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Does Pulse-Wave Velocity Normalize with Increasing Time on ART in Children? Evidence from the CHER Trial Cohort

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Background

- Cross-sectional evidence strongly suggests increased prevalence of vascular disease in HIV+ children on antiretroviral therapy (ART) after adjusting for traditional atherosclerosis risk factors [1-5]
- Long-term outcomes of HIV-related vascular disease in children receiving very early ART is unknown
- Aorto-femoral pulse wave velocity (PWV) is a sophisticated and sensitive measure of arterial wall stiffness (atherosclerosis). Reduced elasticity leads to faster propagation of the arterial pulse wave
- Early PWV elevations strongly predict subsequent incident cardiovascular events in asymptomatic adults [8]

Aim

To determine the relationship between PWV and time on ART in perinatally-HIV-infected primary-school-aged children who initiated LPVr-based ART in the first few weeks of infancy

Methods

- Cross-sectional design
- Cape Town participants in CHER trial [6,7] who 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
- We compared raw PWV; PWV Z-score for height and gender; and PWV Z-score for age and gender
- Simple linear regressions of PWV measures on age and on cumulative time on ART

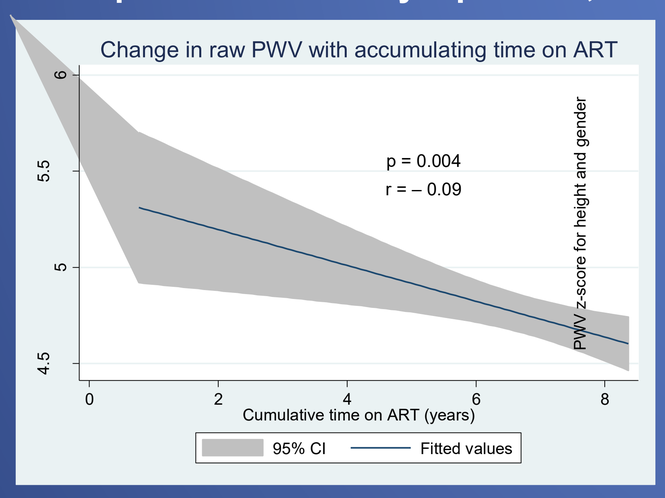
Table 1: Demographics and clinical characteristics
presented as median (interquartile range)

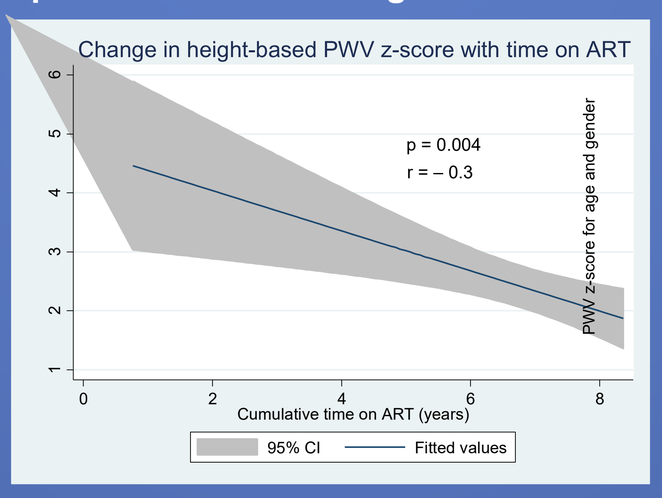
	HIV-infected n = 89	Uninfected controls n = 53	Unadjusted p-value (2-tailed)
Age at study visit (years)	7.7 (7.6 – 7.8)	8.5 (7.8 – 8.7)	<0.0001
Gender (male/female)	46% / 54%	60% / 40%	0.10
Cumulative time on ART (years)	7.1 (6.7 – 7.5)	---	---
% with undetectable HIV RNA PCR (<150 c/ml)	91%	---	---
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
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
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

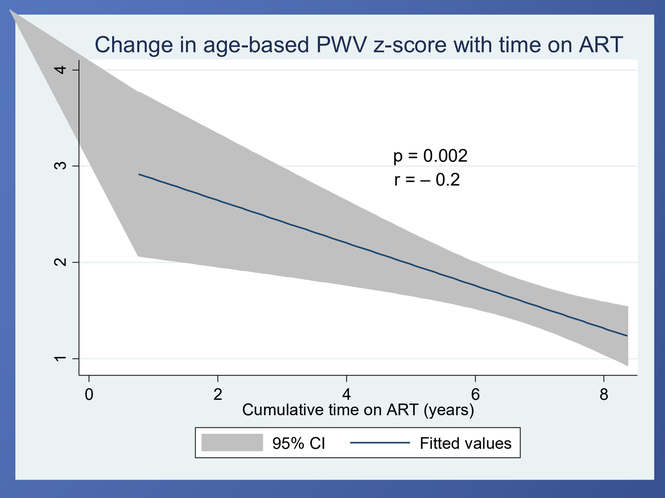
ZDV=zidovudine. 3TC=lamivudine. LPVr=lopinavir/ritonavir.
§ Low CD4 or CD4% was defined as CD4<1000 or CD4%<25% for <12 months of age; CD4 <750 or CD4% <20% for 12-35 months of age; CD4 <500 or CD4% <20% for >36 months

Results (see table 1)

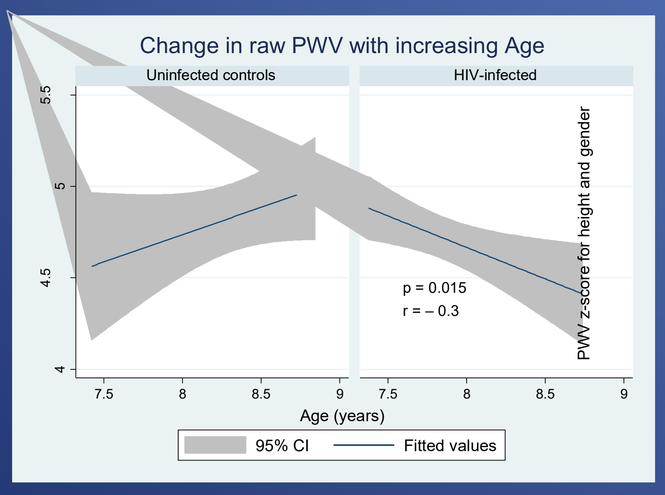
- HIV-infected and uninfected children had similar weight, height, body mass index Z-scores and waist circumference to height ratio (p>0.10)
- Despite substantial dyslipidemia, PWV measures improved with increasing cumulative time on ART in HIV-infected children:

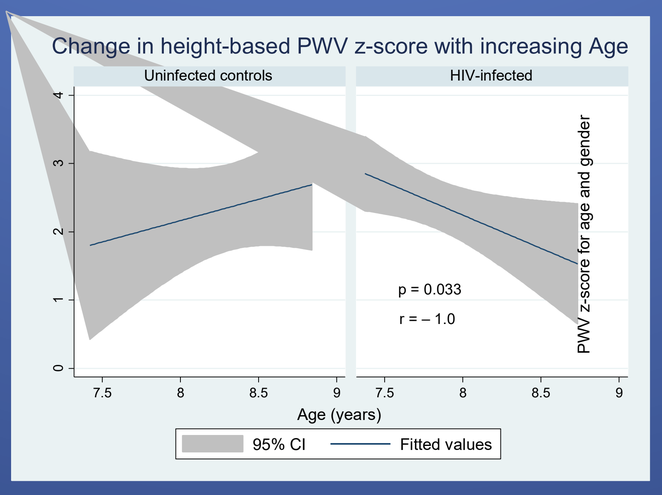


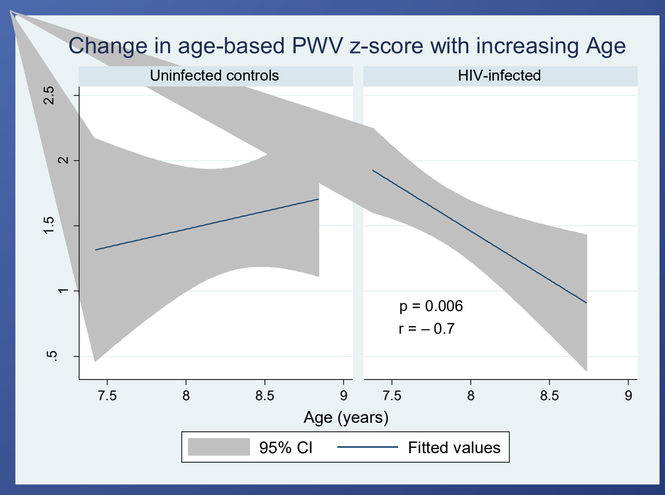




- With increasing age, PWV measures in uninfected controls remained static, but improved with time in HIV-infected children on effective ART:







Conclusion

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

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