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EXECUTIVE SUMMARY

Many countries have made important progress in tackling new HIV infections among children over the past decade. These reductions are far from universal, however. Worldwide, 2.6 million children and 2 million adolescents living with HIV remain significantly disadvantaged regarding access to HIV care and treatment1. Only 31% of children in need of antiretroviral (ARV) treatment received it in 2014, compared with 41% of adults2.

As the epidemic matures, we must also confront the clinical, developmental and psychosocial challenges facing a growing population of adolescents living with HIV. While overall AIDS-related mortality has decreased by 30% in recent years, mortality among this particularly vulnerable group has increased by 50%.

Urgent priorities are improving access to treatment and comprehensive care for paediatric and adolescent populations, integrating programmes that span these key populations to increase early entry and retention in HIV care and treatment, as well as expanding efforts to bridge identified research gaps and support evidence-based policies to improve the treatment and care of infants, children and adolescents living with HIV. Each is essential to achieving an AIDS-free generation.

The Collaborative Initiative for Paediatric HIV Education and Research (CIPHER), a programme of the International AIDS Society (IAS), works to address outstanding research gaps related to the clinical management and delivery of services to infants, children and adolescents affected by HIV. Since its launch in 2012, CIPHER has supported the efforts of several early-stage investigators to fill critical knowledge gaps that impede HIV diagnosis, prevention, treatment and care for infants, children and adolescents in resource-limited settings.

In 2015 alone, CIPHER:

• Promoted the paediatric HIV research agenda by building on the solid core programme developed in its initial phase.
• Awarded five new research grants.
• Announced the launch of its largest-ever research funding round, which will award US$ 1.2 million for cutting-edge paediatric and adolescent research in 2016.
• Extended its activities in paediatric HIV with an advocacy component.
• Convened key stakeholders and industry partners to address challenges associated with making optimal paediatric ARVs available.
• Broadened the scope of CIPHER stakeholders by bringing in additional partners and sponsors committed to advancing the CIPHER research and advocacy agenda.
• Organized two special issues in the Journal of the International AIDS Society (JIAS), “HIV and adolescents: focus on young key populations” and “Getting to 90-90-90 in paediatric HIV: what is needed?”

This 2015 CIPHER Annual Report provides background information on CIPHER and an overview of 2015 activities and events.

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ABOUT CIPHER

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.

Specifically, 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 exchange among paediatric HIV cohorts.

• Advocacy and outreach to support evidence-informed clinical, policy and programmatic decision-making.

CIPHER began in 2012 as a two-year research initiative, with the generous support of an unrestricted grant from founding sponsor ViV Healthcare. At the end of 2013, the IAS reaffirmed its commitment to paediatric HIV by making paediatrics a programme priority.

CIPHER complements existing global initiatives and creates new partnerships to maximize investment in paediatric HIV research and improve paediatric health outcomes. CIPHER’s scientific and programmatic foundation is informed by a comprehensive needs assessment. The initiative is guided by a world-class Scientific Technical and Advisory Committee (STAC) of experts in paediatric HIV convened by the IAS.

RESEARCH PROMOTION

Research Grant Programme

One of the main barriers to effective policy, programmatic and clinical decision-making in paediatric and adolescent HIV is the significant lack of data on these populations. The CIPHER Grant Programme works to support effective decision-making by targeting specific clinical and operational research gaps in paediatric and adolescent HIV in low- and middle-income countries (LMICs). By focusing on early-stage investigators, CIPHER grants also support a new generation of scientists, working to advance paediatric HIV research and foster innovative ideas and evidence-based approaches and interventions.

CIPHER research grants provide up to US$ 150,000 each for up to two years of research, with the requirement that 80% of direct costs of the grant must be spent in resource-limited settings. The high number of applicants for CIPHER grants indicates that the programme fills an important funding gap for early-stage investigators in paediatric and adolescent HIV research.

In 2015, at the 8th IAS Conference on HIV Pathogenesis, Treatment and Prevention (IAS 2015) in Vancouver, Canada, CIPHER was proud to award five new grantees (see page 5), chosen from among 80 eligible applicants. To keep the programme current, an in-committee review of the research priority topics was conducted for the 2015 round. A new round of CIPHER grants - the largest to date, with US$ 1.2 million to be awarded to young investigators - will be presented at the 21st International AIDS Conference (AIDS 2016) in July 2016 in Durban, South Africa.

Since its launch in 2012, the programme has awarded more than US$ 2 million to 14 young researchers conducting innovative research on paediatric AIDS at academic and research institutions in LMICs. With the first seven projects awarded in 2012 now completed, the impact of the programme is clear: as of July 2015, this first group of CIPHER grantees generated more than 20 publications and more than 120 presentations at local, national and international meetings. The CIPHER grant has allowed the grantees to unlock a cumulative US$ 4 million in additional funding, including RO1 funding from the U.S. National Institutes of Health. There has been an unexpected ‘halo’ effect of local capacity building, as well, as Ph.D and Masters students, technicians and nurses have been trained working on CIPHER-funded projects.
2015 CIPHER grantees and their research topics

Suvaporn Anugulruengkitt, Chulalongkorn University, Thailand
Adverse events of 6-week zidovudine/lamivudine/nevirapine antiretroviral prophylaxis regimen for prevention of HIV mother-to-child transmission among high risk new-borns in Thailand.

Heather Bailey, University College London, United Kingdom
Characteristics, outcomes and models of service provision for HIV-positive youth in Ukraine.

Jackson Kijumba B. Mukonzo, Makerere University, College of Health Sciences, Uganda
Optimization of paediatric antiretroviral therapy during co-treatment of HIV-associated cancers.

Irene Nyambura Njuguna, University of Washington Global Assistance Program Kenya, Kenya
Financial incentives to increase paediatric HIV testing.

Birkneh Tadesse, Hawassa University, Ethiopia
Improving treatment of HIV-infected Ethiopian children through earlier detection of treatment failure.

2015 Grantees at the Grant Programme Award Ceremony, at IAS 2015 Vancouver, Canada, with Linda-Gail Bekker, President-Elect of the IAS. From left to right: Heather Bailey, Suvaporn Anugulruengkitt, Jackson Kijumba B. Mukonzo, Irene Nyambura Njuguna, Birkneh Tadesse, Linda-Gail Bekker.

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JIAS Special Issue Series

In 2015, CIPHER continued its series in the Journal of the International AIDS Society (JIAS), focusing on critical topics in paediatric and adolescent research with two special issues.

HIV and Adolescents: Focus on Young Key Populations

Young people are at an increased risk of HIV, and young key populations (young men who have sex with men, transgender people, people who inject drugs, sex workers, and young women) are particularly vulnerable. Yet youth are often not included in studies on key populations, despite the high proportion of the HIV burden they bear. This collection presents a forceful call to address this global public health issue, highlighting where we are leaving adolescent key populations behind in our response to HIV, identifying key research gaps and articulating ways forward.

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Getting to 90-90-90 in Paediatric HIV: What is Needed?

This issue presents a compelling collection of articles underscoring challenges and ways forward in achieving the 90-90-90 targets for children and adolescents, not only within the health sector, but also with partners including funding agencies, policy makers, industry, civil society, children and adolescents themselves. Contributors outline an agenda for expanded academic and programmatic research on paediatric HIV, as well as innovative and integrated approaches to testing, treatment, transitioning to adult care and delivery of health services within a child and youth-friendly framework.

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SUPPORTING COHORT COLLABORATION

CIPHER Cohort Collaboration

Supporting cohort collaboration is another way that CIPHER works to help address knowledge gaps and to support effective policy, programmatic and clinical care decision-making for paediatric populations.

The CIPHER Global Cohort Collaboration is the largest paediatric and adolescent observational cohort collaboration to date, including 12 major cohorts worldwide. At the Global Cohort Collaboration annual meeting on 4–5 May 2015 in Venice, Italy, the group reviewed the results of its first data merge, involving two ongoing projects representing about 170,000 children and adolescents, which addressed these key research questions:

- Time on first-line ARVs in children.
- Global epidemiology of perinatally HIV-infected adolescents.
As part of its commitment to use the cohort collaboration most effectively, and to avoid overlap and duplication of efforts, the group also reviewed the most strategic and appropriate ‘space’ for its work related to issues of major public health impact at the global level, and Northern and Southern Hemisphere comparisons. Within these areas, three main efforts to be addressed collectively through collaboration among all participating cohorts with CIPHER support were identified by the group:

1. Further strategic exploration of the current data set.
2. New research projects requiring a new data merge.
3. Developing the CIPHER collaboration to become the ‘go to’ platform in paediatric HIV cohort research.

In line with the CIPHER objectives, the group also expressed interest in integrating into its activities responses to industry questions to help accelerate the availability of paediatric ARVs and support normative guideline development.

The cohort is governed by an Executive Committee from IAS and CIPHER, and a Steering Committee with representatives of participating cohort networks. Data management is led by a collaboration of major data centres and the Project Oversight Team. Analysis of the two projects is led by Project Teams and is supported by a grant to a young investigator from a LMIC funded through the project and selected through a competitive application process, as a capacity building component. CIPHER was pleased to announce the winner of this award, Amy Slogrove, at IAS 2015.

These cutting edge collaborations are supported by a $500,000 grant from CIPHER, which supports data centers on three continents (University of Cape Town, South Africa; University College London, UK; Harvard School of Public Health, USA).

CIPHER would like to acknowledge the hard work and contribution of all who have contributed to building this project and taking it this far.

**Project partners include:**

- Baylor International Pediatric AIDS Initiative at Texas Children’s Hospital (BIPAI)
- Caribbean, Central and South America Network for HIV Research (CCASAnet)
- The European Pregnancy and Paediatric HIV Cohort Collaboration (EPPICC) including PMTCT and Eastern European cohorts
- Identifying Optimal Models for Care in Africa (Optimal Models ICAP)
- International Epidemiologic Database to Evaluate AIDS Asia-Pacific (IeDEA-A-P)
- International Epidemiologic Database to Evaluate AIDS Central Africa (CA-IeDEA)
- International Databases to Evaluate AIDS East Africa (IeDEA-East Africa)
- International Epidemiologic Database to Evaluate AIDS Southern Africa (IeDEA-SA)
- International Epidemiologic Database to Evaluate AIDS West Africa Collaboration (WADA and pWADA)
- Médecins Sans Frontières Pediatric Cohorts (MSF)
- Pediatric HIV/AIDS Cohort Study: Adolescent Master Protocol (PHACS AMP) and Surveillance Monitoring for ART Toxicities Study (PHACS SMARTT)
- Pediatric Late Outcomes Protocol (PACTG/IMPAACT 219/219c) and A Prospective Surveillance Study of Long-term Outcomes in HIV-infected Infants, Children and Adolescents (IMPAACT P1074)
Adolescent Transition Workshop

As the HIV epidemic matures, thanks to better life-saving paediatric ARVs and advances in clinical care, children with HIV who receive care are now surviving to become adolescents. Many, however, do not remain on treatment, with staggering results: AIDS is now the leading cause of death among adolescents in Africa and the second most common cause of death among adolescents globally. Bridging the gap between paediatric and adult populations to help ensure that HIV-infected adolescents and young adults are retained in care and supported through this developmental transition is a major challenge. There is an urgent need to improve access to ARV treatment and comprehensive care for adolescents.

CIPHER’s Adolescent Transition Workshop, co-hosted by the IAS and the IeDEA Network Coordinating Center, was held in conjunction with the 19th International Workshop on HIV Observational Databases (IWHOD) on 28 March 2015 in Catania, Italy. The objectives of the gathering were to establish a baseline on how paediatric HIV cohorts are tracking, or planning to track, adolescents from paediatric settings to adult care; identify research gaps in adolescent transition; and discuss mechanisms for addressing those gaps. The meeting reached consensus on a broad-stroke research agenda in adolescent transition, and developed a roadmap on the way forward that included the following key issues:

• Defining transition and critical outcomes.
• Identifying key indicators for national and global reporting.
• Developing a common analytical plan for transition studies.
• Engaging with adult cohorts and clinicians.
• Harmonizing and integrating data between paediatric and adult cohorts.

CIPHER Online Database

The CIPHER online paediatric HIV cohort database supports cohort collaboration and research, and promotes the need for research to investigators, funders and policy makers. The database is an open-access platform mapping out paediatric and adolescent observational cohorts worldwide. It features an interactive map and detailed cohort profiles, including the number of participants in each cohort disaggregated by age group, sex and route of HIV transmission.

In 2015, in response to user feedback, new search and information viewing functions were designed and added to the database, allowing users to further refine their information searches to graphically visualize information by specific variables, and to export the data into an Excel format.
ADVOCACY

Thematic Roundtable on Paediatric ARVs

Since 2013, the IAS Industry Liaison Forum (ILF) and CIPHER have collaborated on a series of roundtable discussions with industry partners and other stakeholders designed to expand access to the most needed paediatric ARVs.

One of the main challenges faced by industry partners highlighted in these discussions is the lack of involvement from industry partners in the development of normative guidelines on ARVs. To help address this, the main objective of the Thematic Roundtable on Paediatric ARVs was to provide a forum for feedback with industry partners on the process and discussions leading up to the next World Health Organization (WHO) consolidated ARV guidelines revision, and a report-back from the Paediatric ARV Drug Optimization 2 (PADO 2) meeting. The roundtable meeting also provided an opportunity for a more in-depth discussion on the work being done in the paediatric space on optimal drug formulation (Paediatric HIV Treatment Initiative), coordinated procurement and global supply of paediatric ARVs, and efforts towards alignment of regulatory requirements. This was followed-up with an update from the PADO group in the third quarter of 2015 via a teleconference.

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Thematic Roundtable on Paediatric HIV Diagnostics

Building on the paediatric ARVs roundtable model, and in response to a request from diagnostic industry partners, ILF and CIPHER also convened a thematic roundtable on Paediatric HIV Diagnostics: Early Infant Diagnosis and Beyond on 19 July 2015, in Vancouver, Canada. The discussion brought together key stakeholders in diagnostics and paediatric HIV to identify and discuss challenges along the continuum of diagnostics development and implementation, raise awareness of existing initiatives in paediatric HIV diagnostics and identify opportunities for collaboration.

The roundtable highlighted the investment in product development that has yielded several early infant diagnosis and viral load products that may be used at or near points of care (as well as in the laboratory), and that are suitable for deployment in resource-limited settings. Discussion also focused on the challenges that persist in the rapid adoption and implementation of these products within countries.

At the policy level, the 2015 WHO guidance on infant testing algorithms will help provide direction for developers and implementers towards reliable access to essential testing. A number of demand-side initiatives are also poised to support adoption and implementation. Overcoming regulatory hurdles is a priority and some immediate opportunities, such as consortium efforts, can ensure that emerging technologies reach patients faster. However, overall simplification of regulatory pathways might have to remain a longer-term goal. Consensus on the clinical utility and rational deployment of new electronic identification (EID) technologies will have to be widely accepted, especially at the country level. The utility and optional use of drug resistance testing will also require better understanding.

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INTERNATIONAL WORKING GROUPS

CIPHER continued to be represented in relevant international working groups in 2015. These efforts position the IAS as a stakeholder in paediatric HIV, create stakeholder engagement and help identify strategic activities where resources can be most effective and have the most impact. It also allows for partner engagement, identifying synergies and avoiding overlap.

Working Together

- Adolescent Treatment Coalition.
- Inter-Agency Task Team for Prevention and Treatment of HIV Infection in Pregnant Women, Mothers and Children; Child Survival Working Group (IATT CSWG).
- New Horizons Advancing Paediatric HIV Care Collaborative.
- Paediatric ARV Procurement Working Group (PAPWG).
- Paediatric ARV Working Group (PAWG).
- Paediatric HIV Treatment Initiative of UNITAD, DNDi and the Medicines Patent Pool.

On 6 July 2015, the IAS hosted the Adolescent Treatment Coalition in its Geneva offices for a two day working meeting to review the purpose, structure and work of the coalition, and define a way forward. Following a transparent-bidding process, the IAS was proud to be selected as the next host for the Coalition. Funding was secured in the third quarter of 2015 to hire a full-time Coordinator for the group.