Taylor & Francis
Taylor & Francis Group

AIDS Care

Psychological and Socio-medical Aspects of AIDS/HIV

ISSN: (Print) (Online) Journal homepage: www.tandfonline.com/journals/caic20

Physical functioning in adolescents with perinatal HIV

Nicolette Comley-White, Veronica Ntsiea & Joanne Potterton

To cite this article: Nicolette Comley-White, Veronica Ntsiea & Joanne Potterton (2024) Physical functioning in adolescents with perinatal HIV, AIDS Care, 36:1, 60-69, DOI: 10.1080/09540121.2023.2214862

To link to this article: https://doi.org/10.1080/09540121.2023.2214862


Published online: 25 May 2023.


Submit your article to this journal


Article views: 71


View related articles


View Crossmark data

Full Terms & Conditions of access and use can be found at
https://www.tandfonline.com/action/journalInformation?journalCode=caic20

AIDS CARE
2024, VOL. 36, NO. 1, 60–69
https://doi.org/10.1080/09540121.2023.2214862

Taylor & Francis
Taylor & Francis Group

Check for updates

Physical functioning in adolescents with perinatal HIV

Nicolette Comley-White, Veronica Ntsiea and Joanne Potterton

Department of Physiotherapy, University of the Witwatersrand, Johannesburg, South Africa

ABSTRACT

Perinatal HIV impacts on growth and development in childhood, with physical impairments such as growth limitations, decreased physical activity, reduced exercise tolerance and cardiopulmonary dysfunction continuing into adolescence. There is limited data on other physical functioning domains in perinatally HIV-infected adolescents (PHIVA) thus the aim of this study was to establish the physical sequelae of perinatal HIV in adolescents. This South African cross-sectional study compared PHIVA with HIV-negative adolescents, assessing anthropometry, muscle strength, endurance and motor performance. All ethical considerations were adhered to. The study included 147 PHIVA and 102 HIV-negative adolescents, aged 10–16 years. The majority (87.1%) of PHIVA were virally suppressed however, they still showed significant deficits in height ($p < 0.001$), weight ($p < 0.001$) and BMI ($p = 0.004$). Both groups performed poorly in muscle strength and endurance but did not differ significantly. In motor performance, the PHIVA scored significantly lower for manual dexterity and balance, with significantly more PHIVA with motor difficulty. A regression analysis showed that viral suppression predicted muscle strength ($p = 0.032$) and age positively predicted endurance ($p = 0.044$) and negatively predicated aiming and catching ($p = 0.009$). In conclusion, PHIVA face growth deficits and challenges with motor performance, especially with manual dexterity and balance.

ARTICLE HISTORY
Received 13 December 2021
Accepted 11 May 2023

KEYWORDS
HIV; physical functioning; muscle strength; endurance; growth; adolescence

Introduction

Despite great strides in HIV-related healthcare the disease continues to be a global burden, both in adult and childhood populations (Pandey & Galvani, 2019). In 2019 there were an estimated 1.7 million adolescents living with HIV (UNICEF, 2020a) and as access to antiretroviral therapy (ART) continues to expand so this population increases, shifting paediatric HIV management to that of a chronic disease (Fairlie et al., 2014; Sohn & Hazra, 2013).

Due to the nature of the virus itself, as well as the toxicity of drug therapy [with either highly active ART or combination ART (Menéndez-Arias & Delgado, 2022)], children and adolescents are particularly vulnerable to adverse effects as they go through critical periods of growth and development (Flynn & Abrams, 2019). Research is showing that perinatally HIV-infected adolescents (PHIVA) face neurocognitive dysfunction and mental health issues (Laughton et al., 2013; Lowenthal et al., 2014; Smith & Wilkins, 2015; Willen et al., 2017), as well as physical sequelae such as growth impairment (Arbeitman et al., 2014; Jesson et al., 2019), decreased physical activity (Martins et al., 2017) reduced exercise tolerance (Ferrand et al., 2012) and impaired cardiopulmonary health (Miller et al., 2013). Adolescents themselves have expressed that they experience physical difficulties, with poor endurance, pain and fatigue being the most common complaints (Comley-White et al., 2021).

In 2004, South Africa began with ART rollout (Evans, 2013) and initially the criteria for ART initiation was the presence of an AIDS-defining condition or a CD4 count of less than 200cell/mm^3 (Osler et al., 2018), thus leaving many people (children and adults) with HIV as not eligible for ART initiation for long periods of time. As early initiation of ART and healthcare access improved, so HIV has shifted to a chronic illness, creating a growing population of children with perinatal HIV aging into adolescence in South Africa (Anderson et al., 2020; Fairlie et al., 2014).

With the increasing number of PHIVA there is progressively more research that is becoming available on the long-term effects of perinatal HIV, however, there are still many gaps in the clinical knowledge and a paucity of healthcare options. While it is well-established that children with perinatal HIV are negatively impacted in growth and development (Strehlau et al., 2019; Whitehead et al., 2014) there are areas of concern in PHIVA that need further investigation. Thus the aim of this study was to establish the physical sequelae of

CONTACT Nicolette Comley-White Nicolette.comley-white@wits.ac.za Department of Physiotherapy, University of the Witwatersrand, 7 York Road, Parktown, 2193, Johannesburg, South Africa

© 2023 Informa UK Limited, trading as Taylor & Francis Group

perinatal HIV in adolescents. By determining this, the authors wish to create a background for screening and early intervention for this distinctive population, in turn leading to improved quality of life and health outcomes.

Materials and methods

Design

This study used a cross-sectional design, comparing data between PHIVA and a comparison group of HIV-uninfected adolescents, forming one of the phases of a larger study used for the development of a model of care for PHIVA. Further details on the methodology of this larger study have been published elsewhere (Comley-White et al., 2019).

Study site and participant selection

The study site was a large, urban HIV clinic and research unit in Johannesburg, South Africa. Data was collected from a longitudinal cohort of PHIVA that were followed through childhood as part of the Childhood HAART Alterations in Normal Growth, Genes and AGing Evaluation Study (CHANGES). The HIV-uninfected participants were accessed via a database that forms part of the CHANGES study. These adolescents are HIV negative family members, friends or community members of the PHIVA cohort, and as such are from a similar sociodemographic background as the PHIVA participants.

Adolescence is defined as 10–19 years (UNICEF, 2016; World Health Organization, 2014) and all of the CHANGES children were in the early and middle phases of adolescence, with a cut-off age of 16 years. Participants were excluded if (1) they had any cognitive/physical impairments that prevented them from taking part in the assessment process or that were not related to HIV (for example, a traumatic brain injury); (2) if the mode of transmission for the PHIVA group was not vertically acquired.

Procedure and instrumentation

In 2019 (January to October) suitable adolescents were identified from the clinic's data base and contacted telephonically with information about the study and an invitation to participate. Upon arrival at the study site, the clinic counsellor obtained participant assent and parental consent. Clinical and demographic data were collected from the participants' files and the following variables were assessed by the principal investigator and a research assistant (both of whom were physiotherapists): height, weight, muscle strength, endurance and motor performance. The standing broad jump and the shuttle run test were used to assess muscle strength and endurance, respectively, and the Movement Assessment Battery for Children- Second Edition (MABC-2) evaluated motor performance.

Ethical considerations

The Human Research Ethics Committee (Medical) of the University of the Witwatersrand granted ethical clearance (M180226) and all ethical requirements were adhered to. Potential participants were invited to the study telephonically and/or on the day of their clinic visit. Informed consent and assent were obtained and all data were kept confidential.

Data analysis

The demographic data were described with frequencies, means and standard deviations. Height-for-age z-scores (HAZ) and body mass index (BMI)-for-age z-scores (BAZ) were calculated using World Health Organization reference data (de Onis, 2007; World Health Organization, 2021). Weight-for-age reference data are not available for children over 10 years old since pubertal growth spurts can distort the relativity of height to body mass (World Health Organization, 2021). Stunted was defined as height-for-age < -2 standard deviations (SD) and wasted was defined as BMI-for-age < -2SD (World Health Organization, 2008).

Normality tests were run for all variables and data were normally distributed, with exception of the final standard score of the MABC-2. To compare the two groups, independent sample t tests were used except for the non-normative data that had Mann–Whitney U tests applied. Statistical significance was set at $p < 0.05$ (Vexler & Hutson, 2018). Multivariate linear regression analyses were run to analyse the influence of the clinical variables on the outcome measures.

Data for the MABC-2 were analysed to show the standard score means and standard deviations for each component, as well as the frequency and percentages of the participants whose standard score results placed them in the red, amber or green zones. These zones are indicative of significant motor difficulty, at risk of motor difficulty and no motor difficulty, respectively.

At the time of data cleaning and analysis it was observed that there were sporadic data collection forms with information incomplete. The sample size for each of these outcome measures was adjusted on analysis and is reflected in the tables of results.

Results

Demographic and clinical information

The study included 249 participants, of which 59% (n = 147) were PHIVA and 41% (n = 102) were the HIV-negative comparison group. The mean age for the two groups was the same [12 (SD ± 1–2) years], with the year of birth ranging from 2003 to 2009. Table 1 presents the demographic information for the study population.

Clinical data for the PHIVA group is presented in Table 2. The mean age at which the participants' HIV diagnosis was made was 4.7 months (SD ± 5.9) and the mean age at ART initiation was 8.5 months (SD ± 6.6 months). At the time of assessment, the group had a mean CD4% of 38.3 (SD ± 7.1) and the majority (87.1%) of the participants had viral loads <200 copies/ml.

Anthropometry

The PHIVA group presented with statistically significant lower weight ($p < 0.001$), height ($p < 0.001$) and BMI ($p = 0.004$) when compared to the HIV negative adolescents. Although the mean HAZ and BAZ results for each group were within acceptable ranges (i.e., > −2SD), the PHIVA group scored lower for both variables ($p = 0.246$ and $p = 0.236$, respectively) and significantly more PHIVA were stunted and wasted compared to the HIV negative adolescents (23.1% vs. 2.9% and 6.8% vs. 4.9% respectively; $p = 0.036$). Further data on the anthropometric results are presented in Table 3.

Muscle strength and endurance

The two groups did not differ significantly in their muscle strength or endurance. Table 4 presents the results of the muscle strength and endurance assessments.

Motor performance

On the MABC-2 the PHIVA performed worse than the HIV-negative group, however the difference in the final standard score was not statistically significant (p = 0.144). Despite this, there are important differences on the subscales. The PHIVA group performed significantly worse than the comparison group for manual dexterity ($p = 0.021$) and balance ($p = 0.020$) standard score means. Furthermore, an analysis of the frequencies of participants scoring in the red (i.e., significant motor difficulty), amber (i.e., at risk of motor difficulty) and green (i.e., no motor difficulty) zones showed that significantly more PHIVA than HIV-negative participants were in the red zone for the final MABC-2 scores (13.2% vs. 4.1%, $p = 0.054$). Although not reaching statistical significance, it is noteworthy that there were more PHIVA than HIV negative participants who scored in the red zones for manual dexterity (15.8% vs. 11.1%, $p = 0.064$), and balance (6.3% vs 4.0%, $p = 0.082$); and in the amber zones for manual dexterity (9.6% vs. 3.0%, $p = 0.064$), aiming and catching (6.8% vs. 3.0%, $p = 0.306$) and balance (4.2% vs. 0.0%, $p = 0.082$), Table 5 presents further results on the participants' motor performance.

Clinical predictors

A multivariate linear regression model was used to analyse the influence of the clinical variables of age, sex, height, weight, BMI, viral suppression, current CD4%, age of HIV diagnosis and age of ART initiation on the outcome variables, namely muscle strength, endurance and motor performance. Once the assumptions of multivariate normality, linearity, freedom from extreme values and multi-collinearity were cleared, the regression analysis was performed.

The regression model as a whole (i.e., a combination of all of the clinical variables) was significant for muscle strength ($R^2 = 0.193$; $p = 0.14$) and endurance ($R^2 = 0.213$; $p = 0.006$) however the model was not significant for predicting motor performance ($p = 0.886$). Table 6 presents the results of investigating each clinical variable individually to establish the independent variables prediction of the dependent variables.

Table 1. Demographic data of the study population (n = 249).

	HIV negative adolescents n = 102	HIV positive adolescents n = 147	P value
Male, n (%)	60 (58.8)	73 (49.7)	0.154
Female, n (%)	42 (41.2)	74 (50.3)	0.154
Age in years, mean (SD)	12 (±1)	12 (±2)	0.91
Minimum age	10 years 0 months	10 years 0 months	-
Maximum age	16 years 11 months	15 years 12 months	-

Table 2. Clinical data of the HIV positive participants.

Clinical data	Values
Mean age at HIV diagnosis, months (n = 107)	4.7 (SD ± 5.9)
Mean age at ART initiation, months (n = 147)	8.5 (SD ± 6.6)
Mean CD4 count, cells/mm^3 (n = 147)	1011.6 (SD ± 305.7)
Mean CD4 percentage (n = 145)	38.3 (SD ± 7.1)
Number of participants with viral load < 200 copies/ml (n = 147)	128 (87.1%)
Number of participants with viral load > 200 copies/ml	19 (12.9%)

Table 3. Anthropometric results for the study population (n = 249).

	HIV negative adolescents n = 102	HIV positive adolescents n = 147	P value
Weight in kilograms, mean (SD)	42.8 (±13.2)	36.8 (±10.2)	**<0.001**
Height in metres, mean (SD)	1.5 (±0.1)	1.4 (±0.1)	**<0.001**
BMI, mean (SD)	19.3 (±4.3)	17.9 (±3.2)	**0.004**
HAZ, mean (SD)	−0.3 (±1.0)	−1.1 (±1.1)	0.246
BAZ, mean (SD)	0.3 (±1.4)	−0.3 (±1.2)	0.236
Stunted, n (%)	3 (2.9)	34 (23.1)	**0.036**
Wasted, n (%)	5 (4.9)	10 (6.8)	**0.036**

HAZ = height-for-age z-score; BMI = body mass index: BAZ = BMI-for-age z-score; stunted = <−2SD; wasted = <−2SD.

For the individual clinical variables, only viral suppression statistically significantly predicted muscle strength ($p = 0.032$) while age significantly predicted the endurance ($p = 0.044$). Finally, although the model was not a good fit for motor performance, age was the only variable that was statistically significant in predicting aiming and catching ($p = 0.009$), however it was a negative prediction (while the former two were positive predictions).

Discussion

This study aimed to establish the physical sequelae of perinatal HIV in adolescents through a cross-sectional analysis of PHIVA and an HIV-negative comparison group. The results of this study shows that there are significant physical sequelae that PHIVA face with regards to stunting, wasting and motor performance.

Despite the PHIVA population of this study having early diagnosis (mean age: 4.7 months, SD ± 5.9), early ART initiation (mean age: 8.5 months, SD ± 6.6 months) and majority viral suppression (87.1%), they still presented with multiple physical challenges. This is a concerning finding, especially since this sample of PHIVA were well-managed, with regular follow-up appointments and access to health care via a large, urban HIV research unit. With many PHIVA not accessing regular health care in sub-Saharan Africa (Eba & Lim, 2017; Sam-Agudu et al., 2016) [where more than 88% of children and adolescents with HIV live (UNICEF, 2020b)], these sequelae are potentially even more

Table 4. Muscle strength and endurance results for the study population (n = 249).

	HIV negative adolescents n = 102	HIV positive adolescents n = 145 (2 incomplete records)	P value
Muscle strength: standing broad jump in metres, mean (SD)	120.3 (±21.5)	121.5 (±25.5)	0.716
Endurance: shuttle run test in metres, mean (SD)	277.0 (±132.1)	298.3 (±137.7)	0.225

Table 5. Motor performance results for the study population (n = 249).

	HIV negative adolescents n = 102	HIV positive adolescents n = 147	P value
MABC-2: manual dexterity			
Complete records, n (%)	99 (97.1)	146 (99.3)	-
Standard score, mean (SD)	9.0 (±2.6)	8.2 (±2.7)	**0.021**
Red zone, n (%)	11 (11.1)	23 (15.8)	0.064
Amber zone, n (%)	3 (3.0)	14 (9.6)	
Green zone, n (%)	85 (85.9)	109 (74.7)	
MABC-2: aiming and catching			
Complete records, n (%)	99 (97.1)	146 (99.3)	–
Standard score, mean (SD)	10.2 (±3.7)	10.0 ± (3.3)	0.573
Red zone, n (%)	14 (14.1)	15 (10.3)	0.306
Amber zone, n (%)	3 (3.0)	10 (6.8)	
Green zone, n (%)	82 (82.8)	121 (82.9)	
MABC-2: balance			
Complete records, n (%)	100 (98.0)	144 (98.0)	–
Standard score, mean (SD)	11.87 (±2.7)	10.95 (±3.2)	**0.020**
Red zone, n (%)	4 (4.0)	9 (6.3)	0.082
Amber zone, n (%)	0 (0.0)	6 (4.2)	
Green zone, n (%)	96 (96.0)	129 (89.6)	
MABC-2: total			
Complete records, n (%)	98 (96.1)	144 (98.0)	–
Standard score, mean (SD)	10.3 (±3.0)	9.95 (±6.7)	0.144
Red zone, n (%)	4 (4.1)	19 (13.2)	**0.054**
Amber zone, n (%)	5 (5.1)	5 (3.5)	
Green zone, n (%)	89 (90.8)	120 (83.3)	

MABC-2: Movement Assessment Battery for Children- Second Edition.

Table 6. Regression analysis results reaching statistical significance for individual clinical variables.

Dependent variable	Independent variable	Unstandardized B coefficient	T score	P value
Muscle strength	Viral suppression	13.312	2.176	0.032
Endurance	Age	28.239	2.042	0.044
Aiming and catching	Age	−0.892	−2.667	0.009

prevalent. A review of long-term virologic outcomes in PHIVA living in low- and middle-income countries found that the median age of ART initiation was 4–9 years and that viral suppression ranged from 53% to 68%, and specifically in South Africa, it was 5–11 years and 69% to 81%, respectively (Anderson et al., 2020). Anderson et al.'s (2020) values are substantially poorer than the viral suppression frequency (87.1%) and mean age of ART initiation (8.5 months, SD ± 6.6 months) for this study's population thus indicating the potentially greater prevalence of physical sequelae in other PHIVA. This highlights the necessity of regular healthcare monitoring and access to early diagnosis and ART initiation.

Anthropometry

The PHIVA group had significantly lower height ($p < 0.001$), weight ($p < 0.001$) and BMI ($p = 0.004$) compared to the HIV-negative adolescents, and they were significantly more stunted ($p = 0.036$) and wasted ($p = 0.036$). Perinatal HIV inhibits growth and development in children (Cruz & Cardoso, 2015; Williams & Jesson, 2018) and Jesson et al. (2019) found that a lower CD4 count and later ART initiation were associated with poorer growth in PHIVA. This study highlights that despite early diagnosis, ART initiation and regular follow-up growth deficits continue into adolescence.

Stunting in childhood impacts on pubertal development and it has been well established that pubertal delay occurs in PHIVA (Bellavia et al., 2017; Cruz & Cardoso, 2015; Ferrand et al., 2012; Iloh et al., 2017; Williams & Jesson, 2018). Stunting also has a long-term impact on cognition, academic and economic performance, and maternal reproductive function (Crookston et al., 2011; Dewey & Begum, 2011). Wasting is associated with chronic infections, inflammation and higher levels of morbidity and mortality (Harding et al., 2018). These deleterious effects of stunting and wasting are an indication of the need for regular monitoring of PHIVA in terms of growth, pubertal development, academic performance and cognition.

Muscle strength and endurance

Although there were no differences between the two groups for muscle strength and endurance both performed below the expected norms for their ages (Hardy et al., 2018; Saint-Maurice et al., 2015; Tomkinson et al., 2017). This could be due to the general decreased levels of physical activity that this group of children may be experiencing. One needs to consider that this population is based in a low socio-economic environment and general access to school sport, extramural activities and club sports would potentially be limited.

Many studies include children living with HIV (CLHIV) who are less than 10 years old, i.e., not PHIVA, and present the data of younger children and adolescents together. These studies provide valuable information about the sequelae of perinatal HIV, affecting both younger children and adolescents. Research in CLHIV has shown mixed results on muscle strength, power and endurance. Potterton et al. (2022) and Ramos et al. (2012) found no differences in the muscle strength of CLHIV and HIV-negative participants, however in Ramos et al.'s (2012) study anaerobic power was significantly lower in CLHIV and Somarriba et al. (2013) found significantly decreased lower extremity muscle strength in their population of 7–20 year old participants living with HIV. Although small, deficits in muscle power have been found in another study looking at perinatal HIV in children aged 8–25 years (Macdonald et al., 2017) but further research in this area is lacking.

In our study, although they did not differ significantly, both groups of adolescents performed overall poorly in endurance. Chisati and Vasseljen (2015) assessed aerobic endurance in Malawian young adults with HIV, and found that they had significantly lower endurance compared to the HIV-negative group. Similarly, an assessment of Malawian children and adolescents with perinatal HIV (aged 5–18 years) using the six minute walk test (6MWT) showed that the HIV-positive group walked significantly shorter distances than the HIV-negative comparison group ($p = 0.015$) (Sims Sanyahumbi et al., 2017). Other studies present contrasting findings: a South African cohort of well-managed CLHIV with early ART initiation did not differ significantly from their HIV-negative peers on the 6MWT (Potterton et al., 2022), nor did another South African cohort of PHIVA compared to an age-matched HIV-negative group (Githinji et al., 2019). It should be noted, however, that the 6MWT is an assessment of submaximal endurance and thus is not necessarily sensitive enough to detect mild cardiopulmonary deficits (Githinji et al., 2019).

Other studies have used VO_{2peak} as an outcome measure showing decreased endurance in HIV-positive adolescents (Cade et al., 2002; de Lima et al., 2017; Keyser et al., 2000; Somarriba et al., 2013) and Githinji et al. (2017) assessed lung function in 515 South African PHIVA and found significant lung dysfunction compared to HIV-negative adolescents, thus indicating significant functional aerobic impairment and cardiorespiratory insufficiency for this population.

Aerobic and cardiorespiratory impairments are part of the multifactorial nature of decreased endurance. In addition to the potential low levels of physical activity found in PHIVA, impairments such as moderate to severe dyspnoea have been reported in 34.4% of a PHIVA population (Mwalukomo et al., 2016).

Motor performance

The PHIVA group did poorly in motor performance, with significantly lower performance in the standard score for manual dexterity (0.021) and balance (p = 0.020), and with significantly more PHIVA than HIV-negative adolescents scoring in the red and amber zones for the total MABC-2 score (p = 0.054), thus highlighting the risk of poor motor performance in PHIVA.

Studies have shown a decline in motor function over time in adults living with HIV (Elicer et al., 2018) and that CLHIV face developmental delay (Baillieu & Potterton, 2008; Ruel et al., 2012; Strehlau et al., 2019) but research is lacking in PHIVA. Willen et al. (2017) investigated neurocognitive outcomes in perinatally infected young adults (aged 18–24 years) and found executive dysfunction, with motor speed being significantly worse in the perinatally infected participants compared to a HIV-negative comparison group. Similarly, Horvath et al. (2018) found accelerated epigenetic aging in a group of South African PHIVA which correlated with poorer cognitive functioning, including processing speed. Neurocognitive dysfunction can be caused by delayed cortical maturation and atrophy of the motor cortex that occurs in PHIVA (Yu et al., 2019).

Poor manual dexterity has negative implications for a child's school performance, with handwriting and activities of daily living, such as playing, being affected (Gaul & Issartel, 2016; Mathisen, 2016). Children and adolescents with perinatal HIV already face neurocognitive dysfunction and poor academic performance (Garvie et al., 2014; Phillips et al., 2022; van Opstal et al., 2021) and thus decreased manual dexterity can further disadvantage the adolescent academically.

Balance is important in all daily functioning activities such as mobility, fall prevention and quality of life (Kovács et al., 2013; Schwartz et al., 2012; Surgent et al., 2019). Balance in younger CLHIV and PHIVA has been found to be negatively affected (da Silva Pontes et al., 2019; Debeaudrap et al., 2018; Medeiros et al., 2022).

Clinical predictors

Although the multivariate regression analysis did not reveal multiple significant predictive factors, it is still of value to consider that the overall clinical picture of PHIVA can be used to predict their endurance and muscle strength, more specifically in terms of age (B = 28.239) and viral suppression (B = 13.312), respectively. Further studies involving these variables could be used to create a predictive model for physical functioning in PHIVA, especially since such a model is not currently available.

Viral load has an inverse relation to physical activity (Bopp et al., 2004) and physical functioning (Nieves-Lugo et al., 2017), resulting in a poorer health-related quality of life in people with HIV (Call et al., 2000), thus it is fitting that this study found viral suppression to be predictive of muscle strength, a component of physical health. Another study in South Africa found that BMI and Tanner staging were positively associated with muscle strength in CLHIV (Potterton et al., 2021) however our study did not assess Tanner staging nor did the authors find BMI to be a predictive factor. This may be because the participants in the study by Potterton et al. (2021) were younger (age 5–11 years) than the current study's participants and thus the results cannot be a direct comparison.

This study found age to have a negative prediction on the aiming and catching component of the MABC-2 (B = −0.892). Since PHIVA show smaller increases in physical activity levels with age when compared to HIV-negative peers (Dirajlal-Fargo et al., 2021) it can be expected that with age the skill of aiming and catching would decrease, i.e., as their physical activity levels are lower.

Limitations and recommendations

The participants of this study were accessed from only one clinical site, thus the results are not generalisable to all PHIVA. Furthermore, the HIV-negative participants were mostly siblings of the PHIVA participants and thus may have been HIV-exposed uninfected (HEU) adolescents, however this status was not established during data collection. Studies are showing that many HEU children still face growth and neurodevelopmental sequelae (Wedderburn et al., 2019) and thus the negative outcomes of this study's PHIVA may be even greater when compared to HIV-unexposed uninfected (HUU) adolescents. Future recommendations for research would be to replicate this study using HUU adolescents as a comparative group and to investigate the same outcome measures in PHIVA who are not as well managed medically as this group.

An additional recommendation is for research on endurance in PHIVA using the shuttle run test. To the best of the authors' knowledge, no other studies

have used the shuttle run test to assess endurance in PHIVA and future research would be beneficial, both in the PHIVA population and the general South African adolescent population.

Conclusion

This study aimed to establish the physical sequelae of perinatal HIV in adolescents. The results showed that PHIVA have significant sequelae in height, weight and motor performance. It is of particular concern that these deficits are apparent in PHIVA who are mostly virally suppressed and well managed medically, highlighting the clinical concern for PHIVA across the rest of the globe who do not necessarily have sufficient access to health care and regular monitoring. A population-specific model of care and regular screening of physical sequelae in PHIVA is recommended for clinical practice to try and mitigate these deficits.

Acknowledgements

The authors wish to acknowledge the hard work of the research assistants and all of the staff at the research site, as well as the participants and their caregivers, without whom this research would not have been possible. All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Nicolette Comley-White. The first draft of the manuscript was written by Nicolette Comley-White and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Ethics approval

Approval was obtained from the Human Research Ethics Committee (Medical) of the University of the Witwatersrand (M180226). The procedures used in this study adhere to the tenets of the Declaration of Helsinki.

Consent

All caregivers and children signed consent and assent respectively.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Funding

Funding for this study was obtained through the South African Society of Physiotherapy and the University of the Witwatersrand.

Data availability statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ORCID

Nicolette Comley-White http://orcid.org/0000-0002-6834-4104
Veronica Ntsiea http://orcid.org/0000-0003-4208-5498
Joanne Potterton http://orcid.org/0000-0002-8020-274X

References

Anderson, K., Muloiwa, R., & Davies, M.-A. (2020). Long-term outcomes in perinatally HIV-infected adolescents and young adults on antiretroviral therapy: A review of South African and global literature. *African Journal of AIDS Research*, 1–12. https://doi.org/10.2989/16085906.2019.1676802

Arbeitman, L. E., O'Brien, R. C., Somarriba, G., Messiah, S. E., Neri, D., Scott, G. B., & Miller, T. L. (2014). Body mass index and waist circumference of HIV-infected youth in a Miami cohort. *Journal of Pediatric Gastroenterology & Nutrition*, *59*(4), 449–454. https://doi.org/10.1097/MPG.0000000000000394

Baillieu, N., & Potterton, J. (2008). The extent of delay of language, motor, and cognitive development in HIV-positive infants. *Journal of Neurologic Physical Therapy*, *32*(3), 118–121. https://doi.org/10.1097/NPT.0b013e3181846232

Bellavia, A., Williams, P. L., DiMeglio, L. A., Hazra, R., Abzug, M. J., Patel, K., Jacobson, D. L., Van Dyke, R. B., & Geffner, M. E. (2017). Delay in sexual maturation in perinatally HIV-infected youths is mediated by poor growth. *Aids (London, England)*, *31*(9), 1333–1341. https://doi.org/10.1097/QAD.0000000000001486

Bopp, C. M., Phillips, K. D., Fulk, L. J., Dudgeon, W. D., Sowell, R., & Hand, G. A. (2004). Physical activity and immunity in HIV-infected individuals. *AIDS Care*, *16*(3), 387–393. https://doi.org/10.1080/09540120410001665385

Cade, W. T., Peralta, L., & Keyser, R. E. (2002). Aerobic capacity in late adolescents infected with HIV and controls. *Pediatric Rehabilitation*, *5*(3), 161–169. https://doi.org/10.1080/1363849021000039362

Call, S. A., Klapow, J. C., Stewart, K. E., Westfall, A. O., Mallinger, A. P., DeMasi, R. A., Centor, R., & Saag, M. S. (2000). Health-related quality of life and virologic outcomes in an HIV clinic. *Quality of Life Research*, *9*(9), 977–985. https://doi.org/10.1023/A:1016668802328

Chisati, E., & Vasseljen, O. (2015). Aerobic endurance in HIV-positive young adults and HIV-negative controls in Malawi. *Malawi Medical Journal*, *27*(1), 5. https://doi.org/10.4314/mmj.v27i1.2

Comley-White, N., Potterton, J., & Ntsiea, V. (2019). The physical sequelae of perinatally acquired HIV in adolescents: A research proposal. *BMC Research Notes*, *12*(1), 62. https://doi.org/10.1186/s13104-019-4079-5

Comley-White, N., Potterton, J., & Ntsiea, V. (2021). The perceived challenges of perinatal HIV in adolescents: A

qualitative study. *Vulnerable Children and Youth Studies*, 320–333. https://doi.org/10.1080/17450128.2021.1891358

Crookston, B. T., Dearden, K. A., Alder, S. C., Porucznik, C. A., Stanford, J. B., Merrill, R. M., Dickerson, T. T., & Penny, M. E. (2011). Impact of early and concurrent stunting on cognition: Impact of stunting on cognition. *Maternal & Child Nutrition*, *7*(4), 397–409. https://doi.org/10.1111/j.1740-8709.2010.00255.x

Cruz, M., & Cardoso, C. (2015). Perinatally infected adolescents living with human immunodeficiency virus (perinatally human immunodeficiency virus). *World Journal of Virology*, *4*(3), 277–284. https://doi.org/10.5501/wjv.v4.i3.277

da Silva Pontes, L., Callegari, B., Magno, L., Moraes, A., Silva, B. G., Manso, K., Barros, B., Araújo, A. P., Silva, M. C., Dias, G. A., Vasconcelos, B. H., Costa e Silva, A., Libonati, R. M., & Souza, G. S. (2019). Variations in plantar pressure and balance in HIV-infected children in antiretroviral therapy. *Scientific Reports*, *9*(1), 4344. https://doi.org/10.1038/s41598-019-41028-0

Debeaudrap, P., Bodeau-Livinec, F., Pasquier, E., Germanaud, D., Ndiang, S. T., Nlend, A. N., Ndongo, F. A., Guemkam, G., Penda, C. I., Warszawski, J., Koecher, D., Faye, A., & Tejiokem, M. C. (2018). Neurodevelopmental outcomes in HIV-infected and uninfected African children. *Aids (London, England)*, *32*(18), 2749–2757. https://doi.org/10.1097/QAD.0000000000002023

de Lima, L. R. A., Silva, D. A. S., Silva, K. S. d., Pelegrini, A., Back, I. d. C., & Petroski, E. L. (2017). Aerobic fitness and moderate to vigorous physical activity in children and adolescents living with HIV. *Pediatric Exercise Science*, *29*(3), 377–387. https://doi.org/10.1123/pes.2017-0036

de Onis, M. (2007). Development of a WHO growth reference for school-aged children and adolescents. *Bulletin of the World Health Organization*, *85*(09), 660–667. https://doi.org/10.2471/BLT.07.043497

Dewey, K. G., & Begum, K. (2011). Long-term consequences of stunting in early life. *Maternal & Child Nutrition*, *7* (Suppl 3), 5–18. https://doi.org/10.1111/j.1740-8709.2011.00349.x

Dirajlal-Fargo, S., Williams, P. L., Broadwell, C., McFarland, E. J., Powis, K. M., Jacobson, D. L., Jao, J., & for the Pediatric HIV/AIDS Cohort Study (PHACS). (2021). Brief report: Youth living with perinatally acquired HIV have lower physical activity levels as they age compared with HIV-exposed uninfected youth. *JAIDS Journal of Acquired Immune Deficiency Syndromes*, *87*(1), 700–705. https://doi.org/10.1097/QAI.0000000000002622

Eba, P. M., & Lim, H. (2017). Reviewing independent access to HIV testing, counselling and treatment for adolescents in HIV-specific laws in sub-Saharan Africa: Implications for the HIV response. *Journal of the International AIDS Society*, *20*(1), 21456. https://doi.org/10.7448/IAS.20.1.21456

Elicer, I., Byrd, D., Clark, U. S., Morgello, S., & Robinson-Papp, J. (2018). Motor function declines over time in human immunodeficiency virus and is associated with cerebrovascular disease, while HIV-associated neurocognitive disorder remains stable. *Journal of NeuroVirology*, *24*(4), 514–522. https://doi.org/10.1007/s13365-018-0640-6

Evans, D. (2013). Ten years on ART – where to now? *South African Medical Journal*, *103*(4), 229. https://doi.org/10.7196/SAMJ.6835

Fairlie, L., Sipambo, N., Fick, C., & Moultrie, H. (2014). Focus on adolescents with HIV and AIDS. *South African Medical Journal*, *104*(12), 897. https://doi.org/10.7196/SAMJ.9110

Ferrand, R. A., Desai, S. R., Hopkins, C., Elston, C. M., Copley, S. J., Nathoo, K., Ndhlovu, C. E., Munyati, S., Barker, R. D., Miller, R. F., Bandason, T., Wells, A. U., & Corbett, E. L. (2012). Chronic lung disease in adolescents with delayed diagnosis of vertically acquired HIV infection. *Clinical Infectious Diseases*, *55*(1), 145–152. https://doi.org/10.1093/cid/cis271

Flynn, P. M., & Abrams, E. J. (2019). Growing up with perinatal HIV. *Aids (London, England)*, *33*(4), 597–603. https://doi.org/10.1097/QAD.0000000000002092

Garvie, P. A., Zeldow, B., Malee, K., Nichols, S. L., Smith, R. A., Wilkins, M. L., & Williams, P. L. (2014). Discordance of cognitive and academic achievement outcomes in youth with perinatal HIV exposure. *Pediatric Infectious Disease Journal*, *33*(9), e232–e238. https://doi.org/10.1097/INF.0000000000000314

Gaul, D., & Issartel, J. (2016). Fine motor skill proficiency in typically developing children: On or off the maturation track? *Human Movement Science*, *46*, 78–85. https://doi.org/10.1016/j.humov.2015.12.011

Githinji, L. N., Gray, D. M., Hlengwa, S., Myer, L., & Zar, H. J. (2017). Lung function in South African adolescents infected perinatally with HIV and treated long-term with antiretroviral therapy. *Annals of the American Thoracic Society*, *14*(5), 722–729. https://doi.org/10.1513/AnnalsATS.201612-1018OC

Githinji, L. N., Mahtab, S., Zühlke, L., Lawrenson, J., Myer, L., Gray, D., & Zar, H. (2019). Cardiopulmonary dysfunction in perinatally HIV-infected South African adolescents on antiretroviral therapy: Baseline findings from the Cape Town adolescent antiretroviral cohort. *Journal of the International AIDS Society*, *22*. https://doi.org/10.1002/jia2.25340

Harding, K. L., Aguayo, V. M., & Webb, P. (2018). Factors associated with wasting among children under five years old in South Asia: Implications for action. *PLOS ONE*, *13* (7), e0198749. https://doi.org/10.1371/journal.pone.0198749

Hardy, L. L., Merom, D., Thomas, M., & Peralta, L. (2018). 30-year changes in Australian children's standing broad jump: 1985–2015. *Journal of Science and Medicine in Sport*, *21* (10), 1057–1061. https://doi.org/10.1016/j.jsams.2018.04.005

Horvath, S., Stein, D. J., Phillips, N., Heany, S. J., Kobor, M. S., Lin, D. T., Myer, L., Zar, H. J., Levine, A. J., & Hoare, J. (2018). Perinatally acquired HIV infection accelerates epigenetic aging in South African adolescents. *AIDS (London, England)*, *32*(11), 1465–1474. https://doi.org/10.1097/QAD.0000000000001854

Iloh, O. N., Iloh, K. K., Ubesie, A. C., Emodi, I. J., Ikefuna, A. N., & Ibeziako, N. S. (2017). Comparison of tanner staging of HIV-infected and uninfected girls at the university of Nigeria teaching hospital, ituku/ozalla, enugu, Nigeria. *Journal of Pediatric Endocrinology and Metabolism*, *30*(7), https://doi.org/10.1515/jpem-2016-0356

Jesson, J., Schomaker, M., Malasteste, K., Wati, D. K., Kariminia, A., Sylla, M., Kouadio, K., Sawry, S., Mubiana-Mbewe, M., Ayaya, S., Vreeman, R., McGowan, C. C., Yotebieng, M., Leroy, V., Davies, M., & the IeDEA global

cohort consortium. (2019). Stunting and growth velocity of adolescents with perinatally acquired HIV: Differential evolution for males and females. A multiregional analysis from the IeDEA global paediatric collaboration. *Journal of the International AIDS Society*, *22*(11), https://doi.org/10.1002/jia2.25412

Keyser, R. E., Peralta, L., Cade, W. T., Miller, S., & Anixt, J. (2000). Functional aerobic impairment in adolescents seropositive for HIV: A quasiexperimental analysis. *Archives of Physical Medicine and Rehabilitation*, *81*(11), 1479–1484. https://doi.org/10.1053/apmr.2000.17810

Kovács, E., Prókai, L., Mészáros, L., & Gondos, T. (2013). Adapted physical activity is beneficial on balance, functional mobility, quality of life and fall risk in community-dwelling older women: A randomized single-blinded controlled trial. *European Journal of Physical and Rehabilitation Medicine*, *49*(3), 301–310.

Laughton, B., Cornell, M., Boivin, M., & Van Rie, A. (2013). Neurodevelopment in perinatally HIV-infected children: A concern for adolescence. *Journal of the International AIDS Society*, *16*(1), 18603. https://doi.org/10.7448/IAS.16.1.18603

Lowenthal, E. D., Bakeera-Kitaka, S., Marukutira, T., Chapman, J., Goldrath, K., & Ferrand, R. A. (2014). Perinatally acquired HIV infection in adolescents from sub-Saharan Africa: A review of emerging challenges. *The Lancet Infectious Diseases*, *14*(7), 627–639. https://doi.org/10.1016/S1473-3099(13)70363-3

Macdonald, H., Nettlefold, L., Maan, E., Côté, H., & Alimenti, A. (2017). Muscle power in children, youth and young adults who acquired HIV perinatally. *Journal of Musculoskeletal and Neuronal Interactions*, *17*(2), 27–37.

Martins, P. C., de Lima, L. R. A., Teixeira, D. M., de Carvalho, A. P., & Petroski, E. L. (2017). Physical activity and body fat in adolescents living with HIV: A comparative study. *Revista Paulista de Pediatria*, *35*(1), 69–77. https://doi.org/10.1590/1984-0462/;2017;35;1;00012

Mathisen, G. (2016). Motor competence and implications in primary school. *Journal of Physical Education and Sport*, *16*(1), 206–209. https://doi.org/10.7752/jpes.2016.01032

Medeiros, R. C. d. S. C. d., Silva, R. G. d., Medeiros, R. M. V., Goes, C. J. D. d., Medeiros, J. A. d., Santos, I. K. d., Wilde, P., Barela, J. A., Cabral, B. G. d. A. T., & Dantas, P. M. S. (2022). Performance of postural balance in children and adolescents living with and without HIV. *Gait & Posture*, *91*, 42–47. https://doi.org/10.1016/j.gaitpost.2021.09.204

Menéndez-Arias, L., & Delgado, R. (2022). Update and latest advances in antiretroviral therapy. *Trends in Pharmacological Sciences*, *43*(1), 16–29. https://doi.org/10.1016/j.tips.2021.10.004

Miller, R. F., Kaski, J. P., Hakim, J., Matenga, J., Nathoo, K., Munyati, S., Desai, S. R., Corbett, E. L., & Ferrand, R. A. (2013). Cardiac disease in adolescents with delayed diagnosis of vertically acquired HIV infection. *Clinical Infectious Diseases*, *56*(4), 576–582. https://doi.org/10.1093/cid/cis911

Mwalukomo, T., Rylance, S. J., Webb, E. L., Anderson, S., O'Hare, B., van Oosterhout, J. J., Ferrand, R. A., Corbett, E. L., & Rylance, J. (2016). Clinical characteristics and lung function in older children vertically infected With human immunodeficiency virus in Malawi. *Journal of the Pediatric Infectious Diseases Society*, *5*(2), 161–169. https://doi.org/10.1093/jpids/piv045

Nieves-Lugo, K., del Rio-Gonzalez, A. M., Reisen, C., Poppen, P., Oursler, K. K., & Zea, M. C. (2017). Greater depressive symptoms and higher viral load are associated with poor physical function among Latino Men living with HIV. *Journal of the International Association of Providers of AIDS Care (JIAPAC)*, *16*(1), 30–36. https://doi.org/10.1177/2325957416640363

Osler, M., Hilderbrand, K., Goemaere, E., Ford, N., Smith, M., Meintjes, G., Kruger, J., Govender, N. P., & Boulle, A. (2018). The continuing burden of advanced HIV disease over 10 years of increasing antiretroviral therapy coverage in South Africa. *Clinical Infectious Diseases*, *66*(suppl_2), S118–S125. https://doi.org/10.1093/cid/cix1140

Pandey, A., & Galvani, A. (2019). The global burden of HIV and prospects for control. *The Lancet HIV*, *6*(12), e809–e811. https://doi.org/10.1016/S2352-3018(19)30230-9

Phillips, N., Thomas, K. G. F., Mtukushe, B., Myer, L., Zar, H. J., Stein, D. J., & Hoare, J. (2022). Youth perinatal HIV-associated neurocognitive disorders: Association with functional impairment. *AIDS Care*, *34*(2), 1–5. https://doi.org/10.1080/09540121.2021.1891191

Potterton, J., Strehlau, R., Shiau, S., Comley-White, N., Kuhn, L., & Arpadi, S. (2021). Muscle strength in young children perinatally infected with HIV who were initiated on antiretroviral therapy early. *South African Journal of Child Health*, *15*(2), 107–111. https://doi.org/10.7196/SAJCH.2021.v15.i2.1809

Potterton, J., Strehlau, R., Shiau, S., Comley-White, N., Kuhn, L., & Yin, M., et al. (2022). Evaluation of submaximalendurance in young children living with HIV. *South African Journal of Physiotherapy*, *78*(1), a1613. https://doi.org/10.4102/sajp.v78i1.1613

Ramos, E., Guttierrez-Teissoonniere, S., Conde, J. G., Baez-Cordova, J. A., Guzman-Villar, B., Lopafegui-Corsino, E., & Frontera, W. R. (2012). Anaerobic power and muscle strength in human immunodeficiency virus-positive preadolescents. *PM & R: The Journal of Injury, Function, and Rehabilitation*, *4*(3), 171–175. https://doi.org/10.1016/j.pmrj.2011.11.009

Ruel, T. D., Boivin, M. J., Boal, H. E., Bangirana, P., Charlebois, E., Havlir, D. V., Rosenthal, P. J., Dorsey, G., Achan, J., Akello, C., Kamya, M. R., & Wong, J. K. (2012). Neurocognitive and motor deficits in HIV-infected Ugandan children with high CD4 cell counts. *Clinical Infectious Diseases*, *54*(7), 1001–1009. https://doi.org/10.1093/cid/cir1037

Saint-Maurice, P. F., Laurson, K. R., Kaj, M., & Csányi, T. (2015). Establishing normative reference values for standing broad jump Among Hungarian youth. *Research Quarterly for Exercise and Sport*, *86*(sup1), S37–S44. https://doi.org/10.1080/02701367.2015.1042416

Sam-Agudu, N. A., Folayan, M. O., & Ezeanolue, E. E. (2016). Seeking wider access to HIV testing for adolescents in sub-Saharan Africa. *Pediatric Research*, *79*(6), 838–845. https://doi.org/10.1038/pr.2016.28

Schwartz, I., Kandel, L., Sajina, A., Litinezki, D., Herman, A., & Mattan, Y. (2012). Balance is an important predictive factor for quality of life and function after primary total knee replacement. *The Journal of Bone and Joint Surgery. British*, *94-B*(6), 782–786. https://doi.org/10.1302/0301-620X.94B6.27874

Sims Sanyahumbi, A. E., Hosseinipour, M. C., Guffey, D., Hoffman, I., Kazembe, P. N., McCrary, M., Minard, C.

G., van der Horst, C., & Sable, C. A. (2017). HIV-infected children in Malawi have decreased performance on the 6-minute walk test with preserved cardiac mechanics regardless of antiretroviral treatment status. *Pediatric Infectious Disease Journal*, *36*(7), 659–664. https://doi.org/10.1097/INF.0000000000001540

Smith, R., & Wilkins, M. (2015). Perinatally acquired HIV infection: Long-term neuropsychological consequences and challenges ahead. *Child Neuropsychology*, *21*(2), 234–268. https://doi.org/10.1080/09297049.2014.898744

Sohn, A. H., & Hazra, R. (2013). The changing epidemiology of the global paediatric HIV epidemic: Keeping track of perinatally HIV-infected adolescents. *Journal of the International AIDS Society*, *16*(1), 18555. https://doi.org/10.7448/IAS.16.1.18555

Somarriba, G., Lopez-Mitnik, G., Ludwig, D. A., Neri, D., Schaefer, N., Lipshultz, S. E., Scott, G. B., & Miller, T. L. (2013). Physical fitness in children infected with the human immunodeficiency virus: Associations with highly active antiretroviral therapy. *AIDS Research and Human Retroviruses*, *29*(1), 112–120. https://doi.org/10.1089/aid.2012.0047

Strehlau, R., van Aswegen, T., & Potterton, J. (2019). Interventions addressing neurodevelopmental delay in young children infected with and exposed to HIV: A scoping review. *Rehabilitation Oncology*, *37*(1), 7–16. https://doi.org/10.1097/01.REO.0000000000000150

Surgent, O. J., Dadalko, O. I., Pickett, K. A., & Travers, B. G. (2019). Balance and the brain: A review of structural brain correlates of postural balance and balance training in humans. *Gait & Posture*, *71*, 245–252. https://doi.org/10.1016/j.gaitpost.2019.05.011

Tomkinson, G. R., Lang, J. J., Tremblay, M. S., Dale, M., LeBlanc, A. G., Belanger, K., Ortega, F. B., & Léger, L. (2017). International normative 20 m shuttle run values from 1 142 026 children and youth representing 50 countries. *British Journal of Sports Medicine*, *51*(21), 1545–1554. https://doi.org/10.1136/bjsports-2016-095987

UNICEF. (2016). *Adolescents living with HIV: Developing and strengthening care and support services*, Geneva: UNICEF Regional office for central and Eastern Europe and the commonwealth of independent states (CEECIS). https://www.unicef.org/eca/sites/unicef.org.eca/files/2017-10/Adolescents_Living_with_HIV.pdf.

UNICEF. (2020a). *Adolescent HIV prevention*. UNICEF DATA. https://data.unicef.org/topic/hivaids/adolescents-young-people/.

UNICEF. (2020b). *Hiv statistics—global and regional trends*. UNICEF DATA. https://data.unicef.org/topic/hivaids/global-regional-trends/.

van Opstal, S. E. M., Wagener, M. N., Miedema, H. S., Utens, E. M. W. J., Aarsen, F. K., van der Knaap, L. C., van Gorp, E. C. M., van Rossum, A. M. C., & Roelofs, P. D. D. M. (2021). School functioning of children with perinatal HIV-infection in high-income countries: A systematic review. *PLOS ONE*, *16*(6), e0252746. https://doi.org/10.1371/journal.pone.0252746

Vexler, A., & Hutson, A. D. (2018). *Statistics in the health sciences: Theory, applications, and computing* (1st ed.). Chapman and Hall/CRC. https://doi.org/10.1201/b21899.

Wedderburn, C. J., Evans, C., Yeung, S., Gibb, D. M., Donald, K. A., & Prendergast, A. J. (2019). Growth and neurodevelopment of HIV-exposed uninfected children: A conceptual framework. *Current HIV/AIDS Reports*, *16*(6), 501–513. https://doi.org/10.1007/s11904-019-00459-0

Whitehead, N., Potterton, J., & Coovadia, A. (2014). The neurodevelopment of HIV-infected infants on HAART compared to HIV-exposed but uninfected infants. *AIDS Care*, *26*(4), 497–504. https://doi.org/10.1080/09540121.2013.841828

Willen, E. J., Cuadra, A., Arheart, K. L., Post, M. J. D., & Govind, V. (2017). Young adults perinatally infected with HIV perform more poorly on measures of executive functioning and motor speed than ethnically matched healthy controls. *AIDS Care*, *29*(3), 387–393. https://doi.org/10.1080/09540121.2016.1234677

Williams, P. L., & Jesson, J. (2018). Growth and pubertal development in HIV-infected adolescents. *Current Opinion in HIV and AIDS*, *13*(3), 179–186. https://doi.org/10.1097/COH.0000000000000450

World Health Organization. (2008). *World health organization. Training course on child growth assessment*. WHO.

World Health Organization. (2014). *Health for the world's adolescents: A second chance in the second decade*. http://apps.who.int/adolescent/second-decade/files/1612_MNCAH_HWA_Executive_Summary.pdf.

World Health Organization. (2021). *Growth reference data for 5-19 years—Indicators*. https://www.who.int/tools/growth-reference-data-for-5to19-years/indicators.

Yu, X., Gao, L., Wang, H., Yin, Z., Fang, J., Chen, J., Li, Q., Xu, H., & Gui, X. (2019). Neuroanatomical changes underlying vertical HIV infection in adolescents. *Frontiers in Immunology*, *10*, 814. https://doi.org/10.3389/fimmu.2019.00814