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Modeling Growth Trajectories in Stunted Children Under 5 Years of Age: A Retrospective Analysis of Clinical Data from Guatemala

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Abstract

Background: Stunting is a pervasive issue in low- and middle-income countries, particularly affecting rural and Indigenous populations. Little reported data is available on the growth of clinical populations of children with stunting, including those with more severe stunting.

Objective: This study examines growth trajectories of children under 5 years of age from a long-standing clinical care program to address childhood stunting that provides monthly at-home growth monitoring, family food rations, nutrition counseling, micronutrient supplementation, and childhood illness management.

Hypothesis: We hypothesized that children with stunting are a clinically heterogeneous group, where some experience ongoing growth failure and others catch-up growth.

Methods: We utilized data from 2827 children and 38 864 height measurements. We applied superimposition by translation and rotation modeling to characterize growth patterns.

Results: Median age at first measurement was 9 months (IQR: 3, 16) and median length of growth monitoring was 17 months (IQR: 8, 30). Median height-for-age Z-score at first measurement was −2.51 (IQR: −3.23, −1.68). There was variability in growth dynamics, with some children showing potential catch-up growth, particularly those with the lowest initial height-for-age metrics. In regression analysis, factors significantly associated with growth improvement over time included greater initial severity of stunting, male sex, and geographical region.

Conclusions: These findings underscore the heterogeneity of growth responses among stunted children and the need for individualized intervention strategies. They emphasize the necessity for ongoing investigations of both tailored clinical interventions and novel factors associated with growth variability and catch-up growth.

Plain Language Title

Understanding growth patterns of stunted children under 5 years of age in Guatemala: a chart review

Plain Language Summary

Why did we do the study? Stunting is a widespread issue in less developed countries, especially in rural areas and among Indigenous people. Stunting, a condition in which individuals fail to reach their genetic height potential, is a marker of chronic malnutrition and is associated with hindered childhood development and immune system development and with chronic disease

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development later in life. Little reported data is available on the growth of clinical populations of children with stunting, including those with more severe stunting.
What did we do? We examined the growth patterns of children under 5 years of age who participated in a nutrition program for stunting in rural Guatemala that provides monthly at-home growth monitoring, family food rations, nutrition counseling, vitamin and mineral supplementation, and childhood illness management.
What did we expect to find? We thought that some of the children would show improvement in their height over time, while others would fail to make progress.
How did we do the study? We used data from 2827 children that included multiple height measurements for each child. We used mathematical models to predict heights at different ages for individual children and for groups of children over time.
What did we find? Most children were moderately stunted at first measurement. Different children showed different growth patterns. Some children improved, especially those who were the most behind to begin with. Also, males and children from certain regions of Guatemala improved more than other groups.
What do the findings mean? These findings show that there is significant variability in response to treatment among children with stunting and that individualized treatment strategies are needed. They emphasize the importance of ongoing research into nutrition initiatives that are appropriately adapted to local needs and of research into emerging areas of study related to growth variability.

Keywords
stunting, chronic malnutrition, growth modeling, catch-up growth, Guatemala, clinical nutrition, low- and middle-income country

Introduction

Stunting, or reduced height-for-age, is the most common pediatric growth disorder worldwide.[1,2] It is a significant target of the Sustainable Development Goals and of many national nutritional programs in low- and middle-income countries.[3] As a public health target, stunting is justified because it is a critical marker of a child's nutritional status and the environment in which the child lives. While primarily driven by inadequate nutrition, it is also shaped by sanitation, access to care, chronic illness and caregiver capacity.[1] As a key indicator of social determinants of health, stunting is associated with long-term decreases in intellectual function, educational attainment and economic output, as well as increased risk for noncommunicable chronic diseases such as obesity and hypertension.[4] Given these associations, when clinicians encounter stunted children, a targeted, multi-disciplinary approach to medical management must be pursued.

While most literature on stunting has focused on the effectiveness of public health and nutrition measures to prevent growth faltering in infants and toddlers, the impact of such interventions is small to moderate.[5] Furthermore, understanding of stunting has been greatly impacted by recent research in immunology, gut enteropathy and consideration of environmental toxins and interventions to address these factors. Stunting is a heterogenous disease with multiple presentations and etiologies that must be addressed using a combination of tailored therapies and programs.[6–8] Guatemala has one of the highest burdens of stunting in the world, where often more than 70% of the rural Indigenous population under 5 years of age are severely stunted with height-for-age Z-scores in the range of −6 to −3.[9,10]

Children with stunting often present to community-based feeding programs and other clinical care settings.[11–13] There are few evidence-based clinical guidelines to support the care of these children. This is partly because, with few exceptions, clinical trials of complementary feeding interventions focused on addressing stunting have either excluded children with more severe stunting, enrolled only young infants before the onset of marked growth faltering, or been conducted in settings with a relatively low burden and severity of stunting.[13–18] Children with more pronounced stunting may also be unintentionally excluded from population-based survey efforts, such as the Demographic Health Surveys, because of difficulties in representatively sampling the most remote or resource-poor settings.[19]

Moreover, the literature on stunting often excludes clinical populations with more severe stunting, so there is limited knowledge about growth dynamics and catch-up growth potential across the full clinical spectrum and in subgroups of stunted children.[20] Recently, a compelling analysis from the Institute for Health Metrics and Evaluation showed how dichotomous country-level measures of stunting obscure the picture for children with severe growth failure. While national averages of stunting appeared unchanged, significant gains were made among children with the most severe forms of stunting in countries like Ethiopia and India.[6] This evidence supports the argument that targeted interventions for the most vulnerable children—those with the most initial severity of stunting—can yield substantial improvements in health.

It is also notable to address the ongoing debate on the overall degree to which stunted children exhibit catch-up growth.[20–23] At play are limits on individual biological flexibility imposed by the epigenetic, intergenerational nature of stunting and the interplay with gut inflammation and ongoing environmental exposures. Additionally, "pre-post" interventional designs do not adequately capture the dynamic nature of linear growth faltering in early life, and there is additional uncertainty on whether catch-up growth might be more pronounced for certain baseline nutritional characteristics or within critical

age windows.[12,24,25] Finally, the use of serial height-for-age Z-scores may artificially obscure the ongoing accrual of absolute height deficit. This latter issue is a technical matter related to how Z-scores are calculated as the difference between measured and reference population height/length divided by the population standard deviation. Since the WHO Growth Reference Population standard deviation increases with age, an improvement in Z-score does not necessarily translate to a reversal in height deficit.[26]

Taken together, all these considerations highlight the need for more comprehensive longitudinal data to shed light on the growth characteristics of severely stunted children. In this study we take advantage of a clinical dataset from a large primary care organization in Guatemala with a long-standing support program for children with severe stunting. First, we model and characterize growth trajectories using superimposition by translation and rotation (SITAR). SITAR modeling, by adjusting individual growth curves to the average, facilitates the identification of patterns and thus the interpretation of "real-world" clinical data. Secondly, we identify characteristics of children with improved growth trajectories over time from first to last height measurement. We hypothesized that children with severe stunting are a clinically heterogenous group, where some experience ongoing growth failure and others catch-up growth.

Methods

Background and Context

This work was conducted in collaboration with Wuqu' Kawoq | Maya Health Alliance, a primary care organization based in central Guatemala, providing healthcare primarily in rural Indigenous Maya communities. Maya Health Alliance has a long-standing clinical care program for children under 5 years of age with stunting, which has been described in detail previously.[13,27,28] Core elements of programming include monthly at-home monitoring, family food rations, nutrition counseling, micronutrient supplementation, and management of childhood illness (Tables S2 and S3 of Supplementary Appendix). Children with stunting are referred to this program by community leaders or other public health facilities or clinics, often not until growth faltering is significant and has not responded to first-line community-based interventions.[13]

Ethics

This study was approved by the Maya Health Alliance Institutional Ethics Committee (WK 2020 005), with a waiver of informed consent granted for extraction of electronic health records data.

Data Extraction

Maya Health Alliance's nutritional program data is housed in an open-source electronic health record (OpenMRS 1.9.9, www.openmrs.org). The built-in data extraction function of OpenMRS was used to retrieve relevant clinical data. The search strategy is given in Figure S1 (Supplementary Appendix). Data extraction occurred on March 1, 2023. All pediatric clinical records from the beginning of Maya Health Alliance's implementation of OpenMRS in March 2011 were included in the search. The goal was to extract all growth data from all clinical encounters collected from 0–5 years of age. Exclusion criteria included: (1) children with no growth data prior to 5 years of age; and (2) children enrolled in Maya Health Alliance's complex care program for individuals with severe non-nutritional illness (complex congenital malformations, inborn errors of metabolism, cyanotic heart disease, etc). A total of 7574 records were identified, of which 6415 were retained for growth curve analysis (Figure S1 of Supplementary Appendix). A detailed list of extracted data elements is given in Table S1.

Cleaning of Growth Data and Calculation of Growth Parameters

Data manipulations were performed in R.[29] A flow diagram of the data cleaning process is given in Figure S2 (Supplementary Appendix). Height-for-age Z-scores (HAZ) were calculated using the *anthro* and *zscorer* packages in R.[30] Height-for-age difference (HAD) was calculated as the measured height minus the WHO Multicentre Growth Reference for age and sex.[31] Height-for-age Z-score values above 5 or below −6 were removed. Height values falling outside of the first and 99th percentile of dataset height velocity, as plotted and interpolated through locally estimated scatterplot smoothing (LOESS), were considered outliers and removed (Figure S3a of Supplementary Appendix). Consistent with the requirements for SITAR modeling, observations of individuals with fewer than 7 recorded height measurements were removed. In summary, a total of 38 864 height measurements from 2827 individuals were available for analysis.

Descriptive Analysis and Growth Curve Analysis

We derived basic descriptive statistics of the dataset, overall and disaggregated by sex, using the *gt* package in R and presented them as median (interquartile range), or proportions, as appropriate.[32,33] Given the imbalanced nature of the growth dataset, with data points clustering around 16 months of age, we employed SITAR modeling to predict heights across a range of ages. SITAR modeling uses random effects to model individual growth trajectories in reference to an average curve through an iterative process.[34] It is more robust to data clustering than other modeling methods and is commonly used for growth curve modeling, although it is more commonly applied to adolescents than to young children.[34,35]

We used the *sitar* package in R to generate an overall model that describes trajectories of children within the clinical cohort and plotted average curves for height, HAZ and HAD along with 95% confidence intervals for subgroups of first-measured HAZ. We also modeled individual growth curves for each child

Table 1. Descriptive Characteristics of a Clinical Cohort of Stunted Children in Guatemala.

Characteristic	N	Overall N = 2827[a]	Female N = 1357[a]	Male N = 1470[a]
Female	2827	1357 (48%)	1357 (100%)	0 (0%)
Speaks Mayan language	1102	801 (73%)	380 (73%)	421 (72%)
Indigenous ethnicity	818	765 (94%)	359 (94%)	406 (93%)
Age at first measurement (months)	2827	9 (3, 16)	9 (3, 16)	9 (3, 17)
Length of monitoring (months)	2827	17 (8, 30)	17 (8, 30)	17 (8, 29)
Height measurements per child	2827	10 (8, 16)	11 (8, 16)	10 (8, 16)
First measured height-for-age Z-score	2827	−2.51 (−3.23, −1.68)	−2.40 (−3.08, −1.59)	−2.62 (−3.36, −1.77)
First measured height-for-age difference (cm)[b]	2827	−6.1 (−8.2, −3.8)	−6.0 (−8.2, −3.6)	−6.2 (−8.2, −4.0)
Stunting class at first measurement	2827			
At-risk for stunting or not stunted		926 (33%)	484 (36%)	442 (30%)
Moderately stunted		999 (35%)	507 (37%)	492 (33%)
Severely stunted		902 (32%)	366 (27%)	536 (36%)
Location	2727			
Chimaltenango		1426 (52%)	688 (53%)	738 (52%)
Escuintla		345 (13%)	155 (12%)	190 (13%)
Sololá		488 (18%)	228 (17%)	260 (18%)
Suchitepéquez		420 (15%)	215 (16%)	205 (14%)
Quetzaltenango		44 (1.6%)	20 (1.5%)	24 (1.7%)
Other		4 (0.1%)	3 (0.2%)	1 (<0.1%)

[a] n (%); Median (Q1, Q3) [b] Calculated as the measured height minus the WHO Multicentre Growth Reference for age and sex.

based on the overall average model, accounting for random effects. SITAR-modeled individual growth curves were used to predict height, HAZ and HAD at 6, 12, 18, and 24 months and to construct ridge plots showing the distribution of HAZ and HAD at each of these ages, overall and by sex. For the individually modeled growth curves and ridge plots, we only included predicted height, HAZ, and HAD for ages within 30 days of the first and last measured data points, due to concerns about the reliability of individual predictions farther away from the measured data.

Additionally, to better understand the observed heterogeneity of growth trajectories, we used *ggplot* to generate spaghetti plots of measured HAZ and HAD trajectories over time for each child included in the analysis, disaggregated by sex and quartile of first measured HAZ or HAD, respectively. We highlighted those children who demonstrated improvement in HAZ or HAD between the first and the last height measurement.

Subgroup Analysis of Growth Curves

To identify the characteristics of children with improved growth trajectories over time, we calculated the change in HAD between the first and last height measurements. We then descriptively compared the children who showed an improvement in HAD from the first to the last measurement against those who did not. The characteristics described included demographic, nutritional and anthropometry-related variables, both predicted and measured. Nutritional variables related to food group consumption and breastfeeding were included. We chose to use HAD change rather than HAZ change because of the previously mentioned tendency of HAZ to obscure the ongoing accrual of absolute height deficit. We also chose to use measured rather than predicted change in HAD due to concerns about overextrapolation with SITAR-predicted HAD. We subsequently conducted multivariate median regression analysis with measured HAD change as the dependent variable to identify any characteristics associated with reversal or mitigation of linear growth failure. We included only one height-related measure, first measured HAD, as a predictor due to collinearity among the various height measures. We conducted the regression analysis with and without the nutrition-related variables, because they were missing for approximately half of the children.

Results

Characteristics of Included Population and Growth Data

A total of 2827 unique patients (38 864 height measurements) were included in the descriptive analysis (Table 1). There were a median of 10 height measurements (IQR: 8, 16) per child, with a median time of 17 months (IQR: 8, 30) between first and last measurement. Forty-eight percent of children were female. Patients originated from 15 municipalities pertaining to seven departments in central Guatemala (Figure S4 of Supplementary Appendix). Fifty-two percent of children were from the department of Chimaltenango, and most of the remaining children were from Escuintla, Sololá or Suchitepéquez. Median HAZ at first measurement was −2.51 (−3.23, −1.68), consistent with moderate stunting, and first-measured HAZ and HAD trended lower for males than for females. Given the characteristics of the Maya Health Alliance clinical program,

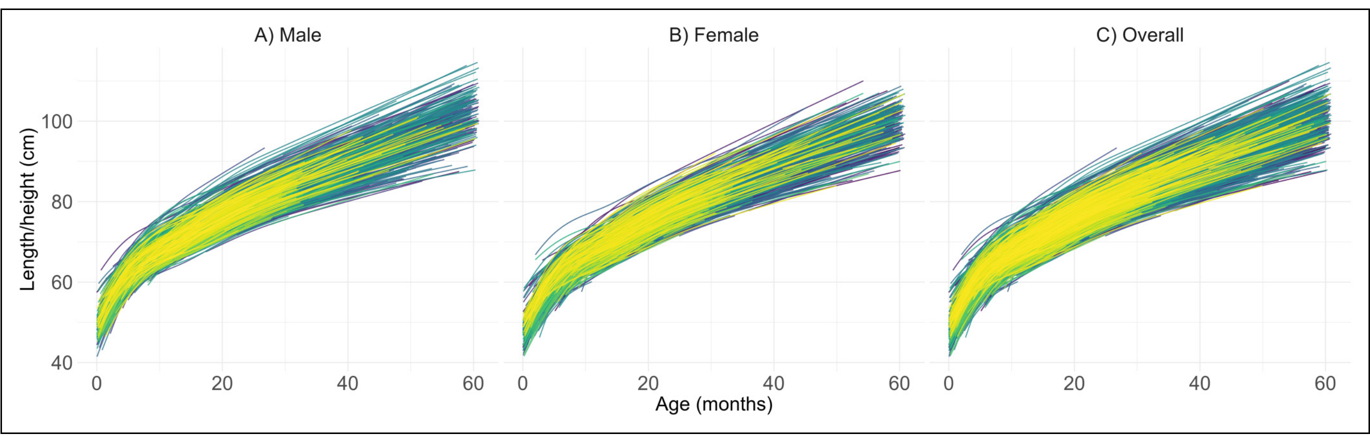

Figure 1. Individual SITAR-modeled height trajectories from a clinical cohort of children with stunting in Guatemala, overall and disaggregated by sex. Data are for all subjects in the dataset with at least seven length/height data points, per restrictions on the SITAR model package (n = 2827). SITAR, Super-Imposition by Translation and Rotation.

the growth data were imbalanced, with peak data point density around 500 days of age, or 16 months (Figure S5 of Supplementary Appendix).

Growth Modeling

Individual SITAR-modeled height trajectories of children from first to last measurement, overall and by sex, are shown in Figure 1. These plots of modeled curves demonstrate the considerable observed variation of heights and height trajectories in this population presenting for clinical care due to stunting. Average SITAR-modeled curves for height, HAZ and HAD along with 95% confidence intervals for subgroups representing distinct groupings of sex and first-measured HAZ are shown in Figure 2. In Figure 2A, more severe stunting at first measurement is associated with lower height at 60 months. In Figure 2B and C, height deficit (HAD) is seen to accrue with age regardless of stunting category upon first measurement, even when Z-scores (HAZ) stabilize or improve. Males from the most severe category of stunting appear to exhibit slightly more Z-score improvement than females between the ages of 24 and 60 months.

Density ridge plots of HAZ and HAD at 6, 12, 18 and 24 months are shown in Figure 3. Several interesting patterns are observed on visual inspection of these plots. First, overall HAZ worsens progressively from 6 to 18 months of age, although the velocity of decline is most rapid between 6 and 12 months. From 18 to 24 months, HAZ remains largely unchanged overall, although the median HAZ shows a very slight improvement for males during the same timeframe. On the other hand, the worsening of the HAD distribution is apparent for each time interval between 6 and 24 months and appears to taper only slightly between 18 and 24 months. These observations persist when the population is disaggregated by sex.

Individual Growth Trajectories

Spaghetti plots of individual HAZ and HAD trajectories over time, grouped by ascending quartiles of the first available HAZ score, are shown in Figure 4. Spaghetti strands that appear in lighter shades indicate an improvement in HAZ or HAD between the first and the last measurement. In addition to the apparent difference in overall HAZ for these three groups, many individuals in the lowest quartile (most severe stunting) demonstrate improvement in HAZ over time, whereas most individuals in the highest quartile demonstrate decline over time. Similar trends, although more subtle, are observed for HAD spaghetti plots (Figure 4B).

Subgroup Analysis of Child Growth Curves

Of the 2827 children included in the analysis, 492 (17%) demonstrated measured improvement in HAD from the first to the last measurement, while 1308 (46%) demonstrated measured improvement in HAZ. This indicates that the majority of children who had improvements in length-for-age Z-score continued to accrue height deficit even as their height-for-age Z-scores improved.

Among children with initial Z-scores of −2 or greater, based on measured data, 85/926 (9%) showed an improvement in HAD, and 188/926 (20%) showed an improvement in HAZ. Among children with initial Z-scores of −3 to −2, 192/999 (19%) showed improvement in HAD, and 477/999 (48%) showed improvement in HAZ. Among children with initial Z-scores of −3 to −4, 155/689 (22%) showed HAD improvement and 462/689 (67%) showed HAZ improvement. Finally, for children with initial Z-scores below −4, 60/213 showed HAD improvement (28%) and 181/213 showed HAZ improvement (85%). Thus, lower initial Z-scores were associated with a greater percentage of children who showed improvement in both HAD and HAZ.

The descriptive characteristics of children whose measured HAD improved from first to last measurement, as shown in Table 2, differed significantly from children whose HAD did not improve. Children with improvement were older at first measurement (16 months [IQR: 7, 21] vs 8 months [IQR: 3,

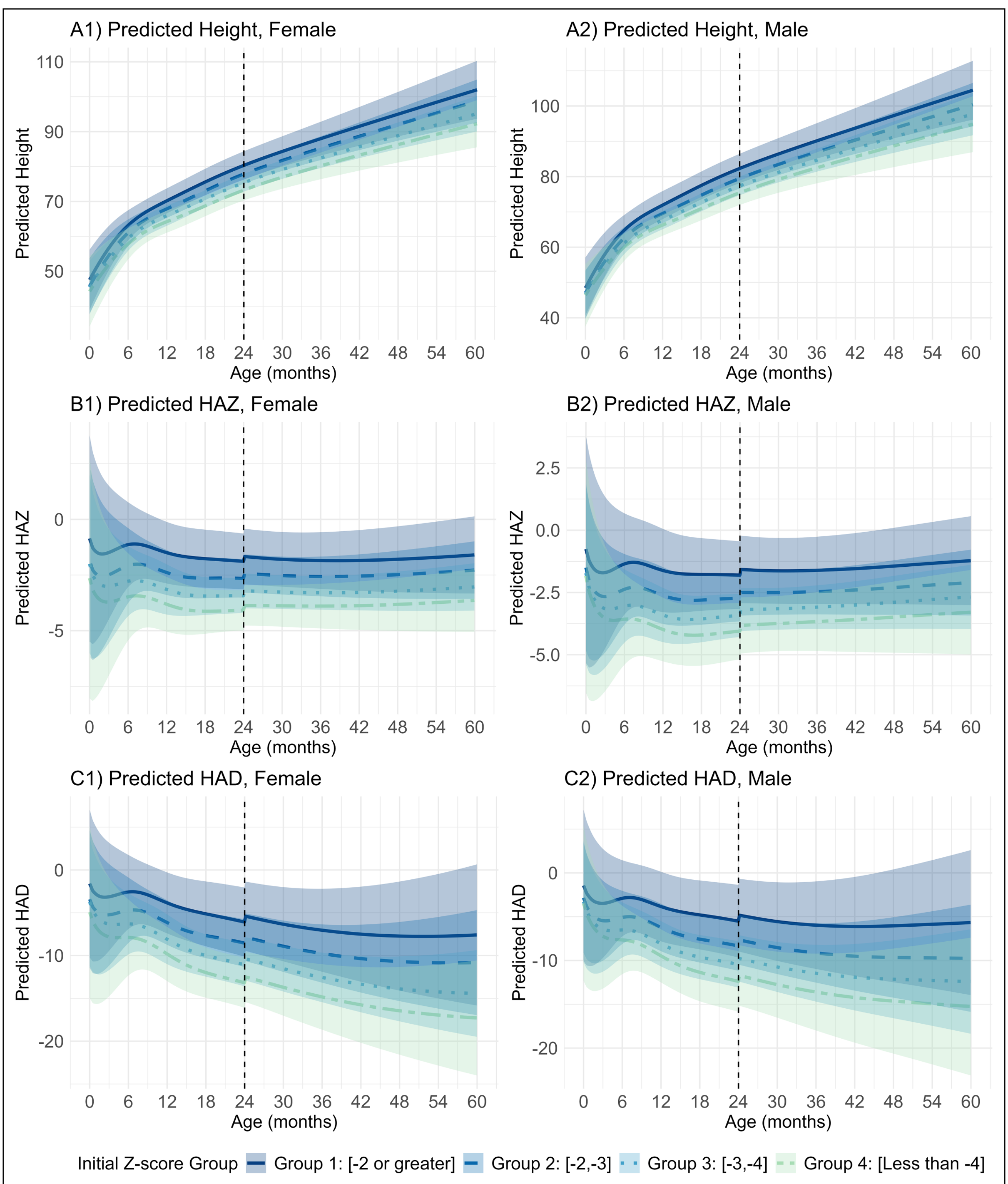

Figure 2. Average curves for SITAR-modeled height, HAZ and HAD from a clinical cohort of children with stunting in Guatemala, disaggregated by sex and by first-measured HAZ. Average curves represent data for subjects in the dataset with at least seven length/height data points, per restrictions on the SITAR model package (n = 2827). Group 4 represents children with the greatest initial severity of stunting. Number included for each combination of sex and first-measured HAZ group: 403 (F/Group 1), 351 (M/Group 1), 545 (F/Group 2), 524 (M/Group 2), 335 (F/Group 3), 451 (M/Group 3), 74 (F/Group 4), 144 (M/Group 4). HAZ, height-for-age Z-score; HAD, height-for-age difference; SITAR, Super-Imposition by Translation and Rotation.

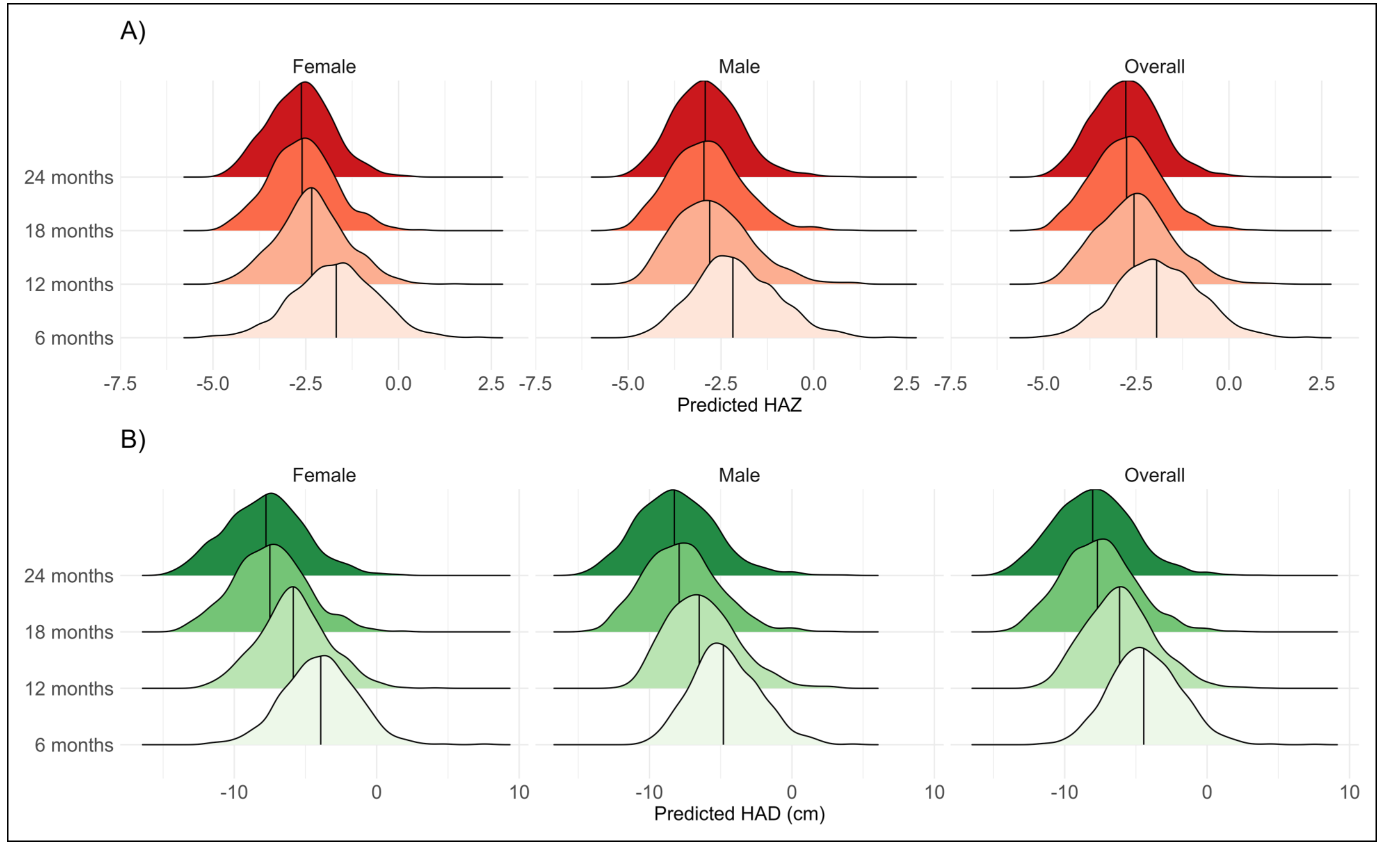

Figure 3. Density ridge plots of SITAR-predicted HAZ and HAD for stunted children from a clinical cohort in Guatemala at 6, 12, 18 and 24 months of age, overall and disaggregated by sex. Plotted values are from SITAR-modeled growth curves (n = 2827). HAZ, height-for-age Z-score; HAD, height-for-age difference; SITAR, Super-Imposition by Translation and Rotation.

15]) and monitored for less time (9 months [IQR: 7, 21) versus 19 months [IQR: 9, 31]). Their median HAZ improved 0.73 (IQR: 0.53, 1.06) and the median HAD improved 0.79 cm (IQR: 0.35, 1.55) during the period of monitoring while median HAZ and HAD declined for rest of the children. First measured HAZ and HAD were also significantly lower for children with improvement, indicating that they began with more severe levels of stunting. Additionally, a lower proportion of the children with improvement came from Chimaltenango and a higher proportion came from Escuintla, Sololá and Quetzaltenango.

Regression Modeling

Table 3 shows associations between predictors and measured change in HAD from first to last measurement. In the first model, which included 2727 children, male sex, an older age at first measurement, more severe stunting at first measurement (as measured by HAD) and location within the departments of Escuintla, Sololá, Suchitepéquez and Quetzaltenango were associated with modestly better HAD change outcomes. In the second regression model that also included dietary data, 1388 children were included. In this model, neither age-appropriate breastfeeding nor child dietary diversity were found to be associated with measured change in HAD from first to last measurement.

Discussion

The data presented here offer an essential look into the growth dynamics of a population of children with chronic malnutrition. Taken together, the data suggest that while there was a continual negative trend in most children's growth trajectories on both HAZ and HAD metrics, the velocity of decline reduced over time. We present both HAZ and HAD to reflect current clinical practice and comparability with prior literature, although we interpret HAD as the more meaningful indicator of absolute growth deficit in this cohort. A subset of children in this clinical cohort did experience improvements in linear growth measures. These improvements were less apparent for the HAD than for the HAZ measure, as HAZ tended to classify significantly more of the children as having improvement over time than did HAD. The improvements observed appear to be driven by those children who initially started with the lowest HAZ or HAD values before apparently stabilizing, and in some cases even recovering slightly over time.

We note that the children identified as having improved, as shown in Table 2, were significantly older at first measurement

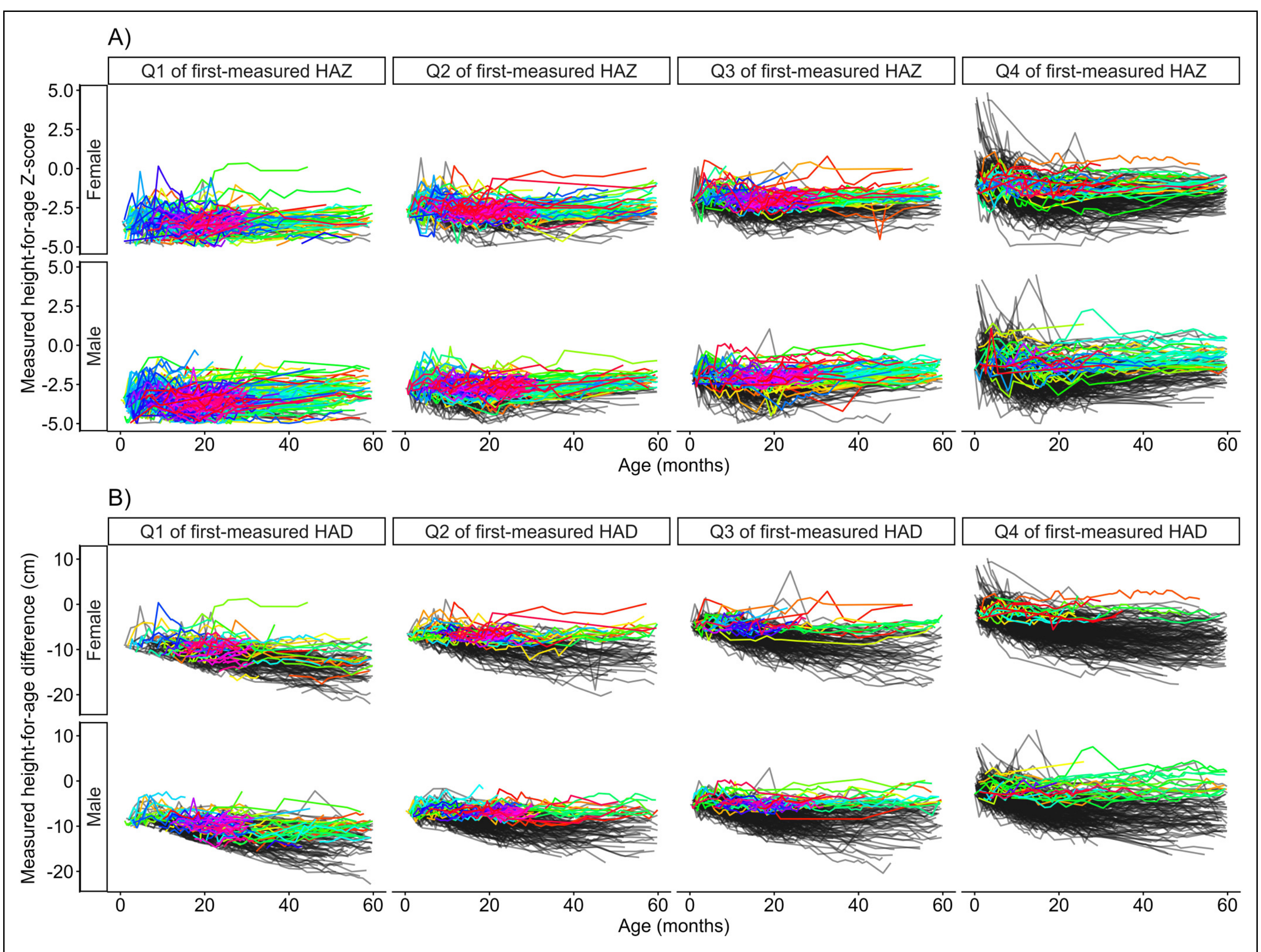

Figure 4. Spaghetti plots demonstrating individual HAZ and HAD trajectories over time for stunted children from a clinical cohort in Guatemala, disaggregated by quartiles of first-measured HAZ or HAD and by sex. For quartiles of first-measured HAZ or HAD, Q1 corresponds to children with the greatest initial severity of stunting. Each "spaghetti strand" represents the growth trajectory of one child. Children showing improvement from first to last measurement are highlighted in lighter shades, whereas those with no improvement are in black (n = 2827). HAZ, height-for-age Z-score; HAD, height-for-age difference.

and were monitored for less time than the children identified as not having improved. This observation could reflect bias related to the uneven distribution of unmodeled growth data. However, we also note that the children who demonstrated apparent improvement did so over a long enough timeframe (9 months, [IQR: 7, 21]) to suggest that improvement was sustained and not simply a function of measurement timing. It is also possible that these children represented referrals to the nutrition program later in life and differed clinically from the children who were recruited at a younger age. The reasons for this would need to be explored further in subsequent studies.

Factors Associated with Growth Trajectories

Regression analysis that included as predictors the limited number of clinical and demographic factors available in the dataset indicated that males and children with lower initial HAD tended to have more favorable changes in HAD over time. Despite this tendency, predictive modeling showed that lower initial HAD was still associated with lower HAD at last measurement. This latter finding is strongly consistent with more definitive population- and clinical trial-based work which clearly demonstrated the predictive nature of early growth metrics on growth outcomes later in childhood.[14,17] We note that males in this clinical cohort exhibited more catch-up growth than females but also started with greater severity of stunting. Disparities in stunting between females and males have been consistently demonstrated in population-based studies.[36]

Slightly more than half of the children from this clinical cohort were from the Department of Chimaltenango, and regression analysis showed that these children had greater accrual of height deficit than children from other areas such as Sololá, Escuintla and Quetzaltenango. This finding

Table 2. Descriptive Characteristics of Stunted Children from a Clinical Cohort in Guatemala for Whom Height-for-Age Difference (HAD) Improved or Did Not Improve from First to Last Measurement.

Characteristic	No Improvement N = 2335[a]	Improvement N = 492[a]	*P*-Value[b]
Female	1132 (48%)	225 (46%)	.3
Age at first measurement (months)	8 (3, 15)	16 (7, 21)	<.001
Length of monitoring (months)	19 (9, 31)	9 (7, 21)	<.001
Number of height measurements	11 (8, 17)	8 (8, 11)	<.001
First measured HAZ	−2.41 (−3.15, −1.57)	−2.81 (−3.59, −2.25)	<.001
First measured HAD (cm)	−5.8 (−7.9, −3.5)	−7.6 (−9.5, −5.8)	<.001
Measured HAZ change (first to last)	−0.25 (−0.82, 0.16)	0.73 (0.53, 1.06)	<.001
Measured HAD change (first to last) (cm)	−2.96 (−5.25, −1.43)	0.79 (0.35, 1.55)	<.001
Acutely malnourished on enrollment	81 (3.5%)	14 (2.8%)	.5
Met Child-MDD[c] (first and last)	340 (26%)	86 (29%)	.4
Age-appropriate breastfeeding (first and last)[d]	993 (77%)	222 (74%)	.3
Location			
Chimaltenango	1247 (55%)	179 (38%)	
Escuintla	249 (11%)	96 (20%)	
Sololá	365 (16%)	123 (26%)	
Suchitepéquez	363 (16%)	57 (12%)	
Quetzaltenango	25 (1.1%)	19 (4.0%)	
Other	2 (<0.1%)	2 (0.4%)	

[a] n (%); Median (Q1, Q3).
[b] Pearson's Chi-squared test; Wilcoxon rank sum test.
[c] Child Minimum Dietary Diversity, adapted to include children beyond the age of 2 years.
[d] Consistent with WHO recommendations to breastfeed through at least 2 years of age.

Table 3. Median Regression of Height-for-Age Difference (HAD) Change (cm)[a] among Stunted Children from a Clinical Cohort in Guatemala.

	Dietary Data Not Included (n = 2727)			Dietary Data Included (n = 1388)		
Characteristic	Beta	95% CI[b]	*P*-Value	Beta	95% CI[b]	*P*-Value
Female	−0.23	−0.39, −0.07	**.012**	0.00	−0.20, 0.14	>.9
Age at first measurement (months)	0.06	0.04, 0.06	**<.001**	0.05	0.02, 0.07	**<.001**
First measured height-for-age difference (cm)	−0.16	−0.20, −0.13	**<.001**	−0.22	−0.29, −0.17	**<.001**
Number of height measurements	−0.02	−0.04, 0.00	**.033**	−0.01	−0.05, 0.00	0.5
Length of monitoring (months)	−0.09	−0.10, −0.08	**<.001**	−0.12	−0.14, −0.10	**<.001**
Location						
Chimaltenango	—	—		—	—	
Escuintla	1.0	0.81, 1.5	**<.001**	0.48	0.08, 0.67	**.004**
Sololá	0.87	0.68, 1.1	**<.001**	0.47	0.28, 0.72	**<.001**
Suchitepéquez	0.44	0.24, 0.72	**.002**	0.47	0.09, 0.70	**.005**
Quetzaltenango	0.53	0.38, 1.0	**.043**	0.22	−0.01, 0.79	.4
Other	2.4	−10, 15	.7			
Met Child-MDD[c] (first and last)				0.18	−0.10, 0.34	.2
Age-appropriate breastfeeding[d] (first and last)				−0.07	−0.31, 0.15	.6

[a] A positive change in height-for-age difference (HAD) (last measurement – first measurement) reflects an improvement in growth trajectory, while a negative change reflects a deterioration. For example, a child with a first measured HAD of −5 cm and a last measured HAD of −2 cm would have a HAD change of 3 cm, representing improvement. [b] CI, Confidence Interval [c] Child Minimum Dietary Diversity, adapted to include children beyond the age of 2 years [d] Consistent with WHO recommendations to breastfeed through at least 2 years of age.

highlights the importance of geographical setting in explaining growth curve variation. However, specific regional factors that might explain the difference were not available in the dataset for analysis. It is noteworthy that dietary diversity and age-appropriate breastfeeding were not found to be associated with clinically meaningful improvements in height deficit over time. Further investigation is merited to determine whether this lack of observed association may reflect limitations

of either the modeling or of the indicators themselves, being qualitative rather than quantitative in nature, or whether dietary diversity and age-appropriate breastfeeding are truly not associated with growth response in this clinical population of already stunted children.

We note that the clinical variables available in the dataset to characterize children with improved growth trajectories were limited and may not have included all salient factors. For example, we lacked access to antenatal maternal nutritional and weight gain data, data on fetal growth and neonatal anthropometrics, which are known predictors of neonatal height and early onset stunting, although their influence on post-natal growth dynamics, including recovery growth, is poorly understood.[37,38] Additionally, many factors associated with growth recovery in stunted children may still be unknown or unexplored. In one recent large path analysis, a large proportion of linear growth variation could not be explained by a comprehensive set of antenatal, pregnancy, and postnatal factors.[17] Recent clinical trials have been focused on understanding the role of various modifiable clinical factors, including environmental exposures such as fungal toxins, the gut microbiome and metabolome, and general environmental enteropathy.[7,8,39] Our team is conducting new research in these areas with a focus on aflatoxin and fumonisin exposure and the mediating effects of the infant gut microbiome on nutrient uptake, inflammation and child growth.[40–44]

Future Research

A consensus on the dynamics of stunting onset and persistence is that, at the population level, it tends to be inexorable and largely irreversible in high-risk groups.[25] This has led to a near-exclusive public health focus on the prevention of stunting in high-risk populations, with virtually no published data on the clinical management of already-stunted children. Notably, children with especially severe stunting are often excluded from the relevant population studies and clinical trials.[13–18] This leaves open the question of which and to what degree, if any, severely stunted children respond to clinical nutrition interventions.[20] Our observational data suggest that at least a small proportion of stunted children receiving nutrition interventions do show improvements. These findings emphasize the necessity of further research involving children with more extreme growth deficits, aiming to better define subgroups with unique growth patterns and to identify differential responses to interventions and factors that predict growth improvements. The leveraging of "real-world" data from clinical programs, like those used in this study, is valuable and may be more likely to capture children with the most severe linear growth deficits than more controlled data from clinical trials, though interpretation may be more complex.

Limitations

Our study has numerous limitations and the results must be interpreted carefully, mainly as a call for further novel research in clinical populations of children with severe stunting. First, as a clinical dataset, the distribution of available growth data was not evenly disbursed, a weakness which we have attempted to overcome through several complementary modeling and descriptive approaches. Nevertheless, there may have been clinical differences that we were not able to measure between children who enrolled early in the program and children who enrolled late. Additionally, the quality of the available anthropometric data could not be verified, as it was obtained through extraction from clinical records. Similarly, the scope of available clinical covariables was limited given the narrow recuperative nutrition focus of the institution's electronic clinical data forms, limiting inferences that could be drawn on both clinical factors and region-specific contextual factors associated with growth improvement.

Conclusion

This study provides valuable insights into the growth trajectories of a clinical cohort of children with stunting from a very high prevalence region of rural Guatemala. Our findings highlight the significant variability in growth responses, with a small subgroup exhibiting growth stabilization and even slight catch-up growth, particularly those with the most severe initial stunting. Given the heterogeneity of growth responses in this population, ongoing investigations of both tailored clinical interventions and novel factors associated with growth variability and catch-up growth will be of great importance.

Abbreviations

HAD	Height for age difference
HAZ	Height/length for age Z score
LCGM	latent class growth modeling
LOESS	locally estimated scatterplot smoothing
SITAR	Superimposition by translation and rotation
WAZ	Weight-for-age Z score
WHZ	Weight-for-height/length Z score.

Author Contributions

CL, LVG, GMB and PR designed research. CL, LVG, SA and PR conducted research, analyzed data, and performed statistical analysis. LVG and PR wrote the paper. GMB, LR, SS, SA and AVS edited the paper. PR had primary responsibility for final content. All authors read and approved the final manuscript.

Consent for Publication

Not applicable.

Consent to Participate

Informed consent to participate was waived by the Maya Health Alliance Institutional Ethics Committee.

Data Availability

Data described in the manuscript, code book, and analytic code will be made publicly and freely available upon publication without restriction at: Rohloff, Peter, 2024, "Replication Data for: Modeling growth

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Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical Considerations

This study was approved by the Maya Health Alliance Institutional Ethics Committee (WK 2020 005), with a waiver of informed consent granted for extraction of electronic health records data.

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Supplemental Material

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