COLLABORATIVE INITIATIVE FOR
PAEDIATRIC HIV EDUCATION AND
RESEARCH (CIPHER)

GRANT PROGRAMME 2013 - 2015

IMPACT REPORT
ACKNOWLEDGEMENTS

Project Team at the International AIDS Society, Switzerland

Marissa Vicari  Manager, CIPHER
Tamara Torri  Project Manager, HIV Programmes
Diddie Schaaf  Project Manager, HIV Programmes

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 Guest  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
Shaffiq Essajee  World Health Organization, Switzerland

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Support

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International AIDS Society, Switzerland

Produced by

Avenue de France 23
CH-1202 Geneva
Switzerland
Tel: +41 22 710 08 00
Fax: +41 22 710 08 99
info@iasociety.org
www.iasociety.org

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INTRODUCTION

The CIPHER Grant Programme was specifically designed to inform policy in paediatric HIV, cultivate a new generation of scientists dedicated to the field, and foster innovative ideas and evidence-based approaches and interventions. It addresses both clinical and operational priority research questions throughout the HIV care cascade for the younger populations, from the effects of in-utero exposure to ARVs in HIV exposed-uninfected infants, through to optimal models for retaining adolescents in care. The priority topics (see page 11, ELIGIBLE RESEARCH TOPICS) were developed through a comprehensive needs assessment, including literature review and key-informant interviews with experts in paediatric HIV.

The programme provides a unique opportunity for early-stage researchers to be the principal investigator (PI) on a sizable grant for the first time. Support from their institution and mentoring by a senior advisor are important components of the proposal.

How it works

All projects must address one of the identified clinical and operational priority research questions. The grants are for up to US$75,000 per year for up to two years; 80% of direct costs of the grant must be spent in low- and middle-income countries (LMICs) and 80% of all funds overall are awarded to applicants from LMICs. CIPHER grantees are brought to the International AIDS Society Conference on HIV Science and International AIDS Conference, for the duration of their grant, to participate in the official awards ceremony and capacity-building events. It is a highly competitive grant with an exigent review process. Letters of intent are submitted in October, and short-listed candidates are invited to submit a full application. Full applications undergo peer review by three independent experts in the field of the proposal.

Objectives

- Address priority HIV research questions to drive improvements in clinical management and service delivery for paediatric and adolescent populations
- Support evidence-informed policy decision making and innovation in paediatric HIV
- Attract early-stage investigators to the field and build research capacity

Some facts and figures

To date, CIPHER has supported 14 grantees from Africa, Asia, Europe and the United States. Grantees have been selected from among a large number of high-quality proposals, demonstrating a significant need for support for early-stage investigators working in paediatric HIV. Seven grantees were awarded in 2013, two in 2014 and five in 2015. With renewed support from CIPHER founding sponsor ViV Healthcare and additional funding from Janssen in 2015, CIPHER launched the fourth and largest round of the Grant Programme, which will award a record US$1.2 million for high-quality paediatric HIV research in 2016.
MEASURING CIPHER’S IMPACT

With the first seven grantees now completing their 2-year projects, the impact of the programme can be seen. CIPHER grants have helped some of the field’s most promising young investigators advance their research efforts, generate more funding support and increase exposure to their work among research leaders, funders and health policy makers. Grantees have reported accelerated promotions, received additional funding, and experienced increased visibility among the international community as a result of the work they conducted with support from CIPHER. After one round, the CIPHER Grant Programme has had a significant impact on the field of paediatric and adolescent HIV research, as indicated by a number of measures.

**Supporting the professional development of grantees**

By providing the first opportunity for researchers to act as independent principal investigators (PIs), CIPHER grants have provided our grantees with a unique level of research and management experience. As a result, CIPHER grantees have received significant exposure to international experts, institutes and platforms, which have greatly improved their profile globally. Grantees have grown the body of research and have generated interest from other funding agencies that are helping many to further the work they initiated with support from the CIPHER Grant. After only two years, many have received promotions and professional recognition.

**Contributing to global knowledge on paediatric HIV**

To date, the first seven CIPHER grants have contributed to 29 publications in respected journals, with an additional number of manuscripts in different stages of pre-publication. CIPHER grantees have also presented their findings of CIPHER-supported research in presentations at national and international events. These publications and presentations, along with the media coverage they generated, have shone a significant spotlight on the key paediatric research gaps identified by CIPHER. The development and dissemination of knowledge about HIV have contributed to local and national ownership of the information.

(see LIST OF PUBLICATIONS and LIST OF PRESENTATIONS)

**Unlocking investment in paediatric and adolescent HIV research**

The initial investment in CIPHER research grants has unlocked close to US$4 million in additional funding for paediatric HIV research from local and international agencies. Besides adding to the body of research, these additional resources invested locally have helped enhance the capacities of local universities, researchers and health systems. Several researchers working on the CIPHER projects have also received additional awards, scholarships and fellowships to continue their work and research educations.
Influencing national and international policy

CIPHER grantees have engaged in local and international policy advocacy related to paediatric HIV issues, and have been invited by their national governments to provide input into national level policies. In some cases, the CIPHER grantees participated and presented their research in international committees, where they are influencing global policy on HIV.

Stronger research through collaboration

CIPHER grantees have built significant partnerships with local and international universities, research institutes and organizations and the health systems in their countries of research. The partnerships are vital in advancing the cause of paediatric HIV.

The Halo effect of CIPHER grants: local capacity building

An unexpected outcome of the CIPHER grants has been their ‘halo’ effect, building local research and healthcare capacity through the employment and training of post-doctoral, doctoral and master’s students as well as nurses and technicians.
MEET THE GRANTEES: AFTER CIPHER

PAUL BANGIRANA

Uganda, Makerere University

Does HIV subtype moderate ART effect neurocognitive functioning in children?

Dr. Bangirana has become the PI of his own R01 from the National Institute of Child Health and Development (NICHD), where he will study mechanisms through which malaria prophylaxis enhances child development. He has also been promoted to Senior Lecturer at Makerere University. He was able to enhance prospects as an independent investigator, to gain experience and insight about managing a grant as a PI. CIPHER funding opened options for future research questions.

CIPHER has allowed Dr. Bangirana, a neuroscientist, to access a valuable network in the paediatrics HIV field. He has entered a collaboration with colleagues at the Department of Pediatrics at University of California at San Francisco and Blood Systems Research Institute in California for HIV subtyping.

Capacity development of research group: gained expertise in performing neuropsychological testing on children. One of his research assistants is now the project coordinator of the R01 study.

DEGU JERENE DARE

Ethiopia, Addis Ababa University

Antiretroviral treatment outcomes among adolescents living with HIV in Ethiopia.

Dr. Dare is now a project director with a non-profit organization, Management Sciences for Health, in Ethiopia where he continues to lead HIV and TB research among adolescents and children. He also became a mentor for another CIPHER grantee. He has presented his work at numerous conferences, including the CIPHER Adolescent Transition Workshop, IAS conferences and the Union World Conference on Lung Health.

The CIPHER grant has opened opportunities for collaboration and networking with experts in the area.

Two members of Dr. Dare’s research team have been selected for NIH/Fogarty HIV research training programme at Johns Hopkins University. The CIPHER project has also supported three MPH theses.
REBECCA HODES
South Africa, University of Cape Town

Promoting adolescent antiretroviral adherence and sexual and reproductive health uptake in South Africa: How can health and social protection services collaborate programmatically with HIV-positive adolescents?

Appointed Director of AIDS and Society Research University at the University of Cape Town; appointed Associate of the Department of Social Policy and Intervention at the University of Oxford, appointed Research Fellow at the Department of Historical Studies, University of Cape Town.

Chaired the Social, Economic Sciences and Human Rights track at the 7th South African AIDS Conference.

Now manages a grant portfolio of nearly US$ 2 million, with grants from the Regional Research and Innovations Fund funded by Evidence for Prevention of HIV in Southern Africa (EHPSA), a DFID programme managed by Mott MacDonald, a Janssen Global Public Health Grant programme and UNFPA/UNICEF grants that focus on adolescent and youth health and mobile health technologies.

National Youth Health Policy for South Africa, National Department of Health and the HIV Pediatric Technical Working Group, Department of Health: The South African National Department of Health has requested a collaborative partnership with the Mzantsi Wakho study regarding the development of their Youth Health Policy. The Director-General of Health has requested that qualitative data be utilized to inform the sections of the policy relating to youth living with HIV and youth sexual and reproductive health. Results from Mzantsi Wakho have also been presented at consultations and high-level meetings from international organizations:

- WHO guidelines on service delivery for HIV-positive adolescents and consultation on developing updated adolescent treatment guidelines
- UNICEF South Africa and Head Quarters, UNICEF ‘All-In for Adolescents’ meeting in Rwanda and high-level meeting of Southern and East African Health Ministers in Zambia
- Office of the Global AIDS Coordinator, President’s Emergency Plan to AIDS Relief (PEPFAR)
- World Bank, UNAIDS, UNICEF, ‘High Level Consultation on Scaling-up Proven Social and Structural Interventions to Prevent HIV Transmission’

Supporting study team member capacity building: Nonzuzo Mbokazi was awarded a research fellowship to develop her doctoral proposal in the Department of Sociology; Mildred Thabeng was provided with research support to fund her undergraduate studies in social work at the University of South Africa; Elona Toska
was awarded a research associateship at the University of Cape Town; Beth Vale was awarded her doctoral degree at Oxford University, and an Oppenheimer Fellowship to support postdoctoral writing; Leslie Gittings was awarded her Master’s degree with a distinction from the University of Cape Town, and doctoral funding.

**STEFAN KELLY**  
The United States, Duke University

**Novel methods for detecting and minimizing chronic cardiovascular, metabolic, respiratory, renal and bone disease in HIV-infected children treated with antiretroviral therapy in Southern Africa.**

As a direct result of the CIPHER award, Steven received a US$50,000 International Research Career Development and Administrative Supplement Award through University of California San Diego, Centre for AIDS Research (UCSD CFAR). His CIPHER project garnered substantial attention and in 2015 he became the PI of his own R01 on atherosclerotic vascular disease in HIV-infected children, representing US$1.64 million over five years.

As a result of the attention he has received from this CIPHER project, Steven was invited in 2015/2016 to act as reviewer on the South African National Research Foundation Rating awards (www.nrf.ac.za/rating); and to participate as review committee member on: (1) Thuthuka grant scheme for research capacity development (www.nrf.ac.za/division/funding/thuthuka-programme-2016-funding); and (2) the Complications subcommittee of the International Maternal Pediatric Adolescent AIDS Clinical Trials group (IMPAACT, www.impaactnetwork.org).

Intensified collaboration with the Center for AIDS Research and the University of California, San Diego (CFAR UCSD).

A newly-qualified study nurse, after mentoring and training, is now an independent study coordinator. A local data manager has been trained to build customized Open Clinical databases.

Project’s data forms the basis for one student’s Master’s degree.

**STEVEN INNES**  
South Africa, Stellenbosch University

**Novel methods for detecting and minimizing chronic cardiovascular, metabolic, respiratory, renal and bone disease in HIV-infected children treated with antiretroviral therapy in Southern Africa.**

Promoted to Deputy Director at Malawi College of Medicine and leads the centre’s HIV research agenda. Awarded a grant by WHO to implement a project on
finding best strategies to improve careers for women scientists involved in infectious diseases of poverty in Africa.

- Grant for US$ 600,000 from UNICEF; Fogarty Global Health post-doctoral fellow; WHO funded INSPIRE PURE-Malawi project provides technical and logistical support at two extra sites.

- Atupele Kapito Tembo has been invited to be a member of the Malawi National HIV Technical Working Group.

- Capacity development of research team as the team gained expertise in performing neurodevelopmental assessments on children. Following the CIPHER project, an R01 research study awarded to Professor Mina Hosseinipour of University of North Carolina for the Lilongwe project has also included neurodevelopment assessment of children.

Supporting and mentoring of a newly CIPHER grantees (2016) McNeil Ngongondo whose project is utilizing her study’s platform.

**MATTHEW KELLY**

The United States, Duke University

**The effect of in utero exposure to HIV and antiretroviral therapy on the microbiology and outcomes of severe pneumonia.**

- Awarded the Burroughs-Wellcome Fund / American Society of Tropical Medicine and Hygiene Postdoctoral Fellowship in Tropical Infectious Diseases, which will provide salary support and research funding from 2016-2018. Preparing a National Institutes of Health (NIH) Career Development Award for submission.

- Received Duke University Centers for AIDS Research (CFAR) pilot grant.

- Has developed collaborations with basic science and translational researchers at Duke University, McMaster University, Boston Medical Center, and the National Institutes of Communicable Diseases (NICD) in Johannesburg, South Africa for developing local capacity in Botswana.

Mentoring 4 paediatric residents and a University of Botswana Masters student who is completing her laboratory-based thesis using specimens collected from participants in this study.

Developed capability for respiratory virus testing of clinical samples at the National Health Laboratory in Gaborone, Botswana in June 2015, the first respiratory virus testing performed in the public sector in Botswana.
NELLEKE LANGERAK

The Netherlands, University of Cape Town

HIV encephalopathy: definition of the natural history, physical characteristics and imaging findings in a group of children with gait abnormalities.

Promoted to Senior Research Officer, became a National Research Foundation (NRF) Research Career Advancement Fellow (NRF RCA), received a NRF rating and was awarded the Claude Leon Merit Award in recognition of early-career researchers with distinction.

Has mobilized ~US$ 250,000, including a NRF RCA, NRF rating grant, Fellowship for Postdoctoral student, Claude Leon Merit Award and a variety of travel grants.

Several collaborations with heads of South African facilities: University of Cape Town - Neurosurgery; Developmental Paediatrics; Radiology; Paediatrics and Child Health; Psychology Department and ACSENT Laboratory; Biomedical Engineering, and Stellenbosch University - Children’s Infectious Diseases Clinical Research Unit and Orthopaedic Surgery.

Mentors and supervises three Master of Science students and two Postdoctoral Fellows.

THANK YOU

Although CIPHER has been instrumental in mobilizing the impact described above, it is understood that the wide footprint of this programme has been made possible through the combined effort of a lot of different agencies and people. CIPHER Grants have played the role of a catalyst to mobilize research, finances and people around paediatric and adolescent HIV. CIPHER would like to thank all of the people who have provided support for the programme and grantees.
# Eligible Research Topics

## Clinical Research:

- Pharmacokinetic, pharmacodynamic and pharmacogenomics studies of paediatric antiretrovirals and of drugs for co-morbid conditions (particularly for TB, and malnutrition) with a focus on pre-term infants and neonates.

- Studies to evaluate the short- and long-term complications of HIV and of antiretroviral therapy and the pathogenesis of such complications, as well as management of HIV, including interventions to treat HIV co-infections children age through adolescence and young adulthood.

- Studies to evaluate the effect of antiretroviral therapy during pregnancy on maternal pregnancy complications, pregnancy outcomes (e.g., prematurity, low birth weight) and neonatal outcomes (morbidity and mortality) in HIV- and antiretroviral-exposed uninfected and HIV-infected neonates, including studies to evaluate potential pathogenesis of adverse effects.

- Studies to evaluate the long-term effects of in utero exposure to maternal antiretroviral therapy in HIV-exposed uninfected children and adolescents, including effects on metabolism, bone mineral density and growth, other laboratory/biologic markers, and physical and cognitive development.

- Studies evaluating and/or validating diagnostic assays to assess neurocognitive and physical development among HIV-infected and HIV-exposed uninfected infants and children in resource-limited settings.

## Operational Research and Implementation Science:

- Evaluations of optimal and innovative strategies for the delivery and implementation of HIV diagnostics (especially for older children), including impact assessment of clinical platforms, point of care technologies, early infant diagnosis and linkage to care.

- Studies evaluating interventions and optimal models for integrating paediatric HIV services with maternal, newborn and child health and other health services.

- Studies evaluating interventions and optimal models for promoting early post-natal and long-term programme retention and reducing loss to follow up.

- Studies evaluating optimal interventions to support childhood and adolescent disclosure and adherence (including for high-risk adolescents and young key populations).

- Studies evaluating the most effective service delivery approaches to support retention in care and transition to adult ART programmes, access to psychosocial and sexual and reproductive health services and delivery of biomedical HIV and STI prevention interventions for adolescents, with emphasis on integrated comprehensive packages of ‘adolescent-friendly’ strategies and services (including for high-risk adolescents and young key populations).
## LIST OF PUBLICATIONS

### Degu Jerene Dare


### Rebecca Hodes


3. Toska E, Cluver L, **Hodes R** and Kidia K. Sex and secrecy: how HIV-status disclosure affects safe sex among HIV-positive adolescents. AIDS Care. 27,1, 2015

4. Cluver L, **Hodes R**, Toska E, Kidia K, Orkin M, Sherr L and Meinick F. ‘HIV is like a tsotsi. ARVs are your guns’: Associations between HIV disclosure and adherence to antiretroviral treatment among adolescents in South Africa. AIDS Special Issue on Parental and Pediatric HIV Disclosure. 29, 1, 2015


### Peer-reviewed, accepted for publication, and forthcoming in 2016


14. **Hodes R,** Toska E, and Gittings L. Babies for bling: Are teenage girls having children to access grants?, HIV Nursing Matters

15. Nattrass N, **Hodes R,** and Cluver L. ‘Changing Donor Funding and the Challenges of Integrated HIV Treatment.’ JAMA Ethics

16. **Hodes R,** Morrell R. ‘South African social science in the global HIV knowledge domain.’ CSSR Working Paper, University of Afepot


### Publications in process


20. Toska E, Cluver L, Boyes ME, Isaacsohn M, **Hodes R,** Sherr L. Combination social protection and reduced unprotected sex among HIV-positive adolescents in South Africa. AIDS and Behaviour.


24. **Hodes R.** Ethical dilemmas in research with HIV-positive adolescents, Medical Humanities.

25. **Hodes R.** Morrell R. HIV Social Science in the Global AIDS Domain, Social Theory and Health.

26. Toska E, Cluver L, Pantelic M, **Hodes R,** Mbiko A. Is knowledge power? HIV-status disclosure and protective sexual practices among adolescent girls and boys in South Africa. In submission to BMC Public Health.


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**Matthew Kelly**


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**Nelleke Langerak**

1. Mann TN, Donald KA, Walker K, **Langerak NG**. Resolved lower limb tone abnormalities in children with HIV encephalopathy receiving standard antiretroviral therapy. AIDS Research and Therapy. 30, 12, 43, 2015


5. Mann TN, Laughton B, Donald KA, Langerak NG. HIV encephalopathy and bilateral lower limb spasticity despite early antiretroviral therapy in South African children. Reviews in Antiviral Therapy & Infectious Diseases. 8:118-119
6. **Langerak NG, Mann TN, Walker KG, Donald KA.** Observation of resolved lower limb tone abnormalities in children with HIV encephalopathy on antiretroviral treatment. Reviews in Antiviral Therapy & Infectious Diseases. 6, 76-77, 2014

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**Peer-reviewed, accepted for publication, and forthcoming in 2016**


# LIST OF PRESENTATIONS

<table>
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<tr>
<th>RESEARCH PRESENTATIONS</th>
<th>NUMBER AND TYPE</th>
<th>SELECT EVENTS</th>
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| International events    | 59 oral presentations  | • AIDS Conference 2014 (6)  
                        | 4 poster presentations | • International Workshop on HIV Paediatrics 2015 (3)  
                        |                          | • IAS Conference 2015 (3)  
                        |                          | • World Conference on Lung Health 2015 (2)  
                        |                          | • Southern African AIDS Conference 2015 (12)  
| National events         | 7 presentations | • South African AIDS Conference 2015  
                        |                          | • University of Cape Town 2015 (2)  
                        |                          | • University of Witwatersrand 2013 (2)  
                        |                          | • Surgical Research Day, Cape Town,  2014  
                        |                          | • 10th South African Neuro-Developmental Therapy Association (SANDTA) Congress, 2014  

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<tr>
<th>PRESENTATIONS FOR POLICY IMPACT</th>
<th>NUMBER AND TYPE</th>
<th>EVENTS</th>
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| International events            | 4 oral presentations | • WHO guidelines on service delivery for HIV-positive adolescents and consultation on developing updated adolescent treatment guidelines  
|                                 |                | • UNICEF South Africa and HQ, UNICEF ‘All-In for Adolescents’ meeting in Rwanda and high-level meeting of Southern and East African Health Ministers in Zambia  
|                                 |                | • Office of the Global AIDS Coordinator, President’s Emergency Plan to AIDS Relief (PEPFAR)  
|                                 |                | • World Bank, UNAIDS, UNICEF, ‘High Level Consultation on Scaling-up Proven Social and Structural Interventions to Prevent HIV Transmission’  
