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Original Article

Height gain after two-years-of-age is associated with better cognitive capacity, measured with Raven's coloured matrices at 15-years-of-age in Malawi

Tiina Teivaanmäki[1,2], Yin Bun Cheung[1,5], Anna Pulakka[§], Jussi Virkkala[7], Kenneth Maleta[6] and Per Ashorn[1,3]

[*]University of Tampere School of Medicine, Department for International Health, Tampere, Finland, [†]Helsinki University Hospital, Department of Paediatrics, Helsinki, Finland, [‡]Tampere University Hospital, Department of Paediatrics, Tampere, Finland, [§]University of Turku, Department of Public Health, Finland, [5]Duke-National University of Singapore Graduate Medical School, Centre for Quantitative Medicine, Singapore, Singapore, [6]School of Public Health and Family Medicine, College Of Medicine, University of Malawi, Malawi, and [7]Sleep Laboratory, Finnish Institute of Occupational Health, Finland

Abstract

Stunting is a measure of chronic undernutrition, and it affects approximately 160 million children worldwide. Cognitive development of stunted children is compromised, but evidence about the association between height gain in late childhood and adolescent cognitive capacity is scarce. We aimed to determine the association between height gains at different ages, including late childhood, and cognitive capacity at 15-years-of-age. We conducted a prospective cohort study in a rural African setting in Southern Malawi. The study cohort was enrolled between June 1995 and August 1996. It originally comprised mothers of 813 fetuses, and the number of children born live was 767. These children were followed up until the age of 15 years. The anthropometrics were measured at one and 24-months-of-age and 15-years-of-age, and cognitive capacity of participants was assessed at 15-years-of-age with Raven's Coloured Matrices score, mathematic test score, median reaction time (RT) (milliseconds) and RT lapses. The associations between growth and the outcome measures were assessed with linear regression. Raven's Coloured Matrices score was predicted by height gain between 24 months and 15-years-of-age (coefficient 0.85, $P = 0.03$) and (coefficient 0.69, $P = 0.06$), but not by earlier growth, when possible confounders were included in the model. The association weakened when school education was further added in the model (coefficient = 0.69, $P = 0{,}060$). In conclusion, in rural Malawi, better growth in late childhood is likely to lead to better cognitive capacity in adolescence, partly through more school education. In light of these results, growth promotion should not only be limited to early childhood.

Keywords: growth, stunting, undernutrition, adolescent, cognitive capacity, school education.

Correspondence: MD Tiina Teivaanmäki, University of Tampere School of Medicine, Arvo-building, FIN-33014 Tampere, Finland. E-mail: tiina.teivaanmaki@gmail.com

Introduction

Stunting is a measure of chronic undernutrition. The prevalence of stunting has decreased over the years worldwide. Recently, it was estimated that 160 million, i.e. 25% of all the children under five-years-of-age are stunted (UN 2015). The improvement has been slow in Sub-Saharan Africa, where the proportion of stunted children is 37% (UN 2015). Stunting is associated with increased mortality, morbidity and developmental problems including neurodevelopment in infancy and early childhood (Black *et al*. 2008; Chang *et al*. 2002; Grantham-McGregor *et al*. 2007; Walker *et al*. 2007; Perignon *et al*. 2014; Sudfeld *et al*. 2015). It also has intergenerational effects (Walker *et al*. 2015). The children of shorter mothers have lower birth weight, grow slower and have smaller head circumference and lighter brain weight (Victora *et al*. 2008; Black *et al*. 2008; Grantham-McGregor *et al*. 2007; Lecours *et al*. 2001).

A large number of cross-sectional studies have demonstrated an association between stunting and cognitive capacity (Grantham-McGregor *et al*. 2007; Berkman *et al*. 2002; Grantham-McGregor 2002). In a recent Cambodian study, school aged children who were stunted at the time of the assessment got lower scores in intelligence tests compared with those with better growth (Perignon *et al*. 2014). A strong association was found between concurrent stunting and cognitive skills in Peruvian children entering school (Crookston *et al*. 2011). In addition to the cross-sectional studies, some longitudinal studies, that assess the association between early childhood growth and later cognitive development, have been conducted. These studies have shown a relationship between faster growth in early childhood and better cognitive capacity later in life (Crookston *et al*. 2011; Grantham-McGregor *et al*. 2007; Walker *et al*. 2007; Crookston *et al*. 2013; Gandhi *et al*. 2011; Fink & Rockers 2014). However, except a recent multicentre study (Fink & Rockers 2014), they have mainly focused on the impact of early childhood growth. In contrast to earlier suggestions (Victora *et al*. 2010) it has recently been proposed that stunted children may also demonstrate catch-up growth after the first 1000 days of life, i.e. 24-months-of-age (Teivaanmäki *et al*. 2015; Crookston *et al*. 2013). This gives a rationale to explore whether there is an association between height gain in late childhood and later cognitive development of children, and whether the circumstances leading to better growth also enhance the cognitive development.

School education may buffer the risks for poor development and is associated with better cognitive function in stunted high-risk populations (Gorman & Pollitt 1996; Sudfeld *et al*. 2015; McCoy 2015). In low-income settings, children who grow better are more likely to be healthier and get more school education (Grantham-McGregor *et al*. 2007). Hence, it is possible that the association between better growth and better cognitive capacity is mediated by schooling.

Our primary study question was whether the growth between birth and 24-months-of-age and between 24 months and 15-years-of-age (180 months) were associated with cognitive development in adolescence. Because cognitive development may be affected by several exposures, our secondary aim was to find out if any observed association was mediated through other exposures, such as education. We hypothesized that better growth during any of the age periods assessed would be associated with better cognitive capacity at 15-years-of-age.

Participants and methods

Study design

This prospective cohort study was conducted in Lungwena, Mangochi District, Southern Malawi. The study area covered approximately 100 km^2, and included 26 villages and 23 000 inhabitants in about 5200 households. Most of the inhabitants were Muslims of the Yao tribe, and the family organization was matrilineal. The literacy rate was low, and the main sources of income were farming and fishing. The study cohort was enrolled between June 1995 and August 1996. It originally comprised 795 mothers who attended antenatal clinic at Lungwena health centre during their pregnancies (Maleta *et al*. 2003). These pregnant

Key messages

- The impact of the timing of stunting and catch-up growth on cognitive capacity later in life is not clear. Recent evidence on possible catch-up growth until adolescence emphasizes the need to explore the association between height gain at different age periods and cognitive development.
- In a resource poor area in rural Malawi, height gain between 24 months and 15 years was associated with better cognitive capacity at 15-years-of-age. This association was partially mediated through school attendance.
- Besides the child's height gain and education, better cognitive performance in adolescence was predicted by male gender and maternal educational attainment.

women carried altogether 813 fetuses, and the number of children born live was 767 (Supplemental Fig. 1). These children were followed up until the age of 15 years.

Ethical approval for the Lungwena Child Survival Study (LCSS) was obtained from the National Health Science Research Committee in Malawi (HSRC 93/94) and the College of Medicine Research and Ethics Committee. Informed consent was obtained from each guardian in the beginning of the cohort study and again from each guardian and adolescent before the visit at 15-years-of-age.

Data collection

We studied the association of height gain between birth and 24 months, and between 24 months and 15 years, respectively, with cognitive capacity at 15-years-of-age with three different regression models. The first anthropometric measurements were taken at one-month-of-age, and these measurements were used as a proxy for weight and height at birth. Subsequent measurements were taken at 24 months and 15-years-of-age. At one-month-of-age, the data collectors measured the participants' length at their homes with locally constructed length boards with reading increments of 5 mm. The data collectors were thoroughly and repeatedly trained and retrained by the investigators with intervals of one to 36 months. In addition, their work was regularly monitored. The measurements at 24 months-of-age were taken at participants' homes with a self-made height board with reading increments of 5 mm. The measurements at 15-years-of-age were done at the study clinic with a stadiometre (Harpenden, Holtain Limited, UK) with reading increments of 1 mm.

The techniques for the measurements have been described in detail earlier by Maleta *et al.* (2003). The study team calibrated all length and height boards and stadiometres weekly.

We used WHO Multi-centre Growth Reference Study (WHO Multicentre Growth Reference Study Group 2006) for children at one and 24-months-of-age and WHO Reference 2007 (De Onis *et al.* 2007) at 15-years-of-age to derive length-/height-for-age *z*-scores (LAZ/HAZ). Reference values for length were used for the measurements at one and height for ≥24-months-of-age. By using the two closely aligned WHO references we were able to cover the whole range of growth in length/height in the cohort. We generated the *z*-scores for anthropometric measurements using a Stata macro (Vidmar *et al.* 2013).

We used Raven's Coloured Matrices to assess cognitive performance at 15-years-of-age (Raven *et al.* 1998). We conducted a pilot study in the same setting and age group with Raven's Standard Progressive Matrices (Raven *et al.* 2000), and received poor results with very little variability. Hence, we used Raven's Coloured Matrices, which is originally designed and standardized for children younger than 15-years-of-age (Raven *et al.* 1998). Raven Coloured Matrices has been found to correlate with the performance component of the Wechsler Intelligence Scale for Children (WISC-III) (The Psychological Corporation 1997).

This assessment had 36 patterns each with a piece missing, and the best possible score was 36. The participants chose the piece that they considered correct to complete the pattern from six alternatives.

The mathematics test had eight questions, each with four answer alternatives. It was developed from a reference test designed for children aged 7–14 years used in the Indonesian Family Life Survey (Strauss *et al.* 2004; Gandhi *et al.* 2011). The test has previously associated with preceding development (Gandhi *et al.* 2013) and changes in HAZ (Gandhi *et al.* 2011), which is an established predictor of cognitive ability in children in low-income countries (Grantham-McGregor *et al.* 2007).

We used computer based Psychomotor Vigilance Task (PVT) (Dinges & Powell 1985) to assess reaction time (RT), which has correlated with intelligence (Wenger & Townsend 2000; Vernon 1983). RT test measures the time between a stimulus and participant's reaction during a 5-min test period with random interstimulus interval of 2 to 10 s. A number appears on a black display, and the participant indicates his or her reaction by pressing the enter key with a forefinger of the dominant hand. We evaluated two PVT performance metrics in our study, the median RT (milliseconds) and the number of lapses (RTs ≥ 500 ms) in a 5-min trial. Before the test each participant performed a test trial to familiarize himself or herself with the procedure.

Statistical analyses

We formulated three regression models to assess the associations between growth between birth and 24 months, and between 24 months and 15 years, and cognitive capacity at 15-years-of-age. Model 1 simultaneously included HAZ at one (HAZ_1) and 24 months (HAZ_24) and 15-years-of-age (HAZ_180) as independent variables without any adjustments. Model 2 was adjusted for gender, gestational duration (weeks), father's occupation, father's literacy, mother's literacy and a wealth index (Filmer & Pritchett 2001). Wealth index was assessed perinatally by interviewing the mothers. It summarized household ownership of radio, bicycle / tricycles, mattress, number of family supporters, ownership of land per person and number of cattle (cow, goats, sheep and chickens). It was derived from factor analysis, and categorized into three levels: poor (below 40 percentile), middle (40–80 percentiles) and rich (top 20 percentile). The gestational duration was estimated by using the nationally used chart for fundal height during the antenatal visits, because ultrasound was not available and the information about the timing of menstrual periods was not reliable (Kulmala *et al*. 2000). Model 3 was further adjusted for the number of years of schooling reported at the age of 15 years. In all three models, the associations between HAZ scores and Raven's Coloured Matrices score, mathematics score, median RT (ms) and RT lapses were assessed with multiple linear regression. Both theoretical and simulation studies showed that the least squares regression is robust in analysis of non-normal data even when the sample size is smaller than the present study's (Cheung 2014; Sullivan & Sr D'Agostino 2003). To further evaluate the robustness of the chosen statistical method, we ran sensitivity analysis with ordered logistic regression.

We included all the cohort members with no missing values in exposure variables, outcome variables at 15-years-of-age and confounders in the analyses. Possible selection bias caused by missing values, loss to follow-up and death data was assessed by comparing the background characteristics and anthropometric measurements of the included and excluded participant with Chi-square test and *t*-test. Previous scholars have discussed that sample size (or power) calculation after completion of statistical analysis is inappropriate (Feinstein & Concato 1998). Instead, they have suggested focusing on confidence interval. As such, for all regression coefficients we included confidence intervals to demonstrate the precision level of the estimates.

We also ran the analyses with HAZ_1 and 'unexplained residual' HAZ at 24 months (rHAZ_24) and 15-years-of-age (rHAZ_180) (Cheung 2014). These residual height values represent the child's deviation from his or her expected HAZ independent of his/her earlier HAZ. The three aforementioned models were also fitted for unexplained residuals of HAZ. In all of the analyses, regression coefficients with *P*-value smaller than 0.05 were considered statistically significant. We performed all the analyses with Stata 12.1 (Stata Corporation, College Station, TX, USA).

Results

Of the 767 live-born infants, 179 (23%) died and 50 (7%) dropped out during the follow-up. Of the 538 who remained in the study at the age of 15 years, 180 had missing values in one or more of the exposure or outcome variables. Thus, 358 formed the final study groups and were included in the analysis (Supplemental Fig. 1).

Among these 358 participants, the mean (SD) duration of pregnancy was 39 (3) weeks, and the newborn weight was and 3140 (525) grams. Twenty per cent of the infants were born preterm (<37 completed gestation weeks) and 9% presented with low newborn weight (<2500 g). The participants who survived but were excluded because of missing data had rather similar socio-demographic baseline characteristics to those included (Table 1). Twenty-seven per cent of the participants had not completed any years at school by the age of 15 years, and 87% of the mothers of the participants were illiterate.

Raven's Coloured Matrices

The mean (SD) HAZ of the included children was −1.61 (1.24) at one-month-of-age, −2.92 (1.23) at 24-months-of-age and −1.59 (0.96) at 15-years-of-age. The mean (SD, range) values for the outcome variables were 15 (6, 0–33) points for Raven's Coloured Matrices, 4 (2, 0–8) points for mathematics test, 408 (165, 229–2332) ms for median RT and 9 (8, 0–40) lapses in RT assessment.

When HAZ at the age of one month, 24 months and 15 years were included in the analysis (Model 1), none of them was statistically significantly associated with the Raven's Coloured Matrices score (Table 2). In Model 2, adjusted for the confounders, Raven's Coloured Matrices Score was predicted by HAZ at 15-years-of-age (coefficient = 0.85, $P = 0.03$), gender and mother's literacy, but not by HAZ at one or 24-months-of-age. In Model 3, further adjusted for the completed years of school education, schooling predicted Raven's Coloured Matrices score, but the association with HAZ at 15 years was weakened (coefficient = 0.69, $P = 0.06$) (Table 2). Raven's Coloured Matrices score was three points lower in females than males ($P < 0.001$) (Table 2). It was two points higher if the mother of the participant was literate ($P = 0.02$) and one point higher with each additional year that the participant had completed at school ($P < 0.001$) (Table 2).

Table 1. Participant characteristics

Variables	Complete data ($n = 358$)	Excluded[a] ($n = 238$)	P-value
Gender, male % (n)	51 (182)	46 (107)	0.22
Mean newborn weight[b], g (SD)	3140 (525)	3020 (470)	0.03
Low newborn weight[b] %, (n)	7.8 (20)	10.7 (14)	0.35
Mean gestational age, weeks (SD)	39.2 (3.3)	39.1 (3.2)	0.65
Preterm births (<37 gestational weeks), % (n)	19.8 (71)	18.3 (41)	0.65
Wealth index, % (n)			
Poor	37.2 (133)	39.0 (85)	
Middle	38.6 (138)	39.0 (85)	0.81
Rich	24.3 (87)	22.0 (84)	
Father's occupation, % (n)			
Fisherman	40.5 (145)	35.5 (81)	
Other	23.5 (84)	19.7 (45)	0.16
Trader	19.0 (68)	21.1 (48)	
Farmer	17.0 (61)	23.7 (54)	
Father's literacy, literate, % (n)	43.3 (155)	41.7 (95)	0.70
Mother's literacy, literate, % (n)	12.9 (46)	17.1 (39)	0.15

[a] Excluded because of loss to follow-up or missing values. The final numbers of participants in the comparison vary between 386 and 596.

[b] Measured at ≤ 7 days of age.

Mathematics score

In Model 1 without any adjustments, there were no significant associations between HAZ at any age and mathematics scores. In Model 2, adjusted for the most important confounders, there were statistically significant associations between the mathematics score, wealth index and mother's literacy (Table 3). In Model 3, further adjusted for the number of years of school education, the mathematics score was statistically significantly associated only with the number of years of school education (Table 3). The mathematics score was 0.2 points better with each additional year completed at school ($P < 0.001$).

Reaction time

HAZ and RT median did not reach statistical significance in Model 1 or in Model 2 (Table 4). In Model 3, further adjusted for number of years of school education, schooling was statistically significantly associated with RT median (Table 4). Each additional year completed at school was associated with a 12 milliseconds shorter median RT ($P = 0.01$).

In the non-adjusted Model 1 there were no statistically significant associations between HAZ at any age and RT at 15-years-of-age (Table 5). In the adjusted Model 2, there was a statistically significant association between gender and RT lapses (Table 5). In Model 3, further adjusted for the numbers of completed years of school education, male gender and the school education were statistically significantly associated with

Table 2. The association between growth and Ravens Coloured Matrices score at 15-years-of-age (180 months)

Regressor	Raven's coloured matrices					
	Model 1[a]		Model 2 [b]		Model 3[c]	
	Coef. [95% CI]	*P*-value	Coef. [95% CI]	*P*-value	Coef. [95% CI]	*P*-value
HAZ_1[d]	0.01 [−0.54,0.56]	0.96	−0.01 [−0.55,0.53]	0.97	−0.02 [−0.53,0.49]	0.95
HAZ_24[d]	0.03 [−0.56,0.62]	0.93	−0.12 [−0.68,0.44]	0.67	−0.02 [−0.56,0.51]	0.93
HAZ_180[d]	0.37 [−0.37,1.10]	0.33	0.85 [0.09,1.61]	0.03	0.69 [−0.03,1.41]	0.06
Female sex			−2.69 [−3.94,−1.43]	<0.001	−2.62 [−3.81,−1.43]	<0.001
Gestational duration, weeks			−0.03 [−0.22,0.15]	0.07	−0.07 [−0.24,0.10]	0.43
Wealth index			0.67 [−0.12,1.47]	0.25	0.24 [−0.52,1.01]	0.53
Father's occupation			−0.43 [−0.99,0.12]	0.13	−0.36 [−0.88,0.17]	0.18
Father's literacy			0.08 [−1.21,1.22]	0.99	−0.31 [−1.46,0.85]	0.60
Mother's literacy			3.43 [1.64,5.21]	<0.001	2.11 [0.37,3.85]	0.02
School education, years					0.89 [0.62,1.17]	<0.001

[a] Model 1 included three HAZ measures as independent variables, adjusted for each other.
[b] Model 2 further adjusted for gender, gestational duration, wealth index, father's occupation, father's literacy and mother's literacy.
[c] Model 3 further adjusted for completed years of school education.
[d] HAZ=height-for-age *z*-score at one and 24-months-of-age and 15-years-of-age (180 months).

less RT lapses (Table 5). Every additional year completed at school was associated with one less lapse ($P = 0.01$).

In sensitivity analyses ran with ordered logistic regression, growth between 24-months and 15-years-of-age was statistically significantly associated with Raven's score (coefficient 0.28, $P = 0.024$). Also female sex (coefficient 0.90, $P < 0.001$) and mother's literacy (coefficient 1.10, $P = 0.002$) were statistically significantly associated with Raven's score as they were in the analysis by least square regression. Similar to the results from least square regression model, there was no association between growth and mathematics score (each $P > 0.38$) nor growth and the number of lapses in RT test (each $P > 0.34$). Mother's literacy was statistically significantly associated with mathematics score

Table 3. The association between growth and mathematics score at 15-years-of-age (180 months)

Regressor	Mathematics					
	Model 1[a]		Model 2[b]		Model 3[c]	
	Coef. [95% CI]	*P*-value	Coef. [95% CI]	*P*-value	Coef. [95% CI]	*P*-value
HAZ_1[d]	0.01 [−0.18,0.19]	0.95	0.02 [−0.17,0.21]	0.86	0.02 [−0.17,0.20]	0.87
HAZ_24[d]	−0.03 [−0.23,0.17]	0.78	−0.03 [−0.23,0.17]	0.78	−0.001 [−0.19,0.19]	0.99
HAZ_180[d]	0.23 [−0.16,0.48]	0.07	0.21 [−0.06,0.47]	0.13	0.16 [−0.10,0.42]	0.22
Female sex			−0.02 [−0.47,0.42]	0.92	−0.005 [−0.43,0.42]	0.98
Gestational duration, weeks			−0.03 [−0.09,0.04]	0.38	−0.04 [−010,0.02]	0.23
Wealth index			0.30 [0.02,0.58]	0.04	0.18 [−0.10,0.45]	0.20
Father's occupation			−0.06 [−0.25,0.14]	0.56	−0.04 [−0.23,0.15]	0.70
Father's literacy			−0.23 [−0.66,0.20]	0.30	−0.31 [−0.73,0.10]	0.14
Mother's literacy			0.68 [0.05,1.31]	0.03	0.32 [−0.31,0.95]	0.32
School education, years					0.24 [0.14,0.34]	<0.001

[a] Model 1 included three HAZ measures as independent variables, adjusted for each other.
[b] Model 2 further adjusted for gender, gestational duration, wealth index, father's occupation, father's literacy and mother's literacy.
[c] Model 3 further adjusted for completed years of school education.
[d] HAZ = height-for-age *z*-score at one and 24-months-of-age and 15-years-of-age (180 months).

Table 4. The association between growth and RT median at 15-years-of-age (180 months)

Regressor	RT median					
	Model 1[a]		Model 2[b]		Model 3[c]	
	Coef. [95% CI]	*P*-value	Coef. [95% CI]	*P*-value	Coef. [95% CI]	*P*-value
HAZ_1[d]	−9.07 [−24.66,6.52]	0.25	−5.77 [−21.81,10.26]	0.48	−5.73 [−21.62,10.17]	0.48
HAZ_24[d]	1.21 [−15.37,17.78]	0.89	4.17 [−12.56,20.89]	0.62	2.87 [−13.74,19.47]	0.73
HAZ_180[d]	0.24 [−20.59,21.08]	0.98	−3.77 [−26.28,18.75]	0.74	−1.63 [−24.00,20.74]	0.89
Female sex			26.63 [−10.73,63.99]	0.16	25.71 [−11.33,62.74]	0.17
Gestational duration, weeks			−3.56 [−9.02,1.90]	0.20	−3.07 [−8.49,2.34]	0.27
Wealth index			−14.14 [−37.76.02,9.48]	0.24	−8.51 [−32.27,15.25]	0.48
Father's occupation			−9.39 [−25.86,7.08]	0.26	−10.39 [−26.73,5.95]	0.21
Father's literacy			−9.90 [−46.08,26.28]	0.59	−5.76 [−41.74, 30.22]	0.75
Mother's literacy			−19.76 [−73.01,33.48]	0.47	−2.42 [−56.67,51.83]	0.93
School education, years					−11.74 [−20.26,−3.21]	0.007

[a] Model 1 included three HAZ measures as independent variables, adjusted for each other.
[b] Model 2 further adjusted for gender, gestational duration, wealth index, father's occupation, father's literacy and mother's literacy.
[c] Model 3 further adjusted for completed years of school education.
[d] HAZ = height-for-age *z*-score at one and 24-months-of-age and 15-years-of-age (180 months).

(coefficient 0.76, $P = 0.002$), and female participants scored statistically significantly more lapses than male participants (coefficient 0.85, $P < 0.001$), as was in the case of least square regression.

In supplementary analyses, we applied an alternative set of regression models that were otherwise identical to the models in Tables 2 to 5 but used conditional growth measures (unexplained residuals) at 24 months and 15 years instead of HAZ at 24 months and 15 years as the exposure variables. Similar findings were obtained that (1) HAZ at one month and conditional growth at 24 months did not show statistically significant association with any of the four outcomes with or without adjustment for the potential confounders in Model 2 of Tables 2 to 5 (each $P > 0.29$); (2) conditional growth at 15 years was associated with Raven's

Table 5. The association between growth and RT lapses at 15-years-of-age (180 months)

Regressor	RT lapses					
	Model 1[a]		Model 2[b]		Model 3[c]	
	Coef. [95% CI]	*P*-value	Coef. [95% CI]	*P*-value	Coef. [95% CI]	*P*-value
HAZ_1[d]	−0.55 [−1.31,0.21]	0.15	−0.56 [−1.33,0.21]	0.15	−0.56 [−1.32,0.21]	0.15
HAZ_24[d]	0.21 [−0.59,1.02]	0.60	0.35 [−0.45,1.15]	0.39	0.29 [−0.51,1.09]	0.48
HAZ_180[d]	0.62 [−0.39,1.63]	0.23	0.14 [−0.94,1.22]	0.80	0.24 [−0.84,1.32]	0.66
Female sex			2.72 [0.92,4.51]	0.003	2.68 [0.90,4.46]	0.003
Gestational duration, weeks			0.06 [−0.20,0.32]	0.65	0.08 [−0.18,0.34]	0.53
Wealth index			−0.04 [−1.18,1.09]	0.94	0.22 [−0.92,1.36]	0.71
Father's occupation			0.06 [−0.73,0.85]	0.89	0.01 [−0.77,0.80]	0.98
Father's literacy			−1.45 [−3.20,0.28]	0.10	−1.27[−3.00, 0.47]	0.15
Mother's literacy			−1.01 [−3.57,1.54]	0.44	−0.21 [−2.82,2.40]	0.88
School education, years					−0.55 [−0.96,−0.14]	0.009

[a] Model 1 included three HAZ measures as independent variables, adjusted for each other.
[b] Model 2 further adjusted for gender, gestational duration, wealth index, father's occupation, father's literacy and mother's literacy.
[c] Model 3 further adjusted for completed years of school education.
[d] HAZ = height-for-age *z*-score at one and 24-months-of-age and 15-years-of-age (180 months).

Coloured Matrices score (coefficient = 0.79, $P = 0.029$) after adjustment for confounders but not schooling; and (3) the regression coefficient for conditional growth at 15 years weakened and the P-values became larger (coefficient = 0.65, $P = 0.07$) after further adjustment for schooling.

Discussion

The primary aim of our study was to assess the association between HAZ at one-month-of-age and height gain during two subsequent age periods and cognitive development at 15-years-of-age. In addition, we investigated whether there are some exposures that would confound or mediate these associations. In the cohort of 358 children we found a significant association between HAZ at 15-years-of-age and Raven's Coloured Matrices score, but not with mathematics score or RT median or lapses. Because the model was adjusted for HAZ at 24 months, the coefficient for HAZ at 15 years represents the association between height gain between 24 months to 15 years and the cognitive outcomes (Cheung 2014). Thus, the finding indicated that height gain after the age of 24 months had an association with the score. Male sex, mother's literacy, higher wealth index and more years of school education were associated with better success in Raven's Coloured Matrices score, mathematics test and RT median and lapses at 15-years-of-age. The results were similar in the models which included HAZ scores and conditional growth measures. These similar findings indicate that the results were not affected by collinearity of the exposure variables. In addition, the correlation coefficients between exposure variables HAZ_1, HAZ_24 and HAZ_180 were <0.46, showing only moderate correlation between them.

The key finding of the present study is that height gain between age 24 months and 15 years predicted scores on the Raven's Coloured Matrices. A secondary finding, based on comparison of regression coefficients without and with adjustment for schooling, is that this association appeared to be partly mediated by schooling. Theoretically, this might indicate a causal pathway, linking good growth to good cognitive development through increased exposure to education. However, given the observational nature of our study, we cannot rule out a possibility of reverse causality, i.e. cognition either co-existing with or influencing later schooling, as documented earlier by Grantham-McGregor at her collaborators (Grantham-McGregor *et al.* 2007). If that were the case, the regression model with adjustment for schooling might be an over-adjustment. Nevertheless, this uncertainty about the causality interpretation does not affect the key finding that height gain predicted the adolescents' Raven's scores even after adjustment for perinatal factors. There is no way to formally establish a causal effect of schooling on cognition in observational studies. There has been recent discussion that the effect of schooling may be influenced not just by years of schooling but also by quality of schooling (Frost & Little 2014). All of the outcome measures used in this study were independently associated with number of years of school education. This may suggest reasonable quality of schooling in rural Malawi, although that was not particularly investigated in this study. Education itself may lead to better cognitive function (Gorman & Pollitt 1996), but the children with experience from school may also be more familiar with the school-work-kind of tasks, and therefore perform better. Altogether, our findings support the view that growth improvement after the first 1000 days of life may also contribute to better development of cognitive capacity (Crookston *et al.* 2010; Fink & Rockers 2014; Cheung & Ashorn 2010). In contrast to some previous studies (Victora *et al.* 2008; Sudfeld *et al.* 2015), we did not find any significant associations between growth before 24 months and cognitive capacity later in life.

The reliability and criterion validity of Raven's Matrices have been found to be good in Africa (Wicherts *et al.* 2010; Costenbader & Ngari 2001). Our finding that Raven's score and the other three outcome measures were associated with schooling also supported their criterion validity. However, there is a concern that, in Africa, it may not measure 'general intelligence', or 'g', as intended (Wicherts *et al.* 2010). More detailed psychometric assessment and analysis will be needed to clarify its properties. Previous research has shown that education of the mother, but not that of the father, is correlated with child development (Kong *et al.* 2015). Our analysis has also demonstrated this pattern for Raven's and the mathematics tests, indicating their convergent and divergent validity. While the validity and reliability of Raven's Coloured Matrices (Raven *et al.* 1998) are relatively well documented compared with the mathematics test (Gandhi *et al.* 2011; Strauss *et al.* 2004) and the RT test (Roach *et al.* 2006; Dinges & Powell 1985; Loh *et al.* 2004), we cannot exclude the possibility that the absence of association between the other measures and child growth was because of insufficient level of measurement properties. Further studies that employed more detailed and locally validated measures are needed.

Female gender and mother's illiteracy were associated with lower score in Raven's Coloured Matrices score, and female gender also with more RT lapses in the model with school education included. This suggests independent associations between gender and cognitive capacity, which are not mediated by schooling. There is previous evidence about gender differences and importance of mother's literacy for cognitive skills in low-income populations (Green *et al.* 2009; Casey *et al.* 2011; Abubakar *et al.* 2010), and these associations were further solidified in our study in a rural African setting. The association between wealth index and mother's literacy and the mathematics score were diluted when number of years of schooling was added in the model. This suggests that higher socioeconomic status leads to better education and better skills in mathematics.

The study cohort comprised 97% of all the newborn infants in the study area during the time of enrolment, and our sample represented the target population well. Approximately one quarter of the original cohort died and one quarter had missing values in some of the variables. Only 7% dropped out. Hence, altogether approximately half of the original cohort members were excluded from the study. Participant characteristics were, however, similar in the included and the excluded groups except that the excluded participants were born smaller. The average birth weight was within a normal range in both groups, and there was no significant difference in the proportion of children with low birth weight. Furthermore, the regression analysis results are unlikely to be biassed materially by sample selection because the estimates were conditional on HAZ at one month, which correlated strongly with newborn weight. According to a statistical theory, factors that are conditioned on cannot cause a bias in regression findings (Cheung 2014; Fairclough 2010).

We used globally applicable WHO Multi-centre Growth References (WHO Multicentre Growth Reference Study Group 2006 (312 pages), De Onis *et al.* 2007). The height measurements were taken by trained data collectors with a proper, regularly calibrated equipment, at each age. Earlier research has shown that (1) while some anthropometric measures such as skinfold thickness may have low level of reliability, length and height measures tend to have reliability levels well above 0.9, and (2) while technical measurement errors may change over age, reliability tends to be stable (Ulijaszek and Kerr 1999). Measurement errors lead to under-estimation of regression coefficients by a factor of (1 – reliability) (Montgomery et al. 2001). As such, we would expect that our findings were neither materially nor differentially affected by measurement errors of HAZ at different ages, even though formal reliability tests were not conducted. In contrast, in the absence of detailed information on measurement error, we cannot positively exclude the possibility that our conclusion on the absence of association between growth and other outcome measures was biassed. Further research is therefore needed to confirm this aspect of the findings. However, because the impact of imperfect reliability is under-estimation, not over-estimation, of association, the key finding that change in HAZ from 24 months to 15 years was positively associated with Raven's scores is unaffected.

Instead of writing, the participants were instructed to point out the correct answer with their finger in Raven's Coloured Matrices test. This may have caused some problems in validity of the test. However, the data collectors were thoroughly trained to perform all the assessments, and the quality of the measurements was regularly monitored. The weaknesses in our study, aforementioned answering technique, the possible problems in validity of Raven's Coloured Matrices in uneducated populations and rather large exclusion rate, are not likely to cause bias in the results. Hence, we believe that the results of this study may be generalized to the target population of rural East African adolescents.

In conclusion, our results support a hypothesis that in rural Malawi height gain between 24 months and 15 years is associated with better cognitive capacity at 15-years-of-age regardless of the child's previous growth. Some of this effect may be mediated through school education. Mother's illiteracy, female gender and less school education were risk factors for worse performance. This emphasizes the importance of the education of girls. In light of these results, it may be further suggested, that in low income settings growth promotion should not be limited to the first 1000 days of life.

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Conflict of interest

The authors declare that they have no conflicts of interest.

Contributions

The authors' responsibilities were as follows. PA and KM formed the original cohort and conducted the early data collection. TT, YBC and PA were responsible for the current research design and TT, AP and JV conducted the study. TT and YBC performed and are responsible for the data analysis. TT wrote the first draft of the manuscript; YBC, AP, JV, KM and PA were involved in data interpretation and writing the final version of the manuscript. All authors read and approved the final manuscript. TT had primary responsibility for the final content.

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