# Physical sequelae of growing into adolescence with perinatally acquired HIV: a scoping review protocol

Nicolette Comley-White • Joanne Potterton • Veronica Ntsiea

*Department of Physiotherapy, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa*

## ABSTRACT

**Objective:** This scoping review aims to identify and describe the physical sequelae experienced by adolescents with perinatally acquired HIV.

**Introduction:** Perinatally acquired HIV is a prevalent condition affecting adolescents. It results in neurocognitive dysfunction and mental health challenges. Data show that some of the physical challenges facing this population include stunted growth and delayed puberty; however, other physical challenges remain largely unknown.

**Inclusion criteria:** This review will consider studies that include adolescents aged 10 to 19 years, with perinatally (vertically) acquired HIV. Adolescents from any geographic area, of any ethnicity or socioeconomic background will be considered. The concepts included will be all physical sequelae of perinatally acquired HIV. Studies of any research design, including quantitative, qualitative, and mixed methods, as well as systematic reviews, will be considered.

**Methods:** This review will utilize a three-step search strategy. There will be an initial search of MEDLINE (PubMed), followed by a full search of MEDLINE (PubMed), PEDro, CINAHL (EBSCO), Scopus (Elsevier), ScienceDirect (Elsevier), and Google Scholar. Gray literature will be searched using CDC Stacks and OpenGrey. Lastly, the reference lists of all articles will be checked for additional studies. Titles and abstracts will be screened by two independent reviewers against the inclusion criteria, and a third reviewer will resolve any discrepancies. Results will be charted on a data extraction tool and presented with a table, diagrammatic representation, and a descriptive narrative.

**Keywords:** adolescence; HIV; human immunodeficiency virus; perinatal

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## Introduction

HIV is one of the leading causes of death in adolescents globally,[1] and especially of concern in Africa.[2] There were approximately 1.7 million adolescents living with HIV worldwide in 2019.[3] The infection in these adolescents is transmitted either vertically (from mother to child) or horizontally (from someone other than the mother), and although data show that the most common route of transmission is vertical, there are no exact numbers on the prevalence of adolescents with perinatal HIV across the globe.[4]

Due to the increasing availability of antiretroviral therapy (ART), there is a growing number of adolescents with perinatally acquired HIV, at which point the disease is considered a chronic condition. This creates the challenge of living with a chronic disease and using lifelong medication.[5,6] Although the pediatric brain has high levels of neural plasticity, it is vulnerable to environmental changes, and adverse environmental factors can affect normal development.[7] HIV is a neurotropic virus that is able to cross the blood-brain barrier, thus changing the environment of the developing pediatric brain.[8] In addition, the blood-brain barrier makes it challenging for ART to penetrate the central nervous system,[9] and ART medications themselves have a variety of neurotoxic effects.[10]

Research has shown the adverse effects of perinatally acquired HIV on neurodevelopment, including cognitive and neurological complications in children.[11-13] Adults also face a range of neurological complications from HIV.[14,15] However, literature is emerging showing the sequelae of perinatally acquired HIV in adolescents, with most of the data

*Correspondence:* Nicolette Comley-White, nicolette.comley-white@wits.ac.za

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pertaining to neurocognitive challenges (as opposed to physical and developmental impairments), and the majority of the studies are from resource-rich countries,[16] despite 84% of adolescents with HIV living in sub-Saharan Africa.[2] These studies show that adolescents with perinatally acquired HIV are at a higher risk of mental health challenges, neurocognitive dysfunction, decreased cognition, and decreased processing speed.[5,16-18]

In addition to neurocognitive sequelae, studies have shown that this population also faces certain physical challenges, such as stunting[19,20] and delayed puberty.[21] Stunted growth in children with perinatal HIV is well-established[22] and appears to continue into adolescence, with up to 34.4% of males and 39.5% of females stunted in adolescence.[19] Poor growth has been shown to mediate a delayed onset of sexual maturation in adolescents with perinatally acquired HIV,[21] resulting in late onset of puberty.[18] Stunted growth and pubertal delay are multifactorial consequences of perinatal HIV, with some of the key factors to consider including chronic inflammation, endocrine dysfunction, other infectious or immunological diseases (eg, tuberculosis, pneumonia), and nutritional disorders.[19,23,24]

There is a call in the literature for further research and development of policies in the field of neurodevelopment in adolescents with perinatally acquired HIV.[16,18] Although there are emerging data on the neurocognitive (and some physical) effects of perinatal HIV in adolescence, there are still gaps in the knowledge base. Establishing the existing evidence will aid researchers in identifying these gaps in knowledge, thus informing future studies and research. Additionally, a scoping review will collate and present the known physical sequelae in this population, which may be useful to clinicians for developing a model of care. The aim of this scoping review is therefore to identify and describe the physical sequelae experienced by adolescents with perinatally acquired HIV.

A preliminary search of the Cochrane Database of Systematic Reviews and *JBI Evidence Synthesis* was conducted, which showed no current scoping reviews or systematic reviews on the topic.

## Review question

What does the literature report about the physical sequelae of perinatally acquired HIV in adolescents?

## Inclusion criteria

The inclusion criteria for this scoping review were guided using the population, concept, and context model (PCC) following JBI methodology.[25]

### *Participants*

This review will consider studies that include participants who are adolescents (ranging from 10 to 19 years of age[26,27]) living with perinatally acquired HIV infection.

### *Concept*

This review will consider studies that identify the physical sequelae for perinatally acquired HIV in adolescence. This incorporates (but is not limited to) body mass index, endurance, muscle strength, fatigue, pain, height, weight, head circumference, and pubertal changes.

Perinatally acquired HIV is defined as the mother-to-child transmission of HIV through pregnancy, birth, or breastfeeding.[28] This is also known as vertical transmission.

### *Context*

This review will consider studies that are from countries of any income classifications, rural or urban location, and any ethnic or socioeconomic background.

### *Types of sources*

This scoping review will include all study designs: quantitative, qualitative, and mixed methods. In addition, systematic reviews and meta-analyses will be considered. Gray (unpublished) literature will also be considered.

## Methods

The proposed review will be conducted in accordance with the JBI methodology for scoping reviews,[25] following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) checklist.[29]

### *Search strategy*

A three-step search strategy will be used. The first step was an initial limited search of MEDLINE (PubMed) and CINAHL (EBSCO) to identify articles on the topic. The text words contained in the titles and abstracts of relevant articles, as well as the index

terms used to describe the articles, were used to develop a full search strategy for MEDLINE (PubMed; see Appendix I). Subsequently, a full second search across all of the included databases will be implemented. Thirdly, the reference lists of all included articles will be searched for additional studies. The reviewers will contact the authors of key studies for further information if needed. All studies published in English will be considered, with no date limit. It is expected that the majority of the studies will be published from 2005 onwards because ART initiation occurred globally between 1996 and 2003,[30] allowing babies with perinatally acquired HIV infection to live into adolescence and beyond. However, the search will not be limited to this time period to allow for maximum citation yield.

The initial keywords searched will be HIV, adolescence, adolescents, perinatal, perinatally acquired HIV, vertically transmitted, and sequelae.

The databases to be searched include MEDLINE (PubMed), PEDro, CINAHL (EBSCO), Scopus (Elsevier), ScienceDirect (Elsevier), and Google Scholar. A search for gray literature will be conducted in CDC Stacks and OpenGrey.

### *Study selection*

Following the search, all identified records will be collated and uploaded into Zotero v5.0.89 (Corporation for Digital Scholarship and Roy Rosenzweig Center for History and New Media, VA, USA), and duplicates removed. Titles and abstracts will then be screened by two independent reviewers (JP and NCW, both of whom are physiotherapists with a clinical research and publication-related background in HIV) for assessment against the inclusion criteria for the review. Studies that meet the inclusion criteria will be retrieved in full and reassessed by the reviewers. Reasons for exclusion of papers at the full-text screening stage will be recorded and reported in the scoping review. Any disagreements that arise between the reviewers at each stage of the selection process will be resolved through discussion and consensus, and if consensus cannot be reached, then a third reviewer (VN) will be consulted. A PRISMA-ScR checklist[29] and the PRISMA flow diagram[31] will be used to present the results of the search.

### *Data extraction*

Results from articles meeting the inclusion criteria will be charted using a data extraction tool under the following headings: author(s), year of publication, title, study design, aim/purpose, population/participants, sample size, concept, context, key findings (specific to physical sequelae), reviewer's summary, and other points of note (see Appendix II). The data will be extracted from the papers by the primary reviewer (NCW) and captured on the data extraction tool. Because charting is an iterative process, the tool will be updated with additional data if it is deemed necessary in the process, and any modifications will be described in the full scoping review. A second, independent reviewer (JP) will verify the data extraction by checking the results against the full-text articles.

### *Data analysis and presentation*

The extracted data will be presented in a table to map the existing literature specific to the key findings of physical sequelae in adolescents with perinatally acquired HIV. A diagrammatic representation will be used to summarize these sequelae, and a descriptive narrative of the available literature will be provided linking the results to the review's objective and question.

## Acknowledgments

This scoping review will contribute toward the completion of a doctoral degree for author NCW.

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## Appendix I: Search strategy

**MEDLINE (PubMed)**
Search performed in August 5, 2020

| No. | Search | Records retrieved |
|---|---|---|
| #10 (#4 OR #9) | Search (((((((perinatal HIV[Text Word]) OR perinatally acquired HIV[Text Word]) OR vertical HIV[Text Word]) OR vertically transmitted[Text Word])) AND adolescen*[Text Word]) AND (((sequel*[Text Word]) OR outcome*[Text Word]) OR complication*[Text Word])))) OR ((((complications[MeSH Subheading]) AND HIV[MeSH Terms]) AND ((adolescent[MeSH Terms]) OR pediatric[MeSH Terms])) AND "infectious disease transmission, vertical"[MeSH Terms]) | 655 |
| #9 (#5 AND #6 AND #7 AND #8) | Search (((complications[MeSH Subheading]) AND HIV[MeSH Terms]) AND ((adolescent[MeSH Terms]) OR pediatric[MeSH Terms])) AND "infectious disease transmission, vertical"[MeSH Terms] | 13 |
| #8 | Search "infectious disease transmission, vertical"[MeSH Terms] | 3639 |
| #7 | Search (adolescent[MeSH Terms]) OR pediatric[MeSH Terms] | 273,740 |
| #6 | Search HIV[MeSH Terms] | 30,854 |
| #5 | Search complications[MeSH Subheading] | 234,688 |
| #4 (#1 AND #2 AND #3) | Search ((((((perinatal HIV[Text Word]) OR perinatally acquired HIV[Text Word]) OR vertical HIV[Text Word]) OR vertically transmitted[Text Word])) AND adolescen*[Text Word]) AND (((sequel*[Text Word]) OR outcome*[Text Word]) OR complication*[Text Word]) | 645 |
| #3 | Search ((sequel*[Text Word]) OR outcome*[Text Word]) OR complication*[Text Word] | 1,958,956 |
| #2 | Search adolescen*[Text Word] | 157,008 |
| #1 | Search (((perinatal HIV[Text Word]) OR perinatally acquired HIV[Text Word]) OR vertical HIV[Text Word]) OR vertically transmitted[Text Word] | 8293 |

## Appendix II: Data extraction form

| Author(s) | Year of publication | Title | Study design | Aim/ purpose | Population/ participant details (eg, age, sex, number) | Sample size | Concept | Context | Key findings (specific to physical sequelae) | Reviewer's summary | Other points of note |
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