

COLLABORATIVE INITIATIVE FOR PAEDIATRIC
HIV EDUCATION AND RESEARCH

2018 ANNUAL REPORT



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TAKING STOCK AND LOOKING FORWARD

Taking stock

It was a watershed year for the Collaborative Initiative for Paediatric HIV Education and Research (CIPHER): 2018 saw the achievement of key milestones across its activities. The Global Cohort Collaboration published its first studies, providing the first global description of the epidemic in adolescents with perinatally acquired HIV. The full research method and data from the Global Research Agendas in Paediatric and Adolescent HIV were published in a *Journal of Acquired Immune Deficiency Syndromes* (JAIDS) supplement with accompanying articles looking at different ways to address knowledge gaps faster and more efficiently. And the first special issue dedicated to paediatric and adolescent HIV in the context of the Sustainable Development Goals (SDGs) was published in the *Journal of the International AIDS Society* (JIAS), pushing forward thinking beyond how the SDGs can support efforts in paediatric and adolescent HIV, to look at the relevance of achieving HIV-related goals in these populations to the attainment of the SDGs.

With the maturation of the grant and fellowship programmes, completion of the studies, publication of results and translation of those results into policy, the measurable impact of these programmes is growing. In parallel, they are impacting the professional development of the grantees and fellows through promotions and additional funding leveraged, as well as local capacity building in terms of additional PhD students, Master's students, nurses and technicians trained through the CIPHER projects.

Looking forward

Over 2018, CIPHER completed its strategy review, aimed at adjusting its vision and objectives over the next five years to the changing requirements in the field. Preliminary results indicate a need for an increased focus on operational science and an accompanying need to link policy makers to ongoing research to ensure that

results are relevant to policy and can be rapidly translated into action.

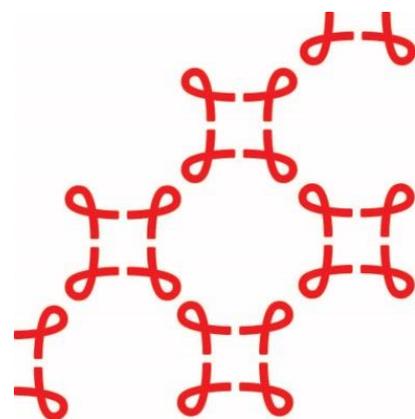
The value of the research component of CIPHER was highlighted, with suggestions on how to increase impact and how to further support the professional development of grantees and fellows both during and after their grant period.

An observational research roadmap was developed, focusing on three key areas: post-marketing surveillance and pharmacovigilance of antiretroviral therapy (ART) in paediatric populations, including pregnancy, infants, children and youth; short- and long-term outcomes of HIV-exposed and uninfected children and adolescents; and informing ART need forecasting in children.

In advocacy, supporting the meaningful engagement of youth in the HIV response, in collaboration with other International AIDS Society (IAS) programmes, as well as the inclusion of pregnant women in research, were primary themes that emerged.

Some of the recommendations were integrated into 2018 activities, and all will be reflected in CIPHER's work from 2019 onwards.

This 2018 annual report describes the main outcomes of activities throughout the year.



RESEARCH

The investment in early-stage investigators through CIPHER grants and fellowships is coming to fruition in full force.

“This opportunity from CIPHER to carry out my project has transformed the services we have been able to provide to at-risk adolescents in reducing their risk for HIV. Personally, it has been a life-changing opportunity for me to establish myself as a researcher in the field of paediatric HIV research both through meeting other investigators and the support they have provided in carrying out the research itself.”

CIPHER 2017 Grantee, Wipaporn Natalie Songtaweessin

Since the launch of the CIPHER Research Grant and Growing the Leaders of Tomorrow Fellowship programmes, CIPHER has supported 32 research projects in 12 countries, providing more than US\$4.6 million to early-stage investigators to address priority evidence gaps across the HIV cascade, including pregnancy, paediatrics and youth, in resource-limited settings. In addition to advancing science, these two-year, intermediate-level grants and fellowships are proving to have a high impact on national and international policy, professional development of the grantees and fellows, and local capacity building. Building on their CIPHER Grant, young investigators have also been able to leverage additional funding to pursue their research and develop new projects.

Advancing science and disseminating research findings



CIPHER Grants and Fellowships have helped some of the field's most promising young investigators advance their research efforts and increase exposure to their work among research leaders, funders and health policy makers.

To date, CIPHER Grants have contributed to 106 publications in scientific journals, with an additional number of manuscripts in different stages of pre-publication.

CIPHER Grantees have also presented their research findings in 107 presentations at national and international events. These publications and presentations, along with the media coverage they have generated, shone a bright spotlight on the key paediatric and adolescent research gaps identified by CIPHER and helped disseminate scientific advancement in this field at the local and international levels. Just in 2018, current and past grantees published 21 scientific articles and gave 33 presentations of their research projects at national, regional and international scientific events.



Influencing policy and practice

CIPHER Grantees have also engaged in local and international policy advocacy related to paediatric and adolescent HIV issues, and their national governments have invited them to provide input into national-level and international policies. To date, CIPHER investigators count 83 instances of informing policy and practice through their participation in key policy events, involvement in advisory committees or expert panels, direct contribution to policy documents or guidelines, and the training of practitioners. This is increasing over time: in 2018 alone, grantees informed 31 instances of policy and practice. Highlights are presented below.



Adrie Bekker, 2017 CIPHER Fellow, contributed as a reviewer of the module on pharmacokinetic modelling for the [Toolkit for Research and Development of Paediatric Antiretroviral Drugs and Formulations](#). The toolkit is an initiative of the World Health Organization (WHO) and its Paediatric ARV Working Group (PAWG), in collaboration with Unitaid, IMPAACT and PENTA-ID. It identifies the challenges and solutions for promoting and accelerating timely and high-quality research and development of antiretroviral drug formulations suitable for infants, children, adolescents and pregnant and breastfeeding women.



Wipaporn Natalie Songtaweessin, 2017 CIPHER Grantee, is part of the expert panel currently writing Thailand national guidelines on the administration of pre-exposure prophylaxis (PrEP) to adolescents, building on her CIPHER project looking at youth-focused strategies to promote adherence to PrEP among youth at risk for HIV in Thailand.

Professional development

Beyond the impact on research and policy, grantees have reported accelerated promotions and professional development. Being a CIPHER Grantee has provided visibility and opportunities for new collaborations, and contributed to allowing them to expand their expertise and establish themselves as leaders in the field of paediatric and adolescent HIV.



The CIPHER Grant *“has given me the opportunity to establish myself as a researcher who is able and willing to collaborate across many departmental boundaries. I have been appointed in 2018 [as] director of the University of Pretoria Research Centre for Maternal, Fetal, Newborn and Child Health Strategies, and have been able to establish myself on a national level as a PMTCT expert and a main contributor to the updated South African National PMTCT guidelines, which are currently being finalized.”* – Ute Feucht, 2017 CIPHER Grantee



Through the CIPHER Grant, Amy Slogrove, 2017 CIPHER Grantee, explains, “*local and international collaborations were developed with concrete projects coming off the ground that have largely been facilitated through the multiple avenues in which CIPHER has invested in me*”. At the CIPHER Global Cohort Collaboration Meeting in San Servolo, Italy, in 2017, Amy was given the opportunity to present the beginnings of a CIPHER HIV-exposed and uninfected (HEU) child concept and argue for investment in this area to the CIPHER community. In 2018, “*this has now fully developed into a CIPHER-funded concept ... This has been an incredible developmental opportunity for me to have started as the CIPHER Cohort Collaboration post-doc at the end of 2015 and, through that, have the opportunity to initiate development of a new CIPHER concept that, within three years, I am now co-chairing and mentoring the next CIPHER post-doc.*”

Leveraging additional funds

CIPHER Grants and Fellowships are filling a real funding niche for investigators from resource-limited settings, helping position them competitively to go on and obtain larger grants from major funding institutions. Overall, the initial investment in CIPHER Research Grants has unlocked more than US\$15 million in additional funding for paediatric HIV research from local and international agencies. These additional resources invested locally have helped enhance the capacities of local universities, researchers and health systems. In 2018, current and past grantees leveraged over US\$2,570,000, winning very competitive grants as illustrated below.



Amara Ezeamama, 2016 CIPHER Grantee, has been awarded a National Institutes of Health (NIH) R21 grant of US\$338,000 for the project, *Caregiver age- and HIV-associated neurocognitive decline in relationship to impaired cognitive development and long-term functional deficits in HIV-infected and uninfected dependent children*. The funding will allow her team to incorporate performance-based neuropsychosocial testing in children and caregivers in her current research in Uganda.

Wipaporn Natalie Songtaweasin, 2017 CIPHER Grantee, received an NIH R21 grant of US\$215,000 for the project entitled *Novel MHealth technologies to enhance PrEP adherence among Thai YMSM: collaborative adaption and evaluation*. Wipaporn met Dr Sarah LeGrand at IAS 2017 in Paris, France, and their collaboration has successfully led to this grant, with Wipaporn and Dr LeGrand as co-principal investigators.



Matthew Kelly, 2013 CIPHER Grantee, received a K23 NIH grant of US\$930,000 for his project involving mother-infant pairs in Botswana. The research will provide insight into the impact of the nasopharyngeal microbiome on the risk of childhood pneumonia. The project will also develop a novel approach for the application of conventional multivariable statistics to the analysis of longitudinal microbiome data.

Profiles of all CIPHER [Grantees](#) and [Fellows](#) were developed in 2018, and can be found online.

2018 CIPHER Grantees and launch of new opportunities

In 2018, CIPHER awarded grants to four outstanding early-career investigators to work on reversing the high impact of HIV among youth in resource-limited settings:

- Alain Amstutz, whose project will test several innovative, targeted interventions along the HIV care cascade for adolescents and young adults in Lesotho, the country with second-highest HIV prevalence in the world, and assess their potential to help reach 90-90-90 UNAIDS targets
- Millicent Atujuna, who will investigate the link between poverty and ART adherence, and identify strategies to improve adherence and retention in care among youth in South Africa
- Sirinya Teeraananchai, whose project will evaluate approaches to improve the treatment cascade in youth, the fastest-growing population of new HIV infections in Thailand, with the dual objective of improving individual health status and limiting HIV transmission among Thai youth
- Elona Toska, who will evaluate different healthcare provision models to improve HIV-related outcomes among adolescent mothers living with HIV and their children, and build capacity to optimize health service delivery for adolescent mother-child dyads in South Africa.

The next round of the grant programme was launched with a focus on paediatric HIV operational science, an area that has been left behind in terms of research and understanding of how to best serve this population. CIPHER was also pleased to launch the second round of the Growing the Leaders of Tomorrow Fellowship, which will provide two fellowship opportunities to early-stage investigators from sub-Saharan Africa in paediatric and adolescent HIV clinical science.

CIPHER Global Cohort Collaboration

The CIPHER Global Cohort Collaboration reached a major milestone this year with the publication of its first papers. The study, [The epidemiology of adolescents living with perinatally acquired HIV: A cross-region global cohort analysis](#), published in *PLOS Medicine* in February, described for the first time ever the epidemiology of this growing population. The study was also covered in “News & Views” in *Nature*, with a [review](#) underlining the policy impact of this work. A second study, published in *JIAS*, showed inequality of outcomes for adolescents with perinatally acquired HIV in sub-Saharan Africa based on country income group ([access study here](#)).

These publications represent a major accomplishment, providing proof of concept that such a diverse group of cohort networks can collaborate to answer questions of high global public health impact. The experience has provided valuable lessons learned for future collaborations and served to increase collaboration in the field overall.

Additionally, first data from the CIPHER “Duration of Second-line ART in children” project was presented at the International Workshop on HIV and Hepatitis Observational Databases (IWHOD), the International Workshop on HIV Paediatrics, the 22nd International AIDS Conference (AIDS 2018) and the New Horizons Workshop.

Looking forward, the collaboration launched new studies to better understand the outcomes of adolescents and youth with perinatal HIV, including on growth and immunology, timing and duration of pubertal growth spurt, and long-term growth after initiation of ART.

As an important component of the work needed to push forward research on HIV-exposed and uninfected child and adolescent outcomes, a scoping project was launched to identify key domains and harmonize definitions that can be used across studies: Data Evaluation and

CIPHER Preparation for an HIV Exposed Uninfected (HEU) Child Cohort Collaboration (DECIPHER). As a capacity-building component, a 15-month post-doctoral fellowship was awarded to Barbara Burman, an early-stage investigator from Kenya, to work with the lead data centre at the University of Cape Town, spend two months with the Paediatric HIV/AIDS Cohort Study (PHACS) Data and Operations Center (DOC) at Harvard University, and spend one month at the Botswana Harvard AIDS Institute Partnership.

The 4th HIV-Exposed Uninfected Child and Adolescent Workshop

The main meeting point of the HEU field, the 4th HIV-Exposed Uninfected Child and Adolescent Workshop was held this year as an official pre-conference of AIDS 2018, and focused on integrating HEU into the early childhood development framework and country monitoring and surveillance systems. The report of last year's HEU workshop was recently published in *Frontiers in Paediatrics*. Access the report [here](#).

POLICY

MIND THE GAP: A roadmap for better use of research resources for an AIDS-free generation

"The IAS/WHO process has helped us to define priority areas for further research, to inform global policies and implementation to bring us closer to an AIDS-free generation for infants, children and adolescents."

WHO HIV Department Director Gottfried Hirsenschall

As a follow up to the [Global Research Agendas](#) for Paediatric and Adolescent HIV released at the 9th IAS Conference on HIV Science (IAS 2017), in 2018, WHO and CIPHER published the methodology and full data set used to develop the agendas in a JAIDS supplement: [Mind the Gap: Filling Knowledge Gaps in Paediatric and Adolescent HIV for an AIDS Free Generation](#). In addition, the supplement contains papers from thought leaders and stakeholders addressing key considerations for implementing the Global Research Agendas, including use of observational data to inform policy change, optimizing clinical trial design, modelling and metamodeling, and the roles of implementation science, innovation and community engagement. The supplement is featured in the [AIDS FREE Toolkit](#), a set of critical resources compiled by WHO and partners to accelerate treatment scale up in children and adolescents living with HIV.

STRUCTURAL BARRIERS

Shining the spotlight on thinking that is needed to move towards an integrated approach to paediatric and adolescent HIV to reach the Sustainable Development Goals (SDGs), CIPHER published a special issue in JIAS on "[Paediatric and Adolescent HIV and the Sustainable Development Goals: the road ahead to 2030](#)". This special issue received news coverage for its article presenting findings that the risk of intimate partner violence is reduced by giving regular cash payments to poor girls ([see AVERT news here](#)) and data from the Mzantsi Wakho study (initially funded through a CIPHER Grant) on adolescent "dream clinics" ([see Evidence](#)

[for HIV Prevention in Southern Africa, EHPSA, Prevention News here](#)). The special issue was distributed in conference bags to every delegate at AIDS 2018 – 14,000 copies in total.

An active stakeholder in paediatric and adolescent HIV

In 2018, CIPHER contributed to the development of several co-branded products through different partnerships, all of which were launched at AIDS 2018:

- [The AIDS FREE Toolkit: Accelerating progress in testing and treatment for children and adolescents with HIV](#)
- [The IATT 2018 optimal formulary and limited-use list for paediatric ARVs](#)
- [Child Survival Working Group: Technical Brief Series: Approaching 2020: Scaling up key interventions for children and adolescents living with HIV](#)
- [Paediatric ARV Working Group: Toolkit for Research and Development of Paediatric Antiretroviral Drugs and Formulations.](#)

See the CIPHER AIDS 2018 roadmap [here](#) for a full list of CIPHER's activities and work throughout the 22nd International AIDS Conference in Amsterdam.

CIPHER is represented as a partner, member or observer in the following fora:

- Adolescent HIV Treatment Coalition (ATC)
- 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

Meetings where CIPHER is present:

- HIV Adolescence Workshop, Virology Education (Organizing Committee)
 - International Workshop on HIV Paediatrics, Virology Education (Steering Committee)
 - SPARK, ViiV Healthcare (Steering Committee)
-

Mission and objectives

CIPHER aims to optimize clinical management and delivery of services to infants, children and adolescents affected by HIV in resource-limited settings through advocacy and research promotion.

In line with the IAS three-pillar approach for programmes of policy, research and structural barriers, CIPHER works to fulfil the following key objectives:

- Promoting and investing in targeted research to address priority knowledge gaps in paediatric HIV
- Convening stakeholders and establishing collaboration mechanisms to strengthen communication, knowledge transfer and knowledge exchange among paediatric HIV cohorts
- Advocacy to support evidence-informed clinical, policy and programmatic decision making.



<http://www.iasociety.org/cipher>

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PAEDIATRIC HIV MATTERS