

Looking back

Annual report 2012



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The Collaborative Initiative for Paediatric Education and Research (CIPHER)

Annual Report 2012

Executive Summary

There has been notable progress in reducing vertical transmission of HIV: 57% of pregnant women with HIV accessed treatment for prevention of mother to child transmission (PMTCT) at the end of 2012 compared with 48% in 2010. Despite this progress, 3.3 million children are living with HIV worldwide and 330,000 were newly infected in 2011.

The paediatric population remains significantly disadvantaged with respect to access to treatment in comparison with adult populations. In addition, there is little data on the effect of antiretroviral therapy (ART) on growth and development of children, nor on how to ensure optimal adherence as they reach adolescence.

Thus, there is an urgent need to address outstanding research questions to inform the preparation of guidelines and to improve access to more effective diagnosis, prevention, treatment and care interventions for children and adolescents. To accelerate the paediatric research agenda, the International AIDS Society (IAS), with the generous support of ViiV Healthcare, has established the Collaborative Initiative for Paediatric HIV Education and Research (CIPHER).

CIPHER was officially launched in 2012 following a comprehensive needs assessment, guided by a Scientific and Technical Advisory Committee (STAC) consisting of leading researchers and policy makers with a track record in the field of paediatric HIV. The needs assessment included a literature review and key informant interviews with experts, and outlined a set of research priorities that has been used to inform and guide implementation of CIPHER.

To meet the objectives of advancing paediatric HIV research, a CIPHER Grant Programme was launched at the [XIX International AIDS Conference](#) (AIDS 2012) in Washington DC, targeting young investigators and welcoming applications in the priority research areas identified in the needs assessment. By its closing date, the grant programme had received 143 letters of intent from around the world, with an even distribution across all priority research questions.

AIDS 2012 also created an opportunity to convene a consultation with paediatric HIV cohort investigators and to initiate a dialogue on how to strengthen paediatric cohort collaboration and support generation of more and more robust evidence that can inform policy makers and programme implementers.

Introduction



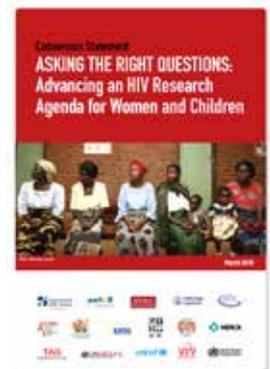
The ambitious global target of eliminating vertical transmission of HIV by 2015 is providing a road map for the international HIV community to scale up efforts to ensure an HIV-free generation. At the end of 2011, 57% of pregnant women with HIV accessed PMTCT compared with 48% in 2010.^{1,2}

Despite notable progress, children continue to be born with HIV and there are 3.3 million children estimated to be living with HIV worldwide³. In 2011, 330,000 children, 90% of whom live in sub-Saharan Africa, acquired HIV infection and 230,000 died of AIDS-related causes. Infants and children remain significantly disadvantaged in their access to ART compared with adult populations; at the end of 2011, only 28% of treatment-eligible children had access to ART compared with 58% coverage for adults in low- and middle-income countries. And while the number of children exposed to antiretrovirals (ARVs) for prophylaxis and maternal treatment is increasing, there is insufficient data on the long-term impact of early and extended ARV exposure on growth and development.

Access to timely, reliable early infant diagnosis remains only one of many key challenges that paediatric populations face in resource-limited settings. Since many HIV-exposed infants are not diagnosed and placed on ART early, HIV-related mortality rates for children younger than two years remain unacceptably high. In addition, clinical management of HIV and other concurrent conditions, such as TB, malaria and malnutrition, remains suboptimal, and contraindications and interactions between ARVs and other drugs and interventions to treat co-morbid conditions are poorly studied in paediatric populations. In addition, there is an urgent need for evidence-based adherence support and sexual and reproductive health interventions tailored to the growing population of perinatally infected adolescents.

The IAS has undertaken significant work to define priority clinical and operational research questions for women and children, and to advocate for increased investments in this research agenda as a strategic priority of the [IAS-Industry Liaison Forum](#). The environmental scan, [Mapping HIV Research Priorities for Women and Children](#), and the [Consensus Statement, Asking the Right Questions: Advancing an HIV Research Agenda for Women and Children](#), released in January 2010, provide the foundation for the IAS's ongoing role in promoting and accelerating HIV research relevant to women and children in low- and middle-income countries.

The generous support of the ViiV Healthcare UK Paediatric Innovation Seed Fund provided an opportunity for the IAS to build on its previous efforts in promoting paediatric HIV research – leveraging its convening power to bring together leading international scientists, clinicians and policy makers to address the needs of infants and children living with HIV – by establishing the Collaborative Initiative on Paediatric HIV Education and Research (CIPHER).



Mapping HIV Research Priorities for Women and Children, and the Consensus Statement, Asking the Right Questions: Advancing an HIV Research Agenda for Women and Children

¹UNAIDS. Global Report: UNAIDS report on the global AIDS epidemic 2012.

²WHO/UNICEF. Global monitoring framework for the global plan towards the elimination of new HIV infections among children by 2015 and keeping their mothers alive (EMTVT), April 2012.

³Global summary of the AIDS epidemic 2011: http://www.who.int/hiv/data/2012_epi_core_en.png.

About CIPHER



Launched in 2012, CIPHER addresses outstanding research gaps related to clinical management and delivery of services to infants, children and adolescents affected by HIV. It is designed to complement existing global initiatives and create partnerships with other organizations to maximize investment in paediatric research and improve paediatric health outcomes.

The key objectives of CIPHER are:

- Promoting and investing in targeted research that addresses knowledge gaps/priority questions that will help optimize service delivery and clinical management of infants and children in resource-limited settings.
- Convening stakeholders and establishing collaboration mechanisms to strengthen communication, knowledge transfer and exchange among paediatric HIV cohorts.

The CIPHER Scientific and Technical Advisory Committee

To provide scientific and technical guidance and networking power for CIPHER, a high-level Scientific and Technical Advisory Committee (STAC) was established. The STAC is composed of technical experts in paediatric research and clinical care from a broad range of stakeholders, including clinicians, academia, normative agencies and non-governmental organizations.

The role of the STAC is to provide scientific and strategic direction and technical advice. In addition, STAC members serve as excellent advocates for paediatric research, championing CIPHER within their organizations and networks, and helping identify opportunities to promote the initiative and its outcomes/findings. STAC members also play an important role in identifying strategic partners and contribute to convening and strengthening collaborations among paediatric HIV cohorts.

Events at AIDS 2012

CIPHER STAC Meeting

AIDS 2012 was used as an opportunity to convene the first in-person meeting of the CIPHER STAC to review the findings of the needs assessment, define the framework for the CIPHER Grant Programme, and discuss challenges and opportunities faced by paediatric cohorts. During the meeting, a Research Grant Working Group was established to provide expert advice and guidance on the grant programme, participate in the initial evaluation process, identify external reviewers and help in the selection process. The STAC furthermore agreed on publication of a special issue on perinatally HIV infected adolescents in the Journal of the International AIDS Society.

Consultation with Paediatric HIV Cohort Investigators at AIDS 2012

A consultation with paediatric cohort investigators was convened at AIDS 2012 as an opportunity to present CIPHER and provide a platform for identifying how CIPHER can support addressing some of the challenges they face and help promote better collaboration. The consultation was well-attended, with representation from 15 paediatric cohorts from around the world. The group warmly welcomed the initiative and emphasized the need for a dedicated meeting for paediatric HIV cohorts. Such a meeting would provide the necessary support by allowing existing paediatric cohort investigators to present an overview of their research and data collection, identify challenges and opportunities, and discuss mechanisms to benefit from CIPHER support. This meeting could serve as a platform for potential new collaborations and partnerships to be formed. The Paediatric European Network for Treatment of AIDS (PENTA) offered that the IAS organize the cohort meeting in conjunction with the PENTAID meeting in May 2013 in Venice, Italy, to ensure more effective use of resources. Based on the feedback from the group, the IAS also decided to develop an online, searchable paediatric cohort database as a long-term tool to serve cohorts and facilitate collaboration.



Needs Assessment

To identify outstanding research priorities and ensure that CIPHER complements rather than duplicates other opportunities available to paediatric researchers, the first phase of the initiative was a comprehensive needs assessment. The needs assessment included a review of peer-reviewed scientific literature, and findings were verified through key informant interviews with technical experts on the STAC.

The final report, [Evidence for Action: A Needs Assessment of Paediatric HIV Research Priorities](#), summarizes the current knowledge gaps in paediatric HIV research and lists the research priorities that provided a basis for the CIPHER Grant Programme. In addition to informing CIPHER objectives, the report supports advocacy and collaboration among key stakeholders, including activities undertaken to strengthen paediatric cohort collaboration.

Priority research topics identified by the CIPHER Needs Assessment

Clinical Research

- Pharmacokinetic and pharmacodynamic studies of paediatric antiretrovirals and drugs for co-morbid conditions (particularly for TB, malaria, other common childhood illnesses and nutritional interventions for malnutrition).
- Studies evaluating optimal ART initiation, long-term management and complications in children (especially children over two years of age) and adolescents.
- Studies evaluating the short-term and long-term impact of *in utero* exposure to maternal antiretroviral therapy and the short-term and long-term impact of paediatric antiretroviral therapy on physical and cognitive development of HIV-infected infants, children and adolescents (key areas include neonatal outcomes, metabolism, bone mineral density, and other clinically-relevant laboratory and biological markers).
- Studies evaluating the short-term and long-term impact of *in utero* exposure to maternal antiretroviral therapy on physical and cognitive development of HIV-exposed uninfected children and adolescents.
- 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.
- Evaluations of the most effective interventions to treat HIV co-infections and co-morbidities among children, including TB, malaria, other common opportunistic infections and malnutrition.

Operational Research

- Evaluations of interventions to improve access to reliable early infant diagnostics, including rapid test protocols.
- Evaluations and/or validation of simplified, standardized diagnostic tools to assess neurocognitive and physical development in HIV-exposed infected or uninfected infants, children and adolescents in resource-limited settings.
- 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 approaches to support childhood and adolescent adherence and transition to adult ART programmes.
- Studies evaluating the most effective interventions to support disclosure, access to psychosocial and sexual and reproductive health services, and delivery of biomedical HIV and sexually transmitted infection prevention interventions for adolescents.



CIPHER Grant Programme

The CIPHER Grant Programme was established to encourage research projects that have the potential to address the priority research questions identified by the needs assessment. To maximize the impact of CIPHER, US\$1 million, representing 43% of the support received by ViiV Healthcare, was allocated to be disbursed as grants to support research projects that have the potential to contribute to the optimization of diagnosis, prevention, treatment and care of infants, children and adolescents affected by HIV. At the same time, the programme intends to attract early-stage investigators to paediatric HIV research in order to cultivate a new generation of scientists dedicated to paediatric HIV research, and foster innovative ideas and evidence-based approaches and interventions.

The programme generated much interest and resulted in a total of 143 letters of intent (LOIs) from 35 countries, 111 of which met the eligibility criteria (Table X). The initial screening and scoring of the LOIs was carried out by the STAC Research Grant Working Group, which evaluated each LOI based on the proposal's potential contribution to addressing the identified research question, its overall quality, and the novelty and innovation of the approach, as well as the applicant's experience. In December 2012, the 24 shortlisted applicants (representing 12 countries) were invited to submit full proposals in 2013.

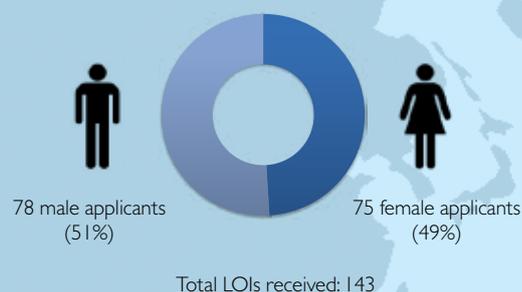
Full proposals received in mid-February 2013 will be submitted for peer-review, with the final selection to be decided by the Research Grant Working Group. Successful applicants will be notified in mid-April 2013, and an awards ceremony will be held at the [7th IAS Conference on Pathogenesis, Treatment and Prevention](#) (IAS 2013) in Kuala Lumpur, Malaysia, on 30 June-3 July 2013.

JIAS special issue

In collaboration with the Journal of the International AIDS Society (JIAS), production of a special issue on Perinatally HIV-infected adolescents was started in 2012. The special issue will contain 10 articles and cover such topics as epidemiology, treatment and resistance, cardiac and metabolic complications, resistance, neurodevelopment, mental health, disclosure and adherence. Guest editors of the special issue are CIPHER STAC members Lynne Mofenson and Marc Cotton. All articles submitted for publication in supplements are subject to peer review. The supplement will be launched at IAS 2013, where it will be distributed in print, and will be fully searchable and freely accessible online; all articles will be peer reviewed and indexed on PubMed. Statistics from the last two JIAS supplements show that they were accessed online around 800 times per day.

CIPHER Grant Applicants

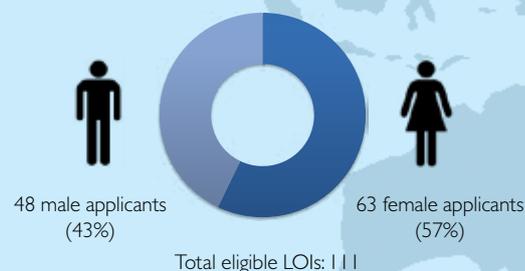
All LOIs Submitted



Total LOIs received: 143



Eligible LOIs



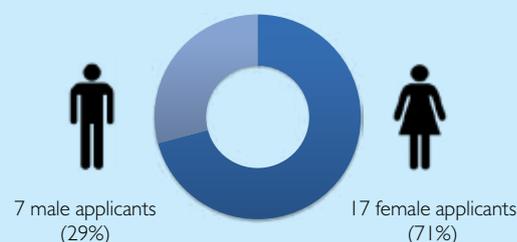
Total eligible LOIs: 111

Research priorities: 57 clinical, 54 operational

Research proposed to take place in 34 countries: Bangladesh, Botswana, Brazil, Burkina Faso, Cameroon, China, Colombia, Democratic Republic of Congo, Ethiopia, Ghana, Guatemala, Guyana, Haiti, India, Indonesia, Jamaica, Kenya, Madagascar, Malawi, Mozambique, Myanmar, Nigeria, Papua New Guinea, Peru, Republic of Congo, Rwanda, South Africa, Thailand, Uganda, Ukraine, United Republic of Tanzania, Viet Nam, Zambia and Zimbabwe.



Shortlisted LOIs



Total: 24

Research priorities: 14 clinical, 10 operational

Research proposed to take place in 13 countries: China, Ethiopia, Kenya, Malawi, Papua New Guinea, Peru, Republic of Congo, South Africa, United Republic of Tanzania, Thailand, Uganda, Zimbabwe



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