

Early Weight and Height Changes in Asian Children Using Cotrimoxazole with ART

David C BOETTIGER¹, Dina MUKTIARTI², Truong Huu KHANH³, Suneeta SAGHAYAM⁴, Torsak BUNUPURADAH⁵, Ly Penh SUN⁶, Rawiwan HANSUDEWECHAKUL⁷, Lam Van NGUYEN⁸ and Azar KARIMINIA¹ for the TREAT Asia Pediatric HIV Observational Database

¹The Kirby Institute, UNSW Australia, Sydney, Australia; ²Cipto Mangunkusumo General Hospital, Jakarta, Indonesia; ³Children's Hospital 1, Ho Chi Minh City, Vietnam; ⁴YRGCARE Medical Centre, CART CRS, Chennai, India; ⁵HIV-NAT, The Thai Red Cross AIDS Research Centre, Bangkok, Thailand; ⁶National Centre for HIV/AIDS Dermatology and STDs and University of Health Sciences, Phnom Penh, Cambodia; ⁷Chiangrai Prachanukroh Hospital, Chiang Rai, Thailand; ⁸National Hospital of Pediatrics, Hanoi, Vietnam

Background

Cotrimoxazole (CTX) prophylaxis remains under prescribed in HIV-infected children starting antiretroviral therapy (ART). In addition to its antimicrobial properties, CTX slows the loss of height- (HFA) and weight-for-age (WFA) when ART is not available. We investigated whether CTX also enhances growth during the early stages of ART use.

Methods

Children enrolled in the TREAT Asia Pediatric HIV Observational Database were included in our analysis if they started ART aged between 1 month - 14 years and had both height and weight measurements available at ART initiation (baseline). They were considered to be using CTX if they were using any form of prophylactic CTX at baseline. Follow-up was censored at: 1) the time of CTX cessation for children using CTX at ART initiation; 2) the time of CTX initiation for those not using CTX at ART initiation; or 3) the last recorded clinic visit whilst still eligible for inclusion. Generalized estimating equations adjusted for time on ART and country income status were used to identify factors associated with change in HFA z-score, change in WFA z-score, follow-up HFA z-score ≥ -2 in those stunted (HFA < -2) at baseline and WFA z-score ≥ -2 in those underweight (WFA < -2) at baseline. Models were adjusted for survival bias by carrying forward the last known height/weight measurements for children that died.

Results

- 3,217 children were eligible for analysis (Table 1).
- Adjusted mean changes in HFA and WFA z-score are shown in Figure 1.
- Table 2 shows the factors associated with recovery during the first 2 years of ART in those stunted (n=1,638) and underweight (n=1,674) at ART initiation.
- When CTX use and baseline CD4% were modelled as an interaction term in our WFA recovery analysis, CTX use increased the odds of achieving a follow-up WFA z-score ≥ -2 in children with a baseline CD4 $\geq 25\%$ (odds ratio [OR] 1.78 vs. not using CTX, 95% confidence interval [CI] 1.24-2.54, $p < 0.01$) and in children with a baseline CD4 10-24% (OR 1.84 vs. not using CTX, 95%CI 1.09-3.11, $p = 0.02$). However, there was no significant effect of CTX use in children with a baseline CD4 $< 10\%$.

Table 1 – Baseline characteristics

	CTX users (n=2,458)	Non-CTX users (n=759)
Years of age, median (IQR)	5.1 (2.6, 8.0)	6.8 (3.4, 9.9)
Male, n (%total)	1,257 (51.1)	379 (49.9)
Perinatal HIV exposure, n (%total)	2,334 (95.0)	714 (94.1)
HFA z-score, median (IQR)	-2.5 (-3.4, -1.5)	-2.2 (-3.2, -1.2)
WFA z-score, median (IQR)	-2.6 (-3.9, -1.4)	-2.2 (-3.4, -1.1)
CD4%, median (IQR)	27 (19, 32)	27 (19, 32)
Initial ART regimen, n (%total)		
NNRTI-based	2,321 (94.4)	677 (89.2)
PI-based	94 (3.8)	74 (9.7)
Other	43 (1.7)	8 (1.1)
Months of CTX use, median (IQR)	0.7 (0.0, 2.6)	0.0 (0.0, 0.0)

Figure 1 – Adjusted mean changes in HFA (a-c) and WFA (d-f) z-score by baseline CD4%. HFA models were adjusted for baseline age, baseline HFA z-score, anemia status, country income status and period of ART initiation. WFA models were adjusted for baseline age, baseline WFA z-score, anemia status, country income status and period of ART initiation. Error bars represent 95% confidence interval around the mean.

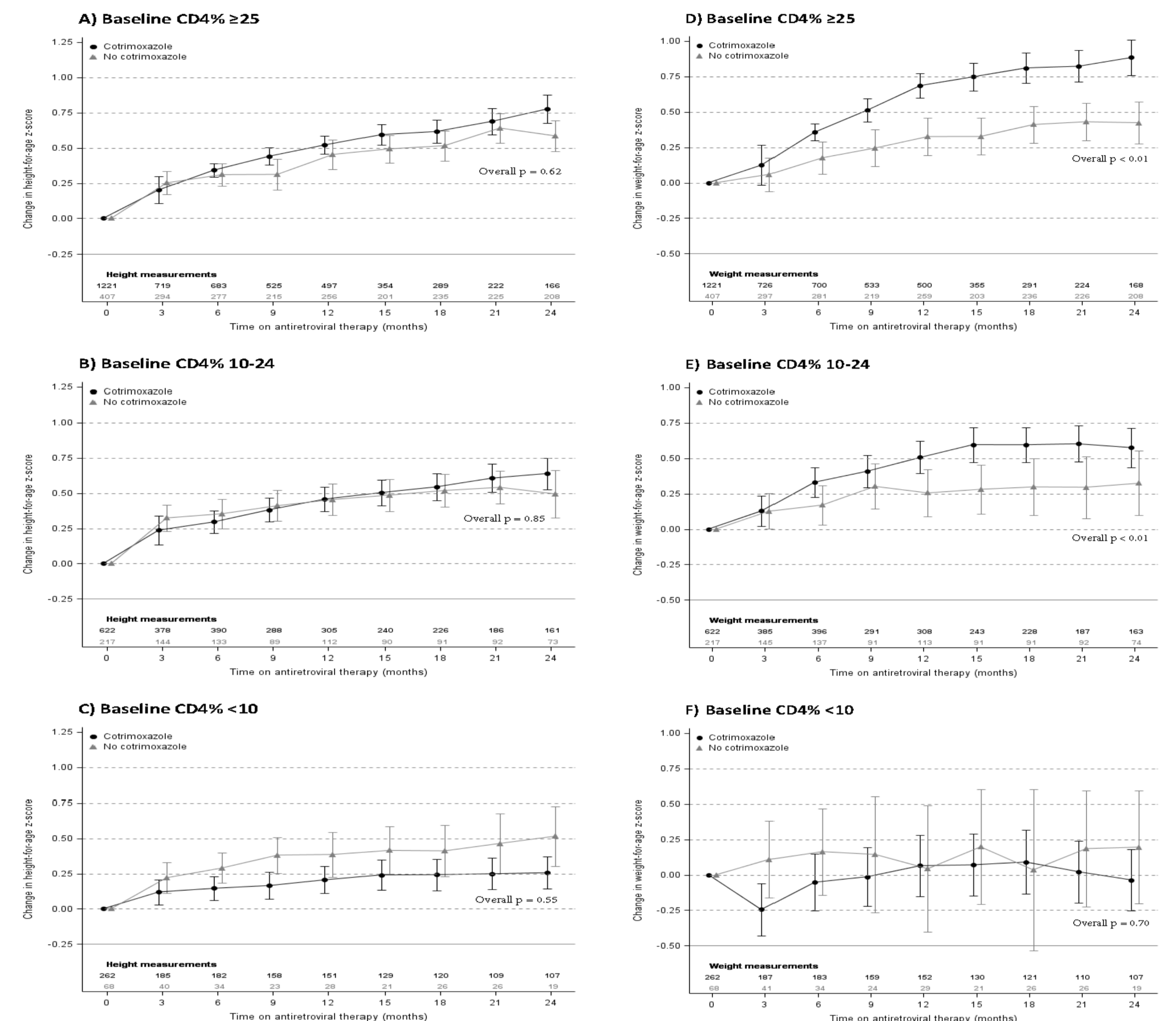


Table 2 – Factors associated with stunting and underweight recovery on ART*

	HFA z-score ≥ -2 Adjusted OR (95%CI), p	WFA z-score ≥ -2 Adjusted OR (95%CI), p
Using CTX prophylaxis (vs. not using)	1.10 (0.79, 1.53), p=0.58	1.70 (1.28, 2.25), p<0.01
Baseline age (per year older)	0.78 (0.74, 0.82), p<0.01	0.85 (0.83, 0.88), p<0.01
Female (vs. male)	-	1.47 (1.21, 1.80), p<0.01
Baseline H/WFA z-score (per unit greater)	4.71 (3.64, 6.09), p<0.01	1.75 (1.55, 1.97), p<0.01
Anemic (vs. normal hemoglobin)	0.61 (0.45, 0.82), p<0.01	0.63 (0.51, 0.77), p<0.01
Baseline CD4 10-24% (vs. $\geq 25\%$)	1.01 (0.74, 1.38), p=0.96	0.89 (0.69, 1.14), p=0.35
Baseline CD4 $< 10\%$ (vs. $\geq 25\%$)	0.29 (0.14, 0.59), p<0.01	0.65 (0.44, 0.96), p=0.03
Prior tuberculosis diagnosis (vs. no prior)	0.66 (0.47, 0.93), p=0.02	-

*Country income status, period of ART initiation and time on ART were included in models but ORs are not shown

Conclusions

CTX use was associated with larger improvements in WFA but not HFA z-score during the first 24 months of ART when compared with non-use of CTX. Benefits to WFA z-score were particularly evident in children starting ART with a high CD4%.

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PS Ly*, and V Khol, National Centre for HIV/AIDS, Dermatology and STDs, Phnom Penh, Cambodia; J Tucker, New Hope for Cambodian Children, Phnom Penh, Cambodia; N Kumarasamy*, S Saghayam, and E Chandrasekaran, YRGCARE Medical Centre, CART CRS, Chennai, India; DK Wati*, LPP Atmikasari, and IY Malino, Sanglah Hospital, Udayana University, Bali, Indonesia; N Kurniati*, and D Muktiarti, Cipto Mangunkusumo General Hospital, Jakarta, Indonesia; SM Fong*†, M Lim, and F Daut, Hospital Likas, Kota Kinabalu, Malaysia; NK Nik Yusoff*, and P Mohamad, Hospital Raja Perempuan Zainab II, Kelantan, Malaysia; KA Razali*, TJ Mohamed, and NADR Mohammed, Pediatric Institute, Hospital Kuala Lumpur, Kuala Lumpur, Malaysia; R Nallusamy*, and KC Chan, Penang Hospital, Penang, Malaysia; T Sudjaritruk*, V Sirisanthana, L Aurpibul, and P Oberdorfer, Department of Pediatrics, Faculty of Medicine, Chiang Mai University and Research Institute for Health Sciences, Chiang Mai, Thailand; R Hansudewechakul*, S Denjanta, W Srisuk, and A Kongphonoi, Chiangrai Prachanukroh Hospital, Chiang Rai, Thailand; P Lumbiganon*‡, P Kosalaraksa, P Tharnprisan, and T Udomphanit, Division of Infectious Diseases, Department of Pediatrics, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand; G Jourdain, PHPT-IRD UMI 174 (Institut de recherche pour le développement et Chiang Mai University), Chiang Mai, Thailand; T Bunupuradah*, T Puthanakit, W Prasitsuebsai, and W Chanthawethip, HIV-NAT, The Thai Red Cross AIDS Research Centre, Bangkok, Thailand; K Choekhaibulkit*, K Lapphra, W Phongsamart, and S Srichaenchai, Department of Pediatrics, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand; KH Truong*, QT Du, and CH Nguyen, Children's Hospital 1, Ho Chi Minh City, Vietnam; VC Do*, TM Ha, and VT An Children's Hospital 2, Ho Chi Minh City, Vietnam; LV Nguyen*, DTK Khu, AN Pham, and LT Nguyen, National Hospital of Pediatrics, Hanoi, Vietnam; ON Le, Worldwide Orphans Foundation, Ho Chi Minh City, Vietnam; AH Sohn*, and C Sethaputra, TREAT Asia/amfAR – The Foundation for AIDS Research, Bangkok, Thailand; DA Cooper, MG Law*, and A Kariminia, The Kirby Institute, UNSW Australia, Sydney, Australia; (*Steering Committee members; † Current Steering Committee Chair; ‡ Co-Chair).