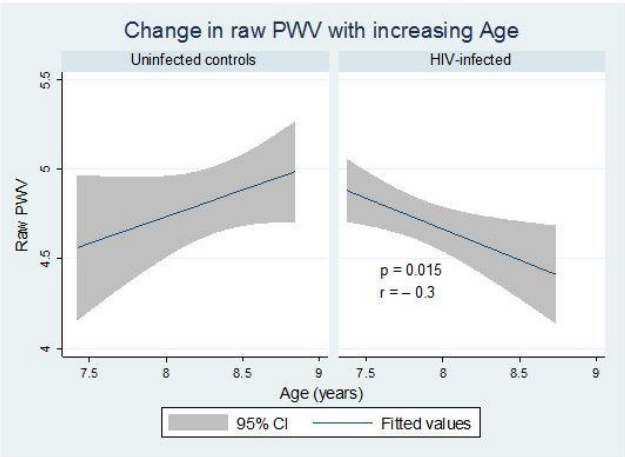
Demographics and clinical characteristics presented as median (interquartile range)	HIV-infected n = 89	Uninfected controls n = 53	Unadjusted p-value (2-tailed)
Current weight-for-age Z-score	-0.4 (-1.0 – +0.3)	-0.2 (-1.0 – +1.1)	0.13
Current height-for-age Z-score	-0.8 (-1.3 – 0.1)	-0.4 (-1.1 – +0.3)	0.12
Current body mass index-for-age Z-score	0.1 (-0.5 – 0.7)	0.0 (-0.5 – 1.2)	0.26
Waist circumference to height ratio	0.5 (0.4 – 0.5)	0.5 (0.4 – 0.5)	0.48
Systolic blood pressure (mmHg)	96 (90 – 100)	96 (92 – 105)	0.10
Total cholesterol (mmol/L)	4.2 (3.7 – 4.8)	3.5 (3.0 – 4.0)	<0.0001
Triglycerides (mmol/L)	0.8 (0.7 – 1.2)	0.6 (0.4 – 0.7)	<0.0001
Triglyceride to HDL cholesterol ratio	0.7 (0.5 – 1.0)	0.4 (0.3 – 0.7)	<0.0001
LDL cholesterol (mmol/L)	2.5 (2.0 – 2.9)	1.9 (1.5 – 2.4)	<0.0001
Glycosylated hemoglobin (%)	5.4% (5.2 – 5.7%)	5.8% (5.5 – 6.0%)	0.11

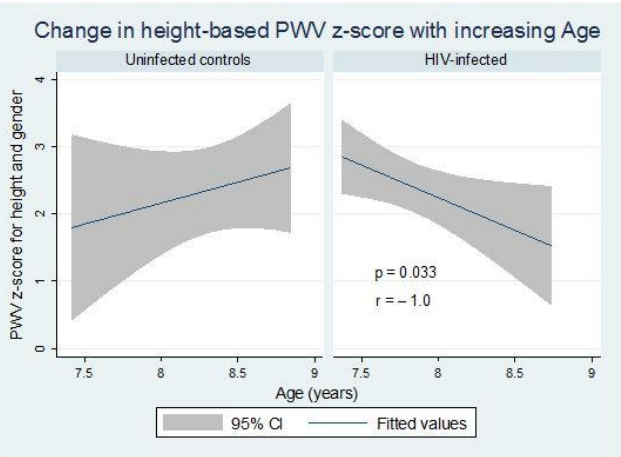
Despite substantial dyslipidemia in HIV-infected children, all PWV measures *improved* with increasing time on ART

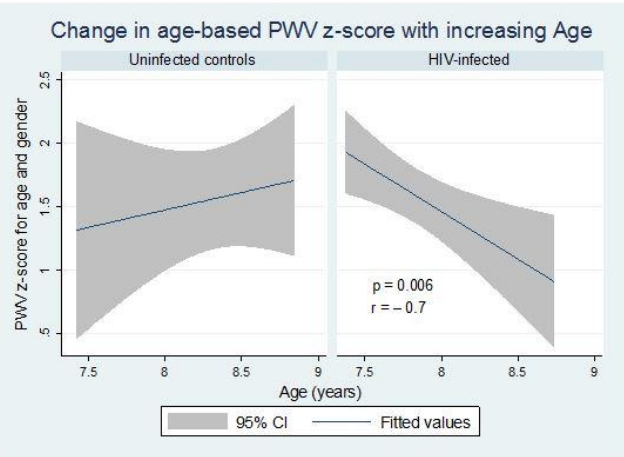












PWV measures remained static with increasing age in uninfected controls, but *improved* with age in HIV-infected children