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Growth Reconstitution following Antiretroviral Therapy and Nutrition Supplementation: Systematic Review and Meta-Analysis

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Abstract

Objective—As antiretroviral treatment (ART) expands for HIV-infected children, it is important to determine its impact on growth. We quantify growth and its determinants following ART in resource-limited (RLS) and developed settings (DS).

Design—Systematic review and meta-analysis.

Methods—We searched publications reporting growth [weight-for-age (WAZ), height-for-age (HAZ), and weight-for-height (WHZ) Z-scores] in HIV-infected children following ART through August 2014. Inclusion criteria: 1) <18 years; 2) ART; 3) sample ≥20; 4) growth at ART; 5) post-ART growth. Standardized and overall weighted mean differences were calculated using random-effects-models.

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Disclaimer: The findings and conclusions in this article are those of the authors and do not necessarily represent official views of the United States National Institutes of Health (NIH).

Results—Sixty-seven articles were eligible (RLS=54; DS=13). Mean age was 5.8 years, and comparable between settings (P=0.90). Baseline growth was substantially lower in RLS versus DS (WAZ −2.1 vs. −0.5; HAZ −2.2 vs. −0.9; both P<0.01). Rate of weight but not height reconstitution during 12- and 24-months was higher in RLS (12-month WAZ change 0.84 vs. 0.17, P<0.01). Growth deficits persisted in RLS after 2-years ART (P=0.04). Younger cohort age was associated with greater growth reconstitution. PI and NNRTI regimens yielded comparable growth. Adjusting for age and setting, cohorts with nutritional supplements had greater growth gains (24-month rate difference: WAZ 0.55, P=0.03; HAZ 0.60, P=0.007). Supplement benefits were attenuated after adjusting for baseline cohort growth.

Conclusions—RLS children had substantial growth deficits compared to DS counterparts at ART; growth shortfalls in RLS persisted despite reconstitution. Earlier age and nutritional supplementation at ART may improve growth outcomes. Scant data on supplementation limits evaluation of impact and underscores need for systematic data collection regarding supplementation in pediatric ART programs/cohorts.

Keywords

growth; antiretroviral therapy; pediatric HIV; nutritional supplementation; systematic review; meta-analysis

Introduction

Antiretroviral therapy (ART) has substantially decreased morbidity and mortality in HIV-infected children [1-5]. ART also results in marked improvements in weight and height in children. Of the 3.3 million children living with HIV, more than 90% reside in resource-limited settings (RLS) [6]. In these settings, malnutrition is prevalent and children may be delayed in receiving ART due to late diagnosis [5, 7]. Both of these issues contribute to suboptimal growth reconstitution. Given prevalent nutritional needs, pediatric HIV treatment programs have varied approaches to nutritional supplementation during ART; with some empirically providing supplementation at initiation of ART [8-10]. It remains unclear whether ART alone or combined with nutritional supplements at initiation is better for long-term growth. It is well established, however, that suboptimal growth is associated with increased risk of mortality, repeat infections, and poor cognitive development [11].

Marked growth reconstitution occurs following ART. Previous reviews of pediatric ART outcomes have focused primarily on immunologic and virologic response, and have been limited to sub-Saharan Africa [3, 12] or resource-limited settings [13]. In a review by Peacock-Villada [14], we noted marked differences in baseline CD4% and viral load, and post-ART mortality in HIV-infected children in resource-limited versus developed countries. We performed a systematic review and meta-analysis to aggregate and compare growth outcomes following ART initiation among HIV-infected children in RLS and DS and to assess determinants of growth in these settings, including the role of nutritional supplementation in RLS.

Methods

Data search

A systematic literature search was conducted for all peer-reviewed literature published in English reporting growth outcomes (weight, length, height, weight-for-age, height-for-age, length-for-age, and weight-for-height Z-scores) in HIV-1 infected children following ART initiation. We searched PubMed, Cochrane, Embase, and Global Health Host through August 2014, using combinations of the following search terms: growth, length, height, weight, Z-score, outcomes, children, pediatric, paediatric, antiretroviral therapy, ART, HAART, HIV. Bibliographies of relevant articles were also examined.

Study selection and inclusion/exclusion criteria

The following inclusion criteria were used to select publications: 1) patients <18 years-old; 2) patients initiating ART (≥3 drugs); 3) sample size ≥20 patients; 4) growth measures at ART initiation; and 5) growth measures following 6, 12, or 24-months of ART. Outcome measures included the following growth parameters: weight-for-age (WAZ), weight-for-height (WHZ), and height-for-age (HAZ) Z-scores.

Studies reporting only clinical outcomes (CD4 count and HIV-1 RNA), limited to growth measures either prior to or following ART only, or lacking stated outcomes of interest were excluded. Manuscripts were also excluded if the outcome of interest was analyzed in terms of weight (kilograms or pounds) and height (centimeters or inches) without Z-score standardization.

Data extraction

Standardized data collection was used to extract all data, including: pre- and post-ART Z-scores, nutritional supplementation, study objective, site, sample size, ART regimen, time on ART, and disease severity at initiation. Articles were classified as having been conducted in a “Resource-limited Setting” (RLS) or “Developed Setting” (DS) based on the United Nations Statistics Division [15], and further subcategorized by geographic location. Studies reporting results from the same cohort or treatment program were compared, and only the most recent publication with relevant growth outcomes was included.

Statistical Analysis

Primary outcomes of interest were change in Z-scores (WAZ, WHZ, and HAZ) at 6, 12, or 24-months post-ART. Data on mean or median change in growth post-ART were either collected directly or calculated from reported results. Change in Z-score [or standard deviation (SD)] was calculated using the following methods: 1) difference between the baseline and 6, 12, or 24-month value; 2) overall rate of change during 6, 12, or 24-month interval, as reported, or 3) monthly rate of change in Z-score as reported from longitudinal analyses, specifically mixed-effects models for longitudinal data. The monthly rate of change estimations differ based on follow-up time as growth reconstitution generally peaks early followed by smaller incremental changes with longer duration on ART. Therefore, studies presenting changes in growth for 6-months may have a greater monthly change than

those with 12-months follow-up (averaged over time). For studies reporting follow-up time in weeks, we included 24, 48 and 96 weeks as 6, 12, and 24-month growth outcomes.

Weighted baseline characteristics were compared between RLS and DS using a two-sample t-test assuming unequal variances, as appropriate. All means were weighted based on the reported sample size within the individual studies. When growth parameters were reported for only a subset of children with follow-up data, the weight for that parameter was adjusted based on reported size of the subset. Standardized mean differences were calculated for individual studies and overall weighted mean differences were calculated by setting (RLS versus DS) and displayed graphically in a Forest Plot. Forest plots display both the weighted mean difference and confidence interval for each study, as shown by a black box and corresponding horizontal line, and the pooled weighted mean difference across all studies, depicted with a diamond. Using methods described in Hozo et al [16], the median, range, and sample size were used to estimate mean and variance where this information was not reported or available. We observed similar meta-analysis results when including means alone versus combined means and medians; thus, results presented include both means and estimations of the mean using medians. Heterogeneity between studies was tested using X^2 tests and the summary I-squared statistic [17]. Random-effects meta-analysis regression models were conducted to account for heterogeneity between studies and to assess the effect of setting and cohort age on growth rate post-ART. Cohort age was defined as the mean or median for each study and categorized as <4 years, 4-6 years, and >6 years at ART. All analyses were conducted using STATA 13.0 (StataCorp LP, College Station, Texas, USA).

Results

Study Selection and Characteristics

Our search strategy identified 1,836 potentially relevant articles. After review of abstracts, 223 articles were selected for full article review. Of these articles, 167 were excluded based on reasons outlined in Figure 1. The remaining 67 articles fulfilled the inclusion criteria and were included for at least one of the primary growth analyses (RLS=54, total N=25,927; and DS=13, total N=1,810). Table 1 describes characteristics of the included cohorts.

Baseline Mean Age and Growth

The mean baseline age at ART initiation was 5.8 years (range, 0.1 to 16 years) in RLS and 6.6 years (range, 0 to 18 years) in DS (P=0.90) (Supplemental Table 1). Baseline growth parameters were well below average (Z-score=0) in RLS children initiating ART. Mean baseline WAZ was −2.1 in RLS compared to −0.5 in DS (P<0.01). Mean WHZ was lower in RLS versus DS (−1.5 and 0.3, respectively, P=0.05). Mean HAZ was −2.2 in RLS versus −0.9 in DS (P<0.01).

Change in WAZ at 6, 12 and 24-Months post-ART

Twenty-seven studies (RLS=33, N=16,841; and DS=6, N=713) reported WAZ at 6-months post-ART (Table 2). Gains in WAZ ranged from 0.01 to 2.19 in RLS and −0.10 to 0.51 in DS. Twenty-nine studies (RLS=23, N=14,032; and DS=6, N=713) with data on mean or median WAZ were included in the estimate of the pooled mean difference (Figure 2a). At 6-

months post-ART, children in RLS gained 0.65 (95% CI 0.35-0.95) in WAZ compared to a gain of 0.19 (95% CI 0.08-0.29) in children in DS (P=0.095). After adjusting for cohort age, the 6-monthly rate of increase in WAZ did not differ between RLS and DS (0.32 SD; 95% CI −0.09-0.73; P=0.12).

At 12-months post-ART, 45 studies (RLS=36, N=17,087; and DS=9, N=1,340) reported mean or median WAZ. Gains ranged from 0 to 3.20 in RLS and −0.20 to 0.53 in DS. Of the 36 studies (RLS=27, N=13,822; and DS=9, N=1,340) included in the pooled estimate (Figure 2a), children in RLS gained an average WAZ of 0.84 (95% CI 0.54-1.14) compared to 0.17 (95% CI 0.05-0.30) among children in DS (P=0.02). Twelve-month gains in WAZ remained greater in RLS than DS (0.56 SD; 95% CI 0.08-1.04; P=0.03) after adjusting for cohort age.

Thirty-four studies (RLS=26, N=11,104; and DS=8, N=789) reported WAZ at 24-months post-ART. Change in 24-month WAZ ranged from 0 to 2.20 in RLS and from 0.11 to 0.70 in DS. After pooling data from 29 studies (RLS=21, N=9,078; and DS=8, N=789), children in RLS experienced greater 24-month gains in WAZ as compared to children in DS (1.03, 95% CI 0.53-1.53; and 0.17, 95%CI 0.08-0.27; respectively, P=0.04) [data not shown]. After adjusting for cohort age, the 2-year rate of increase in WAZ remained higher in RLS (0.60 SD, 95% CI 0.03-1.17; P=0.04).

Figure 3 illustrates WAZ over time in 38 studies in RLS and 12 studies in DS.

Change in HAZ at 6, 12 and 24-Months post-ART

Six-month post-ART growth was reported in 31 studies (RLS=24, N=13,693; and DS=7, N=681) [Table 2]. Change in 6-month HAZ ranged from −0.36 to 0.40 in RLS and from 0 to 0.83 in DS. Of the 26 studies (RLS=19, N=11,585; and DS=7, N=681) included in the pooled analysis (Figure 2b), children in RLS and DS experienced similar 6-month gains in height (0.08, 95% CI 0.02-0.13; and 0.10, 95% CI −0.01-0.20; respectively, P=0.62). After adjusting for cohort age, there was no difference in 6-month HAZ gains by setting.

Thirty-eight studies (RLS=29, N=13,603; and DS=9, N=1,295) reported HAZ at 12-months post-ART (Table 2). Change in HAZ ranged from −0.30 to 1.65 in RLS and −0.01 to 0.70 in DS. Twenty-eight studies were included in pooled analysis (RLS=19, N=10,930; and DS=9, N=1,295) [Figure 2b]. Although not significantly different, children in RLS experienced a mean 12-month gain in HAZ of 0.23 (95% CI 0.14-0.33) compared to a gain of 0.12 (95% CI 0.03-0.21) in children in DS (P=0.34). This remained after adjusting for age.

Twenty-nine studies (RLS=21, N=8,068; and DS=8, N=788) reported HAZ at 24-months post-ART (Table 2). Change in 24-month HAZ ranged from −0.86 to 2.81 in RLS and from 0.11 to 0.90 in DS. Twenty-three studies (RLS=15, N=3,904; and DS=8, N=788) were included in the pooled analysis at 24-months (data not shown). There was no significant difference in gains in HAZ following 24-months of ART between RLS and DS (0.41, 95%CI 0.22-0.60; and 0.18, 95% CI 0.08-0.28; respectively, P=0.42).

Figure 3 illustrates HAZ over time in 29 RLS studies and 12 DS studies.

Change in WHZ at 6, 12 and 24 Months post-ART

Few studies reported post-ART WHZ outcomes. Eleven studies included data on WHZ at 6-months (RLS=9, N=3,361; and DS=2, N=81), 13 studies included data at 12-months (RLS=11, N=3,089; and DS=2, N=81), and 9 studies at 24-months (RLS=8, N=1,750; and DS=1, N=36). Change in WHZ during 24-month follow-up ranged from 0 to 1.71 in RLS and 0.07 to 0.50 in DS [Table 2]. Pooled summary statistics were not performed due to the small number of studies reporting mean WHZ post-ART.

Potential Cofactors for Growth Reconstitution

Age at ART Initiation—Eleven studies reported data regarding associations between age at initiation and post-ART growth [1, 18-28]. Nine of these (RLS=7 and DS=2) reported an association between younger age at ART initiation and greater improvements in WAZ [1, 18-20, 22, 24-27] and HAZ [19, 20, 22, 25-28]. The remaining two studies (Thailand [21] and Malawi [23]) found no difference in growth and age at ART initiation. Adjusting for setting, older median cohort age was significantly associated with lower rate of change in weight (−0.07 SD per 1 year increase in age; 95% CI −0.12, −0.01; P=0.02) 12-months post-ART. Further, cohorts with median age <4 years at ART had greater rate of change in yearly WAZ as compared to cohorts aged >6 years at ART (0.52 SD; 95% CI 0.05-0.99; P=0.03). Similarly, younger cohorts (<4 years) had higher 6-month HAZ increase compared to older cohorts (>6 years) (0.15 SD, 95% CI 0.01-0.30; P=0.04), after adjusting for setting. The relationship between younger cohort age and greater improvements in HAZ did not persist beyond 6-months post-ART.

Nutrition Supplementation and ART—Information on nutrition supplementation was reported in fourteen studies, all in RLS. Types of supplementation included: rice/corn and vegetable oil (Haiti [29]), high-energy protein (Zambia [24]), Plumpy'nut (Malawi [23]), other ready-to-use therapeutic food (Malawi [30]), nutritional porridge (Kenya [18, 31]), corn-soy blend ready-to-eat meal supplement (South Africa [32]), fortified amylase-enriched maize product (South Africa [28]), food supplementation or support (Malawi/Mozambique/Guinea [10], Ethiopia [8], Cambodia [33]), and multivitamins (Kenya [18], South Africa [32], Uganda [34], Uganda/Zimbabwe [35], and India [36]). One (Kenya [18]) study evaluated receipt and duration of nutritional supplementation in growth analyses, while a second (Malawi [30]) evaluated 6-month nutritional recovery in malnourished children initiating ART with ready-to-use therapeutic food. A third (South Africa [32]) evaluated dietary iron intake and changes in hemoglobin 18-months post-ART among children receiving iron-free multivitamins. Specific eligibility criteria for nutritional support were generally not defined. Two studies (US [37] and Kenya [5]) explicitly stated that children received no supplements. After adjusting for cohort age and setting, receipt of nutrition supplements was significantly associated with greater height gains at 12- and 24-months post-ART (0.38, 95% CI, 0.02, 0.74, P=0.04; and 0.60, 95% CI, 0.20, 1.01, P=0.007; respectively); this difference did not remain significant after adjusting for baseline cohort length (0.19, 95% CI −0.19-0.57, P=0.31; and 0.36, 95% CI −0.12-0.83, P=0.13; respectively). Similarly, there was better weight gain at 24-months in studies with supplements than without supplements (0.55, 95% CI 0.06-1.03, P=0.03), however, this

relationship was not as strong after adjusting for baseline cohort weight (0.45, 95% CI −0.03-0.93, P=0.06).

ART Regimen—Nine studies reported post-ART growth comparisons by regimen. Four of these (RLS=3 and DS=1) compared growth among children initiating protease inhibitor (PI) or non-nucleoside reverse-transcriptase inhibitor (NNRTI) based regimen. Two trials (Africa/India [38] and Europe/Americas [39]) reported significantly greater weight gains in nevirapine-naïve children randomized to NNRTI versus PI based regimens. Conversely, an observational study in Brazil [40] reported greater weight gains in children initiating PI-based ART. After adjusting for cohort age and setting, rate of weight gain did not differ between studies reporting NNRTI versus PI-containing regimens (6 mos: 0.13, 95% CI −0.48-0.73, P=0.67; 12 mos: −0.31, 95%CI, −0.98-0.36, P=0.35); similar associations remained after adjusting for baseline cohort weight. Similarly, there was no difference in height velocity by regimen in adjusted analyses (6 mos: 0.19, 95% CI −0.08-0.46, P=0.15; 12 mos: 0.11, 95% CI −0.19-0.40, P=0.44).

Discussion

In this systematic review and meta-analysis of 6, 12, and 24-month growth outcomes in HIV-infected children initiating ART, children in RLS had markedly lower weight and height at ART initiation compared to children in DS. Following ART, children in both settings experienced rapid improvements in weight and height. While the greatest gains in weight were observed during the first 6-months of therapy, gains in height were more modest and occurred later. Children in RLS had significant improvements in WAZ and HAZ at 6 and 12-months post-ART with higher rates of weight gain at 12 and 24-months post-ART compared to children in DS. Despite substantial growth reconstitution following ART, children in RLS continued to be an average of 1 SD below that of children in DS at 12-months post-ART due to baseline differences that never recovered.

Younger age at ART initiation was associated with greater gains in growth in nine studies, irrespective of setting. The most marked improvements in weight and height velocity were observed in children initiating ART prior to three years of age [1, 18-20, 22]. In the two studies reporting no difference in growth based on age at ART, the first consisted of few children less than 2 years of age [21], and the second reported high loss to follow-up rate and missing data [23]. While older children do experience post-ART catch-up growth, they do not reconstitute as rapidly as younger children and they may never reach population age-norms, particularly in height. These results emphasize the need for early identification and treatment of HIV in pediatric populations, as early ART initiation would be expected to avoid further growth compromise.

A few studies provided information on nutritional supplements, all from RLS [5, 8, 10, 18, 23, 24, 29-32, 34, 37]. While many ART programs in RLS provide nutritional supplements during ART, most studies did not clearly specify eligibility criteria or duration of supplementation, and only two evaluated the impact of supplements on growth. A Kenyan study reported greater post-ART weight gain in children receiving food supplements, and greater gains in height with multivitamins [18]. In a South African study of dietary iron

intake, post-ART height gains were associated with higher hemoglobin levels [32]. In other studies mentioning nutritional support [23, 24, 29], the greatest gains in weight were among children with the lowest baseline WAZ at ART initiation. In the absence of HIV, catch-up growth to population norms following malnutrition depends on severity, duration, and age at onset [41]. International adoptees experience remarkable catch-up growth, with younger adoptees gaining as much as 2 SD in weight and height [42]. In Malawi, 80% of children recovered from moderate acute malnutrition after treatment with ready-to-use therapeutic supplementary food [43]. While food supplements as an adjunct to ART may accelerate weight recovery, it is unclear whether ART alone would produce the same rebound in a slightly longer timeframe or if underlying poverty contributes to the persistence of undernutrition. Our pooled analysis suggests greater 12 and 24-month height and 24-month weight gains in cohorts using supplements, however lack of direct comparison of growth outcomes by timing and supplement type make it difficult to interpret these results. Further research is needed to determine effectiveness and optimal supplement regimens as adjuncts to ART.

Prior studies have yielded inconclusive data on the influence of ART regimen on growth reconstitution. The IMPAACT P1060 trial, undertaken in sub-Saharan Africa and India, reported better weight gains in the NVP group compared to LPV/r group [38]. However, this difference did not remain after 1 year [44]. Conversely, the PENPACT trial in Europe and North and South America showed greater weight gain in the PI group [45]. Similarly, a large observational study reported better weight and height growth among children initiating PI- versus NNRTI-based regimens [46]. In practice, younger children are preferentially provided LPV/r-based regimens to reduce the likelihood of NVP resistance among those exposed to PMTCT, which may confound ability to determine role of regimen in growth reconstitution. Despite concerns regarding LPV/r's poor palatability which could compromise adherence [27, 28], a recent Cochrane review [47] concluded that LPV/r was a more efficacious first-line regimen than NVP among younger children. The relationship between post-ART growth gains and immune and viral response is not well understood. Post-ART gains in weight have been shown to correlate with improvements in CD4 and viral load [48, 49]; conversely, other studies have shown no association between post-ART virologic response and growth recovery suggesting other factors are required to promote growth [22, 50, 51]. We found no difference in growth response between studies reporting PI- and NNRTI-based regimens, and many studies lacked statistical power to compare growth outcomes by regimen.

This study has limitations inherent to systematic reviews and meta-analyses. Retention varied across studies. Children no longer in care may have been more likely to have died or worse growth outcomes than those in care. This would lead to overestimating growth reconstitution following ART. The studies included older children (mean age 7 years) and could be affected by survivor bias. Studies of younger children may have greater post-ART growth recovery compared to older cohorts. However, there was no difference in mean age at baseline between RLS and DS. This analysis excluded some studies reporting growth in weight and length rather than Z-scores. However, most studies included Z-scores and we believe exclusion of studies without Z-scores does not introduce substantial bias into our estimates of pooled changes in growth. Lastly, a few studies included children with prior

mono/dual therapy. Compared to treatment-naïve children initiating ART, children with prior treatment may have a slower rate of post-ART growth.

This is the first systematic review of post-ART growth outcomes in children in RLS and DS. Previous reviews of pediatric post-ART outcomes have included only baseline growth measures [14] or provided limited data on follow-up growth in sub-Saharan Africa or RLS [3, 12, 13]. We expanded upon this by systematically screening, evaluating, and selecting studies including post-ART growth outcomes irrespective of study setting. Meta-analysis techniques were then used to provide standardized summary statistics of change in growth at 6, 12, and 24-months post-ART; affording a unique opportunity to compare the rate of change in weight and height in children receiving ART across studies in RLS and DS.

While post-ART rates of growth reconstitution in RLS and DS were comparable or higher in RLS, children in RLS had continued marked lower growth at 12- and 24-months post-ART. Projecting from 2-year growth reconstitution rates, if rates persisted at similar or lower reconstitution, it may take 4-5 years to reach population norms for WAZ while HAZ is likely to never fully recover. Few studies reported data on nutritional supplementation, making it difficult to assess the potential benefits of supplementation. Current programs often provide empiric nutritional supplementation to children starting ART, but it is not clear if this is beneficial because ART alone results in substantial growth reconstitution. Despite empiric nutritional supplementation in pediatric ART programs evidence of the effectiveness of nutritional therapy on growth and morbidity in children on ART is lacking. Improvements in programmatic data regarding nutritional supplements can help inform policies to optimize nutritional therapy for growth reconstitution in children on ART. Our study demonstrates marked persistent growth compromise in ART-treated children. Earlier diagnosis and treatment of children and further data regarding the role of supplementation will be important to enhance growth in these children.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Abbreviations

WAZ	weight-for-age Z-score
WHZ	weight-for-height Z-score
HAZ	height-for-age Z-score
HAART	highly active antiretroviral therapy

ART	antiretroviral therapy
DS	developed setting
RLS	resource-limited setting

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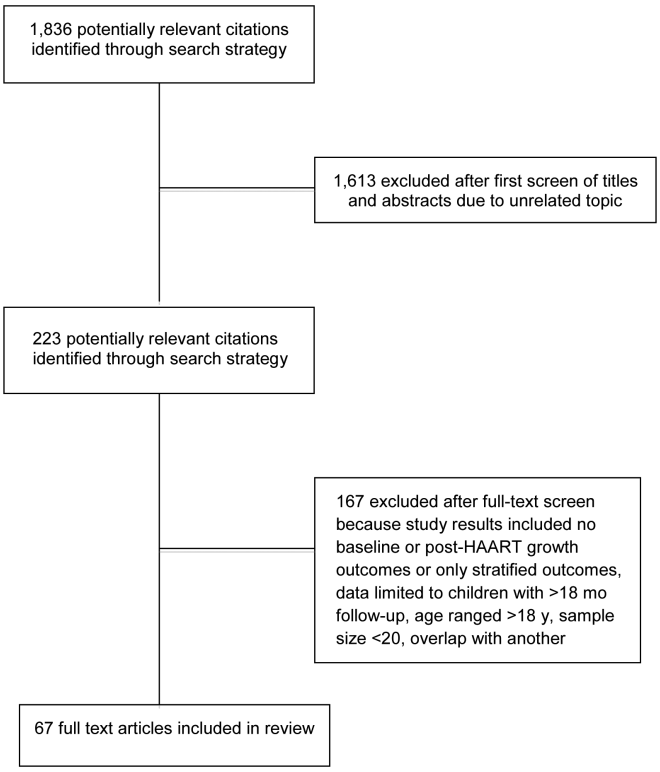

Fig 1.
Study flow chart describing the selection of publications for review

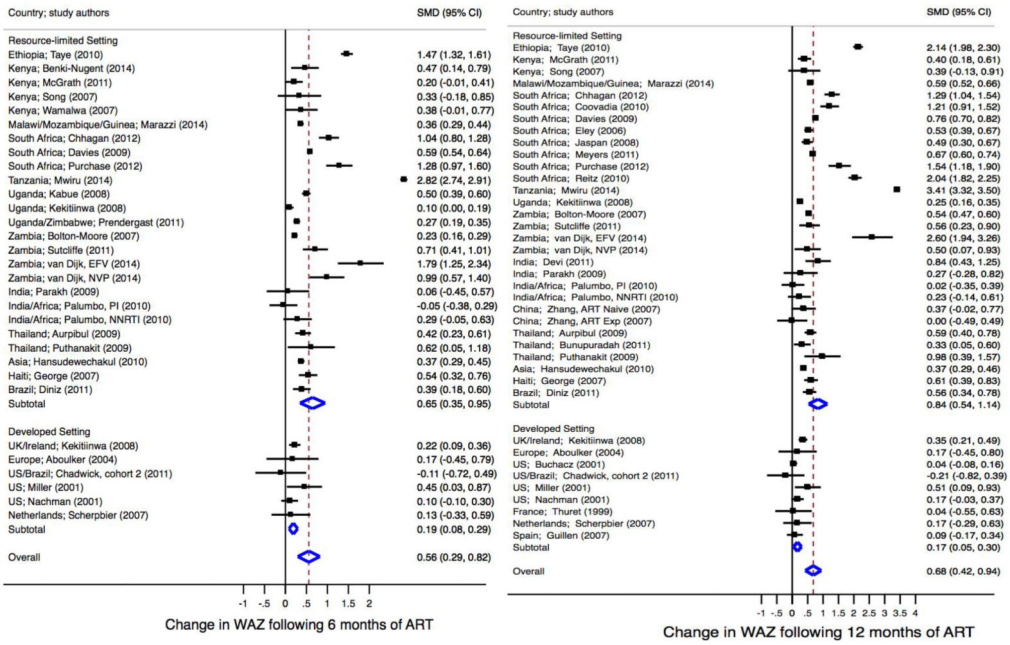

Fig 2a. Standardized mean difference in WAZ at 6 months (left) and 12 months (right) post-antiretroviral therapy

Meta-regression comparing SMD at 6 months in RLS vs. developed settings, *P*=0.12. Meta-regression comparing SMD at 12 months in RLS vs. developed settings, *P*=0.03. ART, antiretroviral therapy; RLS, resource-limited setting; SMD, standardized mean difference.

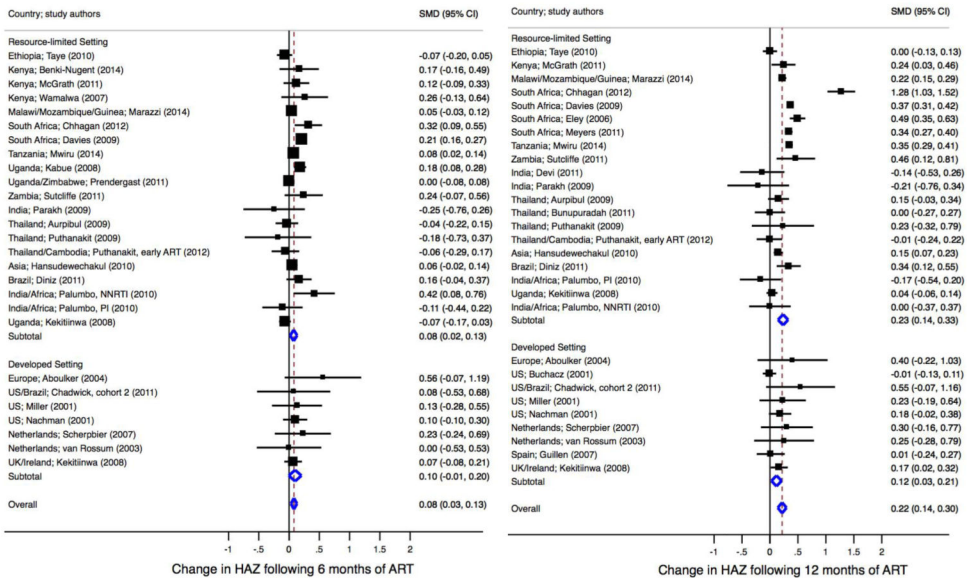

Fig 2b. Standardized mean difference in height-for-age at 6 months (left) and 12 months (right) post-antiretroviral therapy

Meta-regression comparing SMD at 6 months in RLS vs. developed settings, p=0.62. Meta-regression comparing SMD at 12 months in RLS vs. developed settings, p=0.73. ART, antiretroviral therapy; RLS, resource-limited setting; SMD, standardized mean difference.

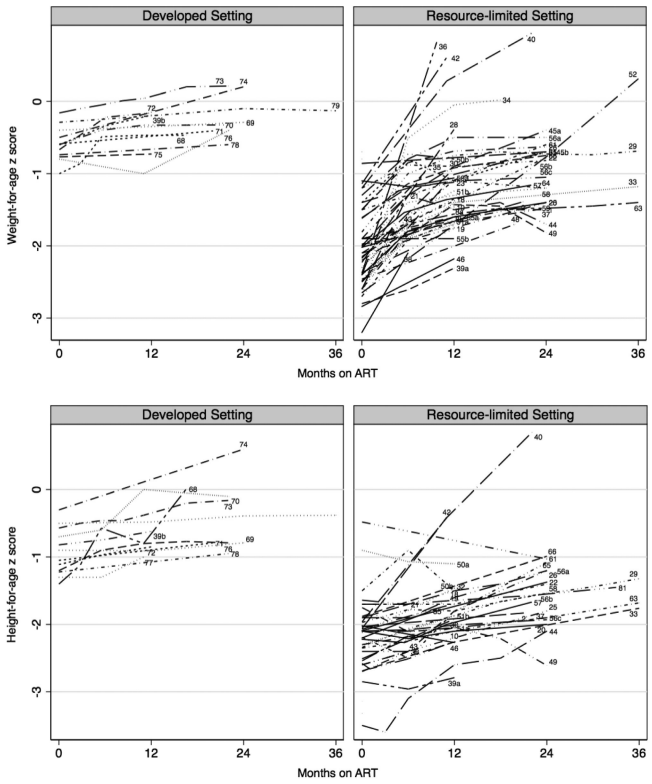

Fig 3. Change in weight-for-age (top) and height-for-age (bottom) following initiation of antiretroviral therapy

Numbers correspond to articles as listed in the References. ART, antiretroviral therapy.

Table 1

Characteristics of studies included in a systematic review of pediatric growth following ART

Study authors (Year)	Location	N	Age, mean (a) or median (b)	Study details, protease inhibit-based (a) or NNRTI-based (b) ART	Months follow-up, mean (a), median (b) or total (c)
RLS (n=54)					
Nacro *et al.* [18] (2011)	Burkino Faso	51	6.8 years[a]	ANRS 12103, phase-II pediatric ART, EFV[b]	12[c]
De Beaudrap *et al.* [19] (2008)	Cote d'Ivoire	177	5.8 years[b]	ANRS 1244/1278, protease inhibitor, 74%; NNRTI, 26%	30[a]
Fassinou *et al.* [2] (2004)	Cote d'Ivoire	60	7.2 years[b]	ANRS 1244, NFV[a], 78%; EFV[b], 22%	21[a]
Hagströmer *et al.* [8] (2013)	Ethiopia	A: 658	52% <6 years	Pediatric HIV Care: Hospital, NR	37[b]
		B: 230	52% <6 years	Health Centre Clinics, NR	26[b]
Taye *et al.* [20] (2010)	Ethiopia	475	NR	Malnutrition and mortality study, NVP[b]	12[b]
Benki-Nugent *et al.* [21] (2014)	Kenya	73	3.7 months[b]	OPH03, <5 months at ART, LPV/r[a], 38%; NVP[b], 62%	6[c]
McGrath *et al.* [22] (2011)	Kenya	169	4.7 years[b]	Treatment-naive, NNRTI	19[b]
Song *et al.* [23] (2007)	Kenya	29	8.5 years[a]	Treatment-naive, NVP[b]	15[c]
Wamalwa *et al.* [5] (2007)	Kenya	52	4.4 years[b]	First-line ART, EFV[b], 27%; NVP[b], 69%	9[b]
Kim *et al.* [24] (2012)	Malawi	55	1.6 years[a]	Nutritional therapy at ART, NVP[b]	6[c]
Weigel *et al.* [25] (2010)	Malawi	419	8.0 years[b]	77% severely immunosuppressed, NVP[b]	23[b]
Marazzi *et al.* [10] (2014)	17 sites Malawi, Mozambique, Guinea	2215	4 years[b]	DREAM Cohort, LPV/r[a], 3%; NVP[b], 97%	16[b]
Chhagan *et al.* [26] (2012)	South Africa	151	5.1 years[b]	Pediatric ART programme, LPV/r[a], 24%; NVP[b], 76%	24[c]
Cotton *et al.* [27] (2013)	South Africa	A: 126	7.4 weeks[b]	CHER Trial: ART 40 weeks, LPV/r[a]	57[b]
		B: 126	7.5 weeks[b]	ART 96 weeks, LPV/r[a]	57[b]

Study authors (Year)	Location	N	Age, mean (a) or median (b)	Study details, protease inhibit-based (a) or NNRTI-based (b) ART	Months follow-up, mean (a), median (b) or total (c)
		C: 125	7.1 weeks[b]	Deferred ART (not included), LPV/r[a]	57[b]
Coovadia *et al.* [28] (2010)	South Africa	99	11 months[b]	NEVEREST: <2 years and NVP-exposed, LPV/r[a] (control)	12[c]
Davies *et al.* [29] (2009)	South Africa	2966	3.6 years[b]	IeDEA, treatment-naïve, LPV/r[a], 52%; EVF[b], 29%	36[c]
Eley *et al.* [30] (2006)	South Africa	409	1.9 years[b]	63% severe clinical disease, protease inhibitor, 51%; NNRTI, 49%	12[c]
Jaspan *et al.* [31] (2008)	South Africa	A: 126	2.2 years[b]	LPV/r[a] or RTV[a]	24[c]
		B: 146	2.2 years[b]	NVP[b] or EFV[b]	24[c]
Kruger *et al.* [32] (2013)	South Africa	53	6.8 years[a]	Dietary iron intake and iron status, EFV[b]	18[c]
Meyers *et al.* [33] (2011)	South Africa	1734	4.3 years[b]	Large public clinic, LPV/r[a] <3 years at ART; NVP[b] ≥3 years	17[b]
Purchase *et al.* [34] (2012)	South Africa	94	8.6 months[b]	<1 year at ART, LPV/r[a], 79%; NVP[b], 4%	18[c]
Reddi *et al.* [35] (2007)	South Africa	151	5.7 years[b]	Pediatric programme, LPV/r[a] <3 years, 15%; EFV[b] ≥3 years, 66%	8[b]
Reitz *et al.* [36] (2010)	South Africa	254	8.8 months[b]	ART Strategy Trial, LPV/r[a], 72%; RTV[a], 28%	9[c]
Mwiru *et al.* [37] (2014)	Tanzania	2133	51% <6 years	Growth post-ART, NVP[b] <3 y; EFV[b] or NVP[b] ≥3 y	17[b]
Kabue *et al.* [38] (2008)	Uganda	749	7.5 years[a]	Pediatric treatment programme, NR	6[a]
Kekitiinwa *et al.* [39] (2008)	Uganda	A: 853	7.6 years[b]	Mulago Cohort, EFV[b] or NVP[b], 98%	12[c]
	UK & Ireland	B: 436	5.0 years[b]	CHIPS, LPV/r[a] or NFV[a], 29%; EFV[b] or NVP[b], 63%	12[c]
Barlow-Mosha *et al.* [40] (2012)	Uganda	104	5.4 years[b]	Adult fixed-dose ART, NVP[b] (Triomune)	22[c]
Musiime *et al.* [41] (2012)	Uganda	A: 449	11.9 years[a]	Urban, EFV[b] or NVP[b]	33[b]
		B: 499	11.4 years[a]	Rural, EFV[b] or NVP[b]	33[b]
Musoke *et al.* [42] (2010)	Uganda	124	5.0 years[b]	Adult fixed-dose ART, NVP[b] (Triomune)	11[c]

Study authors (Year)	Location	N	Age, mean (a) or median (b)	Study details, protease inhibit-based (a) or NNRTI-based (b) ART	Months follow-up, mean (a), median (b) or total (c)
Prendergast *et al*. [43] (2011)	Uganda & Zimbabwe	1168	6.0 years[b]	ARROW Trial, EFV[b] or NVP[b]	6[c]
Bolton-Moore *et al*. [1] (2007)	Zambia	1926	6.8 years[b]	Pediatric ART programme, EFV[b], 11%; NVP[b], 88%	12[b]
Sutcliffe *et al.* [44] (2011)	Zambia	119	2.9 years[b]	65% ART-naïve, EFV[b] or NVP[b]	13[b]
van Dijk *et al*. [45] (2013)	Zambia	A: 39	17.4 months[b]	EFV[b]-based ART and anti-TB treatment	17[b]
		B: 58	20.2 months[b]	NVP[b]-based ART	13[b]
Devi *et al.* [46] (2011)	India	49	6.2 years[b]	TB Research Centre, NR	12[c]
Kumarasamy *et al*. [47] (2009)	India	67	6.3 years[a]	Treatment-naïve, EFV[b], 58%; NVP[b], 21%	12[c]
Lodha *et al.* [48] (2005)	India	26	5.7 years[a]	Tertiary care hospital, IDV[a], 3%; NVP[b], 97%	20[a]
Parakh *et al*. [49] (2009)	India	30	7 years[b]	First-line ART in treatment-naive, NVP[b]	36[c]
Palumbo *et al.* [50] (2010)	India & sub-Saharan Africa	A: 82	0.7 years[b]	P1060 cohort 1 (prior NVP): LPV/r[a]	22[c]
		B: 82	0.7 years[b]	NVP[b]	22[c]
Violari *et al.* [51] (2012)	India & sub-Saharan Africa	A: 140	1.7 years[b]	P1060 (no prior NVP): LPV/r[a]	16[b]
		B: 147	1.8 years[b]	NVP[b]	16[b]
Isaakidis *et al.* [52] (2010)	Cambodia	220	6 years[b]	Long-term ART outcomes, NVP[b]	24[b]
Janssens *et al.* [53] (2007)	Cambodia	212	6.0 years[b]	Split fixed-dose combination, NVP[b]	17[b]
Sophan *et al.* [54] (2010)	Cambodia	23	5.5 years[b]	Modified directly observed therapy, NVP[b]	18[c]
Zhang *et al.* [55] (2007)	China	A: 51	10 years[b]	ART-naive, NVP[b]	12[c]
		B: 32	12 years[b]	ART-experienced, NVP[b]	12[c]
Zhao *et al.* [56] (2013)	China	A: 302	2.0 years[b]	National data: <36 months at ART, EFV[b], 8%; NVP[b], 92%	24[b]

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Study authors (Year)	Location	N	Age, mean (a) or median (b)	Study details, protease inhibit-based (a) or NNRTI-based (b) ART	Months follow-up, mean (a), median (b) or total (c)
		B: 366	4.1 years[b]	36-59 months at ART, EFV[b], 30%; NVP[b], 70%	24[b]
		C: 1150	8.8 years[b]	>59 months at ART, EFV[b], 28%; NVP[b], 72%	24[b]
Aurpibul *et al*. [57] (2009)	Thailand	225	7.2 years[a]	Growth post-ART, EFV[b]: 62%; NVP[b]: 38%	50[b]
Bunupuradah *et al.* [58] (2011)	Thailand	107	6.2 years[b]	NNRTI study, EFV[b]: 30%; NVP[b]: 70%	22[c]
Hansudewechakul *et al*. [59] (2012)	Thailand	410	8.6 years[b]	Community-based pediatric HIV care network, EFV[b]: 13%; NVP[b]: 83%; PI: 4%	28[b]
Phongsamart *et al.* [60] (2014)	Thailand	1139	7.1 years[b]	Pediatric database, PI: 4%; NNRTI: 74%	35[b]
Puthanakit *et al*. [61] (2009)	Thailand	26	9.8 months[b]	≤2 years at ART, NVP[b]	22[c]
Puthanakit *et al*. [62] (2012)	Thailand & Cambodia	A: 149	6.4 years[b]	PREDICT Trial: Early ART, LPV/r[a], 5%; NVP[b], 94%	33[c]
		B: 150	6.5 years[b]	Deferred ART (not included), LPV/r[a], 2%; NVP[b], 41%	33[c]
Hansudewechakul *et al*. [63] (2010)	5 Asian countries	1189	7.0 years[b]	TApHOD: PI, 6%; NVP[b], 93%	35[b]
George *et al.* [64] (2007)	Haiti	163	6.3 years[b]	GHESKIO Centers, treatment-naïve, EFV[b], 68%; NVP[b], 24%	20[b]
Pierre *et al.* [65] (2008)	Jamaica	197	5.0 years[b]	38% Treatment-naïve, NVP[b], 85%	23[b]
Diniz *et al*. [66] (2011)	Brazil	196	3.4 years[b]	Treatment-naïve, NFV[a] or LPV/r[a], 68%; NNRTI, 32%	33[c]
DEVELOPED SETTINGS (n=13)					
Babiker *et al*. [67] (2011)	Europe, N. & S. America	A: 131	7.1 years[b]	PENPACT 1 Trial: LPV/r[a] or NFV[a]	48[c]
		B: 132	6.4 years[b]	EFV[b] or NVP[b]	48[c]
Aboulker *et al*. [68] (2004)	5 European sites	20	2.5 months[b]	PENTA 7: <3 months at ART, NFV[a]	22[b]
Buchacz *et al.* [69] (2001)	US	544	3 months to 18 years	PACTG 219: NFV[a], 43%; RTV[a], 38%; IDV[a], 11%; SQV[a] 11%	24[a]

Study authors (Year)	Location	N	Age, mean (a) or median (b)	Study details, protease inhibit-based (a) or NNRTI-based (b) ART	Months follow-up, mean (a), median (b) or total (c)
Chadwick *et al.* [70] (2011)	17 sites US & Brazil	21	<6 months	IMPAACT-P1030: Cohort 2, LPV/r[a]	28[b]
Dreimane *et al.* [71] (2001)	US	27	6.5 years[a]	Protease inhibitor added to ART, NR	20[a]
Miller *et al.* [72] (2001)	US	45	6.8 years[a]	NFV[a] or RTV[a] or IDV[a] or SQV[a]	5[b]
Nachman *et al*. [73] (2005)	US	192	4 months to 17 years	PACTG 377, RTV[a], 21%; NFV[a], 79%	22[c]
Faye *et al.* [74] (2002)	France	31	3.7 months[b]	French Perinatal Cohort, RTV[a], 32%; NFV[a], 68%	24[c]
Thuret *et al*. [75] (1999)	France	22	6.6 years[b]	Protease inhibitor study, RTV[a]	15[b]
Scherpbier *et al*. [76] (2007)	Netherlands	36	6.6 years[b]	NNRTI-based ART, EFV[b]	16[b]
van Rossum *et al*. [77] (2003)	Netherlands	27	5.5 years[b]	Growth recovery, IDV[a], 89%; NFV[a], 11%	11[c]
Verweel *et al.* [78] (2002)	Netherlands	24	5.2 years[b]	Growth and ART, IDV[a], 83%; NFV[a], 17%	22[c]
Guillen *et al.* [79] (2007)	Spain	122	6.0 years[b]	39% treatment-naive, NR	71[b]

N is the total number of children initiating ART with at least 1 anthropometric measure and not always representative of the cohort with follow up growth measures. ANRS, French National Agency for AIDS Research; ARROW, Antiretroviral Research for Watoto; ART, antiretroviral therapy; CHER, Children with HIV Early Antiretroviral; CHIPS, Collaborative HIV Paediatric Study; DREAM, Drug Resource Enhancement against AIDS and Malnutrition; EFV, efavirenz; IeDEA, International Epidemiologic Databases to Evaluate AIDS; IDV, indinavir; IMPAACT, International Maternal Pediatric Adolescent AIDS Clinical Trials Group; LPV/r, lopinavir/ritonavir; NEVEREST, Nevirapine Resistance Study; NFV, nelfinavir; NNRTI, nonnucleoside reverse-transcriptase inhibitor; NR, not reported; NVP, nevirapine; OPH03, Optimizing Pediatric HAART 03; PENTA, Paediatric European Network for Treatment of AIDS; PREDICT, Pediatric Randomized Early vs. Deferred Initiation in Cambodia and Thailand; RLS, resource-limited settings; RTV, ritonavir; SQV, saquinavir; TApHOD, TREAT Asia Pediatric HIV Observational Database; TB, tuberculosis.

Table 2

Change in growth from baseline at 6, 12, and 24-months following ART in HIV-infected children in resource-limited and developed settings.

Country (study authors)	N	Change in WAZ at months				Change in HAZ at months				WHZ at months			
		base	6	12	24	base	6	12	24	base	6	12	24
RLS (n=44)													
Burkino Faso (Nacro *et al.* [18])	51	−2.01[a]	-	0.63[a]	-	−2.12[a]	-	0.57[a]	-	-	-	-	-
Cote d'Ivoire (De Beaudrap *et al.* [19])	177	−2.37[a]	-	0.61%[a]	-	−2.07[a]	-	0.38%[a]	-	-	-	-	-
Cote d'Ivoire (Fassinou *et al.* [2])	60	−2.02[a]	-	-	0.63[a,c]	−2.03[a]	-	-	0.20[a,c]	-	-	-	-
Ethiopia (Hagströmer *et al.* [8])													
Hospital	658	−2.50[b]	0.65[b]	0.90[b]	-	-	-	-	-	-	-	-	-
Health Centers	230	−2.50[b]	0.60[b]	0.80[b]	-	-	-	-	-	-	-	-	-
Ethiopia (Taye *et al.* [20])	475	−2.40[b]	0.60[b]	0.80[b]	1.00[b]	−2.10[b]	−0.11[b]	0.00[b]	0.10[b]	−0.99[b]	0.90[b]	1.26[b]	1.48[b]
Kenya (Benki-Nugent *et al.* [21])	73	−2.00[b]	0.70[b]	-	-	−1.90[b]	−0.20[b]	-	-	−0.60[b]	0.00[b]	-	-
Kenya (McGrath *et al.* [22])	169	−1.98[a]	0.30[d]	0.60[d]	1.20[d]	−2.09[a]	0.18[d]	0.36[d]	0.72[d]	−0.96[a]	0.36[d]	0.72[d]	1.44[d]
Kenya (Song *et al.* [23])	29	−1.61[a]	0.42[a]	0.49[a]	-	-	-	-	-	-	-	-	-
Kenya (Wamalwa *et al.* [5])	52	−2.30[b]	0.63[b]	-	-	−2.54[b]	0.37[b]	-	-	-	-	-	-
Malawi (Kim *et al.* [80])	55	-	-	-	-	−3.60[a]	-	-	-	−1.49[a]	1.80[a]	-	-
Malawi (Weigel *et al.* [25])	419	−2.10[b]	-	-	0.70[b]	−2.60[b]	-	-	0.80[b]	-	-	-	-
Malawi/Mozam/Guinea (Marazzi *et al.* [10])	1226	−2.16[b]	0.44[a]	0.70[a]	-	−2.58[b]	0.07[a]	0.09[a]	-	−0.74[b]	0.57[a]	0.74[a]	-

Country (study authors)	N	Change in WAZ at months				Change in HAZ at months				WHZ at months			
		base	6	12	24	base	6	12	24	base	6	12	24
South Africa (Chhagan *et al.* [26])	151	−1.26[b]	0.22[d]	0.43[d]	0.86[d]	−2.05[b]	0.34[d]	0.69[d]	1.37[d]	-	-	-	-
South Africa (Coovadia *et al.* [28])	99	−2.23[a]	-	1.84[a,c]	-	−3.14[a]	-	-	-	-	-	-	-
South Africa (Cotton *et al.* [27])													
40 weeks	126	−0.80[b]	-	-	0.47: 4.8 years	-	-	-	-	-	-	-	-
96 weeks	126	−0.70[b]	-	-	0.02: 4.8 years	-	-	-	-	-	-	-	-
South Africa (Davies *et al.* [29])	2966	−1.81[b]	0.81[b]	1.06[b]	1.08[b]	−2.34[b]	0.28[b]	0.47[b]	0.80[b]	−0.39[b]	0.97[b]	1.13[b]	0.91[b]
South Africa (Eley *et al.* [30])	409	−2.17[b]	-	1.24[b]	-	−2.51[b]	-	0.59[b]	-	−0.63[b]	-	1.06[b]	-
South Africa (Jaspan *et al.* [31])													
Protease inhibitor	126	−2.80[b]	-	1.70[b]	2.20[b]	-	-	-	-	-	-	-	-
NNRTI	146	−2.40[b]	-	1.57[b]	1.70[b]	-	-	-	-	-	-	-	-
South Africa (Kruger *et al.* [32])	53	-	-	-	-	−1.70[a]	0.00[a]	0.20[a]	-	−0.40[a]	0.30[a]	0.00[a]	-
South Africa (Meyers *et al.* [33])	1734	−2.40[a]	-	1.00[a]	-	−2.69[a]	-	0.43[a]	-	-	-	-	-
South Africa (Purchase *et al.* [34])	94	−2.70[a]	2.19[a]	2.65[a]	-	-	-	-	-	-	-	-	-
South Africa (Reddi *et al.* [35])	151	−1.90[b]	-	1.00[b,c]	-	−2.20[b]	-	0.40[b,c]	-	-	-	-	-
South Africa (Reitz *et al.* [36])	254	−2.38[a]	-	3.20[a,c]	-	−3.45[a]	-	-	-	-	-	-	-
Tanzania (Mwiru *et al.* [37])	2133	−2.60[a]	0.80[a]	0.92[a]	1.12[a]	−2.19[a]	0.02[a]	0.09[a]	0.17[a]	−1.78[a]	0.80[a]	0.97[a]	1.11[a]
Uganda (Barlow-Mosha *et al.* [40])	104	−1.20[a]	-	1.48[a,c]	2.14[a,c]	−1.96[a]	-	1.55[a,c]	2.81[a,c]				

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Country (study authors)		N	Change in WAZ at months				Change in HAZ at months				WHZ at months			
			base	6	12	24	base	6	12	24	base	6	12	24
Uganda (Kabue *et al.* [38])		749	−3.20[a]	1.10[a]	-	-	−2.70[a]	0.30[a]	-	-	−1.50[a]	1.30[a]	-	-
Uganda (Kekitiinwa *et al.* [39])		853	−2.80[b]	0.19[b]	0.49[b]	-	−2.85[b]	−0.11[b]	0.06[b]	-	-	-	-	-
Uganda (Musiime *et al.* [41])														
	Urban	449	−4.90[a]	-	-	3.4: 2.8 years	−7.30[a]	-	-	5.0: 2.8 years	-	-	-	-
	Rural	499	−4.60[a]	-	-	4.2: 2.8 years	−5.70[a]	-	-	5.1: 2.8 years	-	-	-	-
Uganda (Musoke *et al.* [42])		124	−1.14[a]	-	0.54[a,c]	-	−2.06[b]	-	1.65[a,c]	-	-	-	-	-
Uganda/Zimbab (Prendergast *et al.* [43])		1168	−2.10[b]	0.40[b]	-	-	−2.40[b]	0.00[b]	-	-	−0.50[b]	-	-	-
Zambia (Bolton-Moore *et al.* [1])		1926	−2.20[a]	0.40[a]	0.60[a]	0.70[a]	-	-	-	-	-	-	-	-
Zambia (Sutcliffe *et al.* [44])		119	−2.40[a]	1.10[a]	0.90[a]	0.70[a]	−3.50[a]	0.40[a]	0.90[a]	1.40[a]	-	-	-	-
Zambia (van Dijk *et al.* [45])														
	EFV	39	−2.60[a]	1.30[a]	1.70[a]	2.20[a]	−2.30[b]	0.12[a]	0.25[a]	-	-	-	-	-
	NVP	58	−1.40[b]	0.60[a]	0.30[a]	0.70[a]	−2.30[b]	0.21[a]	0.43[a]	-	-	-	-	-
India (Devi *et al.* [46])		49	−2.84[b]	-	0.66[b]	-	−2.02[b]	-	−0.25[b]	-	−2.41[b]	-	1.33[b]	-
India (Kumarasamy *et al.* [47])		67	-	-	-	-	-	-	-	-	0.53[a]	-	0.05[a]	-
India (Lodha *et al.* [48])		26	−2.46[b]	-	-	0.70[b,c]	−2.48[b]	-	-	1.49[b,c]	−1.01[b]	-	-	1.01[b,c]
India (Parakh *et al.* [49])		30	−1.98[b]	0.12[b]	0.55[b]	0.16[b]	−1.75[b]	−0.36[b]	−0.30[b]	−0.86[b]	-	-	-	-

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Country (study authors)	N	Change in WAZ at months				Change in HAZ at months				WHZ at months			
		base	6	12	24	base	6	12	24	base	6	12	24
India/Africa (Palumbo *et al.* [50])										-	-	-	-
Protease inhibitor	82	−1.10[b]	0.01[b]	0.01[b]	0.00[b,e]	−1.00[b]	−0.20[b]	0.10[b]	0.30[b,e]	-	-	-	-
NNRTI	82	−1.30[b]	0.30[b]	0.70[b]	1.40[b,e]	−1.50[b]	0.30[b]	0.40[b]	0.60[b,e]	-	-	-	-
India/Africa (Violari *et al.* [51])										-	-	-	-
Protease inhibitor	140	−2.70[b]	0.78[a]	1.04[a]	-	−2.30[b]	0.12[a]	0.25[a]	-	-	-	-	-
NNRTI	147	−2.60[b]	1.03[a]	1.36[a]	-	−2.30[b]	0.21[a]	0.43[a]	-	-	-	-	-
Cambodia (Isaakidis *et al.* [52])	220	−2.65[b]	-	-	1.88[b]	-	-	-	-	-	-	-	-
Cambodia (Janssens *et al.* [53])	212	-	-	-	-	-	-	-	-	−1.59[a]	-	0.81[a]	-
Cambodia (Sophan *et al.* [54])	23	−2.97[a]	0.45[b]	0.60[b]	0.78[b,c]	−3.32[a]	0.10[b]	0.60[b]	0.48[b,c]	−1.57[a]	-	-	0.64[b,c]
China (Zhang *et al.* [55])													
ART naive	51	−1.90[b]	-	0.30[b]	-	-	-	-	-	-	-	-	-
ART experienced	32	−1.90[b]	-	0.00[b]	-	-	-	-	-	-	-	-	-
China (Zhao *et al.* [56])										-	-	-	-
<36 months at ART	302	−1.50[a]	0.70[a]	1.00[a]	1.00[a]	−1.90[a]	0.00[a]	0.30[a]	0.70[a]	-	-	-	-
36-59 months at ART	366	−1.20[a]	0.32[a]	0.30[a]	0.38[a]	−1.97[a]	0.19[a]	0.17[a]	0.44[a]	-	-	-	-
>59 months at ART	1150	−1.40[b]	0.20[a]	0.30[a]	0.35[a]	−2.10[b]	0.00[a]	0.05[a]	0.20[a]	-	-	-	-
Thailand (Aurpibul *et al.* [57])	225	−2.02[a]	0.48[a,c]	0.66[a,c]	0.86[a,c]	−2.22[a]	−0.05[a,c]	0.22[a,c]	0.55[a,c]	-	-	-	-

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Country (study authors)	N	Change in WAZ at months				Change in HAZ at months				WHZ at months			
		base	6	12	24	base	6	12	24	base	6	12	24
Thailand (Bunupuradah *et al.* [58])	107	−1.50[b]	-	0.40[b,c]	0.30[b,c]	−1.70[b]	-	0.00[b,c]	0.30[b,c]	−0.50[b]	-	0.40[b,c]	0.20[b,c]
Thailand (Hansudewechakul *et al.* [59])	410	−1.90[b]	-	-	0.50[b]	-	-	-	-	-	-	-	-
Thailand (Phongsamart *et al.* [60])	1139	−1.80[b]	-	-	0.80: 6.4 years	−1.80[b]	-	-	0.70: 6.4 years	-	-	-	-
Thailand (Puthanakit *et al.* [61])	26	−2.49[a]	0.86[a]	1.40[a]	1.89[a]	−2.19[a]	−0.31[a]	0.38[a]	1.11[a]	-	-	-	-
Thailand/Cambodia (Puthanakit *et al.* [81])	149	−1.30[b]	-	-	-	−1.60[b]	−0.06[a,c]	0.01[a,c]	0.07[a,c]	-	-	-	-
Asia (Hansudewechakul *et al.* [63])	1189	−2.15[b]	0.45[b]	0.59[b]	0.67[b]	−2.35[b]	0.10[b]	0.25[b]	0.45[b]	-	-	-	-
Haiti (George *et al.* [64])	163	−2.00[b]	0.60[b]	0.70[b]	0.80[b]	-	-	-	-	-	-	-	-
Jamaica (Pierre *et al.* [65])	197	−0.86[a]	-	-	0.16[a]	−0.48[a]	-	-	−0.55[a]	−1.58[a]	-	-	1.71[a]
Brazil (Diniz *et al.* [66])	196	−1.62[a]	0.48[a]	0.70[a]	0.87[a]	−1.88[a]	0.22[a]	0.45[a]	0.89[a]	-	-	-	-
DEVELOPED SETTINGS (n=14)													
Europe/America (Babiker *et al.* [67])													
Protease inhibitor	131	−0.80[a]	-	-	0.53: 4 years	−1.00[a]	-	-	0.61: 4 years	-	-	-	-
NNRTI	132	−0.80[a]	-	-	0.77: 4 years	−1.00[a]	-	-	0.74: 4 years	-	-	-	-
Europe (Aboulker *et al.* [68])	20	−1.00[b]	0.51[b,c]	0.53[b,c]	-	−1.40[b]	0.83[b,c]	0.60[b,c]	-	-	-	-	-
United States (Buchacz *et al.* [69])	544	−0.40[a]	-	0.05[a]	0.11[a]	−0.90[a]	NR	−0.01[a]	0.11[a]	-	-	-	-
United States/Brazil (Chadwick *et al.* [70])	21	−0.80[b]	−0.10[b,c]	−0.20[b,c]	0.40[b,c]	0.70[b]	0.10[b,c]	0.70[b,c]	0.60[b,c]	-	-	-	-

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Country (study authors)	N	Change in WAZ at months				Change in HAZ at months				WHZ at months			
		base	6	12	24	base	6	12	24	base	6	12	24
United States (Dreimane *et al.* [71])	27	−0.59[a]	-	-	0.18[a,c]	−1.05[a]	-	-	0.26[a,c]	-	-	-	-
United States (Miller *et al.* [72])	45	−0.67[a]	0.45[a,c]	0.51[a,c]	-	−1.11[a]	0.15[a,c]	0.26[a,c]	-	0.25[a]	0.50[a,c]	0.43[a,c]	-
United States (Nachman *et al.* [73])	192	−0.16[a]	0.11[a,c]	0.20[a,c]	0.37[a,c]	−0.57[a]	0.11[a,c]	0.19[a,c]	0.40[a,c]	-	-	-	-
France (Faye *et al.* [74])	31	−0.50[b]	-	-	0.70[b]	−0.30[b]	-	-	0.90[b]	-	-	-	-
France (Thuret *et al.* [75])	22	−0.77[b]	-	0.04[b]	-	-	-	-	-	-	-	-	-
Netherlands (Scherpbier *et al.* [76])	36	−0.60[a]	0.20[a,c]	0.27[a,c]	0.27[a,c]	−1.20[a]	0.30[a,c]	0.40[a,c]	0.41[a,c]	0.28[a]	0.10[a,c]	0.09[a,c]	0.07[a,c]
Netherlands (van Rossum *et al.* [77])	27	-	-	-	-	−1.30[b]	0.00[b]	0.30[b]	-	-	-	-	-
Netherlands (Verweel *et al.* [78])	24	−0.74[b]	-	-	0.34[b]	−1.22[b]	-	-	0.20[b]	-	-	-	-
Spain (Guillen *et al.* [79])	122	−0.29[a]	-	0.12[a]	0.30[a]	−0.50[a]	-	0.11[a]	0.25[a]	-	-	-	-
UK/Ireland (Kekitiinwa *et al.* [39])	436	−0.60[b]	0.26[b]	0.41[b]	-	−0.82[b]	0.08[b]	0.20[b]	-	-	-	-	-

Increases in WAZ, WHZ, and HAZ are reported in difference in mean or median values from baseline to 6, 12, and 24 months. ART, antiretroviral therapy; HAZ, height-for-age; RLS, resource-limited setting; WAZ, weight-for-age; WHZ, weight-for-height.

[a] Mean.

[b] Median.

[c] Follow-up time varied slightly around 6, 12, and 24 months.

[d] Estimates based on mean monthly change from longitudinal models.

[e] <12 children at this time point.