COLLABORATIVE INITIATIVE FOR PAEDIATRIC HIV EDUCATION AND RESEARCH

2019 ANNUAL REPORT
ACKNOWLEDGEMENTS

CIPHER Scientific and Technical Advisory Committee
Annette Sohn, TREAT Asia/amfAR, Thailand
Celia Christie-Samuels, University of West Indies, Jamaica
Chewe Luo, UNICEF, USA
Diana Gibb, MRC Clinical Trials Unit, UK
François Dabis, INSERM, Université Victor Segalen Bordeaux, France
Laura Guay, Elizabeth Glaser Pediatric AIDS Foundation / George Washington University, USA
Linda-Gail Bekker, Desmond Tutu HIV Centre, University of Cape Town, South Africa
Lynne Mofenson, Elizabeth Glaser Pediatric AIDS Foundation, USA
Mark Cotton, Stellenbosch Children’s Hospital, South Africa
Martina Penazzato, World Health Organization, Switzerland
Rohan Hazra, US National Institutes of Health, NICHD, USA
Russell Pierre, University of West Indies, Jamaica
Shaffiq Essajee, UNICEF, United States

Support

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Produced by

Avenue de France 23, CH-1202 Geneva, Switzerland
Tel: +41 22 710 08 00 / Fax: +41 22 710 08 99
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AN UPDATED STRATEGY FOR 2019-2023

“The Global Research Agendas for Paediatric and Adolescent HIV have been a valuable resource for EDCTP during the process of setting our strategic research agenda priorities and for identifying research gaps that could be covered through EDCTP calls for proposals, to ensure that we are supporting policy-relevant and impactful research.”

Lara Pandya, Strategic Partnerships Officer, EDCTP, 2019

In 2019, the Collaborative Initiative for Paediatric HIV Education and Research (CIPHER) launched its new strategy building on findings of an in-depth review designed to ensure it adapts to progress and to new challenges, and to identify where it will have the most impact over the next five years. The review consisted of three components:

1. A global, in-depth research gap study in paediatric and adolescent HIV, in collaboration with WHO;
2. An expert consultation on the best use of observational paediatric and adolescent HIV cohort data;
3. Input gathered from CIPHER stakeholders and high-level policy makers and programmers not currently involved in the initiative.

1. Global research agendas
Using an established methodology for setting priorities in health research, CIPHER partnered with the World Health Organisation (WHO) to conduct a global study on what evidence is most needed to reach an AIDS free generation by 2030. Through this process, stakeholders worldwide – researchers, implementers, communities and young people living with HIV – were engaged in identifying the top five research themes in HIV testing, treatment and service delivery. The result was the development of the Global Research Agendas in Paediatric and Adolescent HIV, which provide guidance and aim to focus diminishing resources where they are needed most. These research agendas define the topics for the CIPHER Grant Programme, and are influencing funders and stakeholders in their decision-making processes (see above quote from Lara Pandya).

2. A collective vision for cohort research
Building on its experience with the Global Cohort Collaboration, CIPHER convened leading experts, Global Cohort Collaboration leads, implementers, WHO and UNAIDS to develop a collective vision for cohort research over the next five years. The focus was on identifying critical questions of high global public health impact where collaboration amongst cohorts is needed to inform programme planning and policy:

- Informing efforts to forecast ART need in children, and continuing to help inform the UNAIDS global estimates of the number of children living with HIV globally.
- Working together for enhanced safety and effectiveness monitoring of existing ARVs, and as new ARVs are rolled out.
- Developing tools and collaborations to provide much needed data on the epidemiology and outcomes of the rapidly growing population of HIV- and ART-exposed and uninfected children and adolescents.

3. Identifying strengths and strategic opportunities
Further to the strategy review conducted in 2018, CIPHER finalised its new strategy reflecting on the key outcomes of the review:

- The research niche of CIPHER is well defined and highly relevant; it is the strongest component of the initiative. For greater impact, new funding mechanisms and requests for proposals with strategic focus on specific topics or underserved regions, and in
languages other than English, should be developed to help address changing needs and gaps over the next five years, such as in French, for West and Central Africa.

- The capacity building of young researchers from resource-limited settings is particularly valued. This value could be enhanced by providing additional support to grantees and potential applicants in terms of networking, mentoring and training.
- With the increased need for operational and implementation science, there is a need to increasingly involve policy makers and implementers more directly in all stages of the research process, including in research that is already ongoing. This will help increase the impact of research and facilitate faster translation of evidence into action.
- Given the rapidly changing landscape and global 2020 targets for children and adolescents, a mid-term review should be done to re-align the five-year strategy in 2021.

In 2019, CIPHER applied these learnings across the initiative, galvanizing activity with an updated mission and objectives.

CIPHER mission and objectives
The mission of CIPHER is to accelerate an evidence-informed, human rights based and integrated HIV response for infants, children, adolescents and young people living with and affected by HIV. This is achieved through a capacity-building approach, supporting the development of young investigators building evidence and translating research into action in low-and-middle-income countries. CIPHER has three primary objectives:

- **Research**: Address priority knowledge gaps in paediatric and adolescent HIV through grants and fellowships, innovative capacity building and collaborative approaches.
- **Evidence to Action**: Accelerate the translation of evidence into policies, programmes and care.
- **Advocacy**: Use evidence to spotlight critical issues for children, adolescents and young people in the HIV response, and enable opportunities for meaningful engagement of children, adolescents and young people.

CIPHER Strategy 2019-2023

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RESEARCH

Strategic focus on paediatric operational science and reaching francophone investigators

CIPHER Grant and Fellowship Programmes

The 2019 round of the CIPHER Grant Programme had a strategic focus on paediatric operational science, targeting this underrepresented area highlighted both in the CIPHER/WHO Global Research Agenda for Paediatric HIV and the CIPHER strategy review. After a large response and a highly competitive selection process, at the 10th IAS Conference on HIV Science in Mexico in July 2019 (IAS 2019), CIPHER awarded three young investigators grants to address critical operational research questions for children in resource limited settings.

Recipients of the CIPHER Grant Programme:

- **Ceri Evans**: The impact of improved water, sanitation and hygiene (WASH) on cytomegalovirus co-infection in HIV-affected mothers and children in rural Zimbabwe. Read more [here](#).
- **Sarah Skeen**: Khwezi Lokusa (Early Morning Star) Project: Integrating an evidence-based intervention component to promote HIV testing of young children into community-based parenting programmes. Read more [here](#).
- **Tongdiyen Jasper**: The impact of structured caregiver peer support (CaPS) on ART adherence and viral suppression among children living with HIV in Nigeria: A randomized controlled trial, Nigeria. Read more [here](#).

Janan Dietrich was awarded a CIPHER Growing the Leaders of Tomorrow Fellowship for her project: An investigation of factors associated with viral suppression among adolescent girls and young women living with HIV and participating in the HERStory Study in six South African districts. The Fellowship programme aims to build and support clinical research leadership in paediatric and adolescent HIV in low- and middle-income countries, particularly high-burden countries in sub-Saharan Africa. CIPHER Fellows are medical practitioners from sub-Saharan Africa with clinical research experience and the potential to become the next generation of leaders in paediatric and adolescent HIV. Read more about Janan [here](#).
Impact
To date, through the grant and fellowship programmes, 35 young investigators have been awarded, representing a total of US$5 Million in grants and fellowships to enable these young investigators to address critical research gaps in low- and middle-income countries. CIPHER grants and fellowships have contributed to advancing and disseminating research findings, influencing policy and practice and leveraging additional funding for paediatric HIV research from local and international agencies as further detailed below.

Research highlights
Birkneh Tadesse and Degu Jenere’s article Hepatic and renal toxicity and associated factors among HIV-infected children on antiretroviral therapy: a prospective cohort study published in HIV medicine made the news on aidsmaps in January 2019. This study demonstrates that among HIV-positive children with liver and kidney abnormalities, liver enzyme abnormalities improved while kidney function progressively deteriorated the longer the children were on antiretroviral therapy (ART).

Through her CIPHER funded study, Wipaporn Songtaweesin was invited to attend the Thai National PrEP Forum on 29 October 2019 to celebrate the appointment of Her Royal Highness Somsawali of Thailand as the UNAIDS Goodwill Ambassador for HIV Prevention for Asia and the Pacific. Wipaporn presented the progress of her CIPHER study to Her Royal Highness (poster and oral presentation). The event, attended by Ambassador Deborah Birx (US Global AIDS) as well as senior members of the Thai Government, was broadcast on Thai National TV.

Influencing policy and practice
Adrie Bekker (2017 CIPHER fellow) has been making a tremendous policy impact. Her CIPHER study contributed to the US Pediatric Guidelines, looking at the post-natal age at the start of lopinavir/ritonavir (LPV/r) treatment. Additionally, following her presentation at the International Workshop on HIV Paediatrics in Mexico, Adrie was invited to assist with the South African nevirapine (NVP) treatment guidelines for premature infants and essential medicines list for South Africa. Adrie also received US$1.2 Million through the UNITAID Benefit Kids Grant to evaluate the PK and safety of abacavir/lamivudine/lopinavir/ritonavir (30/15/40/10mg) “4-in-1” fixed-dose combination granule formulation in HIV-exposed neonates.
Ute Feucht (2017 CIPHER grantee), as member of the National PMTCT and Paediatric HIV Technical Working Group, is a lead author of the updated South African National PMTCT Guidelines. With funding provided by the Global Fund and the World Health Organization, the updated guidelines were officially released in October 2019. Among the changes in the guidelines, there is an enhanced focus on linking of mother-infant pairs to care, and the care of HIV-exposed and uninfected children. Ute was also part of the core team to develop the accompanying PMTCT training slides being made available nationally to train health workers throughout the entire country.

Finally, CIPHER grantees and fellows also contributed to inform the UNAIDS Programme Coordinating Board (PCB) meeting held in Geneva in December 2019:

- The research of CIPHER fellow Jane Mutanga has been referenced in the UNAIDS background note document on the thematic segment "Reducing the impact of AIDS on children and youth" in preparation for the UNAIDS PCB.
- Data from the CIPHER funded “Mzantsi Wakho” and “Hey Baby” studies, led by Rebecca Hodes and Elona Toska, was presented by their mentor Lucie Cluver. Data from this group shows the impact of kindness on adolescent health and well-being. A combination of programming for safe schools, cash transfers (to cover basic necessities such as food), and parenting support synergize to hit seven Sustainable Development Goals targets for adolescents. CIPHER provided seed funding for the Mzantsi Wakho study, which now has over 25 sponsors and is informing the ACCELERATE Achievement for Africa’s Adolescents UKRI GCRF Hub.

Leveraging additional funds for future research

Birkneh Tadesse (2015 CIPHER grantee) received an EDCTP2 grant of €4 Million for a clinical trial (PREGART) on optimizing treatment options for pregnant women living with HIV and their children. Specifically, the project will explore the safety and efficacy of dolutegravir and efavirenz 400 for pregnant and breastfeeding women in Ethiopia.

“Certainly, the CIPHER project has enabled me to position myself as a principal investigator in this project. The CIPHER grant also helped me to establish collaborations with scientists all over the world, with whom I have made the application for this grant. The data generated through the CIPHER grant has helped me to gain visibility and also to assume a coordinator position for this prestigious grant” - Birkneh Tadesse, 2015 CIPHER grantee.

Elona Toska (2018 CIPHER grantee) and her mentor Lucie Cluver are part of one of the twelve international teams selected by United Kingdom Research and Innovation (UKRI) to establish large interdisciplinary research hubs that address the world’s complex development challenges. Lucie Cluver is the principal investigator and Elona Toska is a co-investigator of the Global Challenges Research Fund Accelerating Achievement for Africa’s Adolescents Hub (ACCELERATE Hub). The £18.5 Million grant aims to discover which combinations of services can most efficiently and most cost-effectively help adolescents achieve their potential across multiple life domains: health, education, employment and safety. The goal is to provide policy makers with the evidence they need to choose programmes that work and are cost-effective and scalable. Working with partners, the team aims to reach 20 million adolescents in 34 African countries. As shared by Lucie Cluver, “much of the work that led to the ACCELERATE Hub has come directly from the studies that CIPHER has supported (2013 CIPHER grantee, Rebecca Hodes) and is supporting (2018 CIPHER grantee, Elona Toska)".
2020 round of CIPHER grants open to application in French
For the first time, the next round of the CIPHER grant programme will be open to applications in French. West and Central Africa (WCA) experience one of the highest HIV burdens among children and adolescents in the world. The IAS recognizes that one of the reasons for this gap is the language barrier that many francophone researchers from the region face in the grant application process which, to date, has been run in English. Over the past years, the members of the CIPHER Scientific and Technical Advisory Committee have continuously recommended to make the application process more accessible to francophone applicants. Experts in WCA have been convened to provide their input with regard to the translation of the programme materials into French, ensuring its scientific accuracy and an Advisory Committee has been formed to support this expansion in the region. The new round of the grant programme, open to applications in both English and French, was launched at IAS 2019.

CIPHER Global Cohort Collaboration

Developing a global paediatric safety and effectiveness platform
With informing efforts to forecast ART need in children and the UNAIDS global estimates of the number of children living with HIV globally, as well as enhanced safety and effectiveness of existing and new ARVs identified as next steps in the CIPHER observational data strategy review, the CIPHER Global Cohort Collaboration has been asked to serve as the basis of the monitoring component of the Global Accelerator for Paediatric-formulations (GAP-f). The MRC-UCL will be the lead data centre.

The Global Accelerator for Paediatric Formulations (GAP-f)

Informing global forecasting efforts
Contributing to global forecasting efforts, the CIPHER Cohort Collaboration data was cited at the Joint WHO/UNAIDS Annual Consultation with Pharmaceutical Companies, Partner Organizations and Stakeholders, held in July 2019 in Geneva. CIPHER data was cited as contributing to the paediatric ARV forecasting module under development by the Cost Effectiveness of Preventing AIDS Complications (CEPAC) Paediatric Team.

New global study published suggesting increased need for 2nd line ART for children
The CIPHER Global Cohort Collaboration published the largest study to date on “Incidence of switching to second-line antiretroviral therapy and associated factors in children with HIV: an international cohort collaboration” in The Lancet HIV in February 2019. The study, which brings together individual patient data on more than 95,000 children worldwide, shows an incidence of switch to second-line ART in children at three years of age ranging from 6.8% to 0.8% and
suggests that there will be an increased need for second-line ART for children with the roll out of viral load monitoring in low- and middle-income countries.

**Bi-annual meeting**
The Cohort Collaboration meeting took place on 3-4 June 2019 in Baveno, Italy, alongside PENTA-ID. The main aims of the meeting were to review the progress of current projects, identify potential new concepts, discuss policy impact and advocacy messaging and review the inclusion of CIPHER grantees in current and future projects. Updates were provided on the DECIPHER, Duration of 2nd line and Adolescent growth, immunology and pubertal growth spurt projects. A robust discussion was held around the upcoming post-marketing safety and effectiveness and forecasting projects, including guest presentations from WHO, New Horizons and the African pharmacovigilance network PAVIA. The group was largely in favour of proceeding with another data merge, led by EPPICC/PENTA, and featured as part of GAP-f.

**EVIDENCE TO ACTION**
Leading in linking evidence to policy makers and implementers at the international and regional levels

**CIPHER Evidence to Action Forum**

With the aim of placing greater emphasis on translating evidence from research into tangible action, the CIPHER Evidence to Action Forum was held at IAS 2019. The forum provided a platform for CIPHER grantees and fellows to directly engage with implementers and other relevant stakeholders at an early stage in the research process. Participants joined a facilitated poster walk during which they had the opportunity to discuss the projects directly with the grantees.

For a full description of CIPHER activities at IAS 2019, see the CIPHER IAS 2019 roadmap here.

**Workshop on Children and Adolescents HIV-Exposed and Uninfected**

The 5th Workshop on Children and Adolescents HIV-Exposed and Uninfected (HEU) focused on the first 1,000 days for HEU children, exploring the impact of maternal HIV infection and *in utero* ARV-exposure on infants and children’s growth and development up to the age of two years. Panel discussions explored how to partner for progress, ensuring that all children, including HEU children, survive and thrive. Participation of Ministry of Health representatives from Zambia and South Africa linked the research children who are HEU directly to policy making. Over 150 participants attended this pre-conference at IAS 2019 in Mexico. More details on the programme can be found here.

Following her presentation at the workshop, CIPHER fellow Jane Mutanga was invited to take part in the Biologics Effectiveness and Safety Team (BEST) of the FDA. The research focuses on finding innovative ways to use routinely collected electronic health records and claims data to actively search for signals of adverse health outcomes. Jane shared that “this experience will be very useful to my research in Zambia because my CIPHER project relies on data from electronic health records and I am learning new ways of effectively linking mother-infants pairs”.

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Bringing CIPHER Evidence to Action fora to the regional level

The first regional CIPHER Evidence to Action forum, *The drive to thrive – How are the children and adolescents HIV-Exposed yet Uninfected doing?*, was held on 5 December 2019, alongside ICASA in Kigali, Rwanda. Over 250 participants were in attendance. The forum aimed to generate awareness among implementers, policy makers and advocates about the risk of poorer health and developmental outcomes experienced by children who are HEU and sought to foster new collaboration between CIPHER grantees involved in this research and implementers. Following presentations from four grantees on their HEU research, a panel discussion was held with representatives from the UNICEF Eastern and Southern Africa regional office, PATA, and the Coalition for Children Affected by AIDS Youth Ambassador. As the topic was relatively new to the audience, this was a unique opportunity to raise awareness among participants that often do not attend the IAS and AIDS conference (including national and regional policy makers, healthcare practitioners and representatives from West and Central Africa).

ADVOCACY

IAS-CIPHER Forum on inclusion of pregnant and lactating women in HIV clinical trials

On 10 July in Geneva, CIPHER engaged over 45 representatives from industry, clinical research, regulatory authorities and other key stakeholders to:

- Review the approaches for including pregnant and lactating women in clinical trials put forward through the PADO4 group;
- Identify challenges to including pregnant and lactating women in clinical trials from an industry perspective; and
- Outline potential solutions in order to move this agenda forward.

The group agreed that a business case informed by multi-stakeholder discussions is needed, informed in particular by industry, community and country-level policy makers. Additionally, the group identified the need to relax trial inclusion and withdraw criteria and develop clear definitions of what constitutes a safety signal in reproductive toxicity studies. As next steps, CIPHER will lead on the development of the business case.

Supporting meaningful participation of young people across the IAS

Preparations and planning began for the “Youth Advisor” project. The IAS will award six stipends to young people (under 30) to work with the IAS to identify strengths and weaknesses in the ways the organization works with young people while simultaneously building their capacity to meaningfully engage in the HIV response themselves. Each Youth Advisor will work with an IAS department focal point to co-create a roadmap for future improvements and sensitise the wider organization to the importance of meaningfully engaging young people.
CIPHER actively participates in numerous initiatives across the paediatric and adolescent HIV response:

- Accelerate Hub for Adolescent Health in Africa (Strategic Advisor)
- Adolescent HIV Treatment Coalition (ATC) (host)
- Child Survival Working Group (CSWG)
- Global Accelerator for Paediatric formulations (GAP-f)
- New Horizons Collaborative
- Paediatric ARV Drug Optimization Group (PADO)
- Paediatric ARV Procurement Working Group (PAPWG)
- Paediatric ARV Working Group (PAWG)
- PHASES Pregnancy + HIV/AIDS Seeking Equitable Study
- HIV Adolescence Workshop, Virology Education (Organizing Committee)
- International Workshop on HIV Paediatrics, Virology Education (Steering Committee)
- SPARK, ViiV Healthcare (Steering Committee)