



Collaborative HIV Paediatric Study (CHIPS) Annual Report 2010/11

June 2011

Introduction

CHIPS is a multi-centre cohort study of HIV infected children in the UK and Ireland. It was established in 2000 and is a collaboration between clinical centres that care for HIV infected children, the National Study of HIV in Pregnancy and Childhood (NSHPC) at the Institute of Child Health, and the Medical Research Council (MRC) Clinical Trials Unit which also coordinates the Paediatric European Network for the Treatment of AIDS (PENTA) trials.

The main objectives of CHIPS are to describe clinical, laboratory and treatment data for these children, and to describe the use of paediatric HIV services. CHIPS aims to enhance the exchange of information and expertise between clinics in order to promote standardised high quality paediatrician-led care of all HIV-infected children in the UK and Ireland.

CHIPS is primarily funded by the NHS London Specialised Commissioning Group.

How CHIPS works

Children born to HIV infected women or those found to have HIV infection after birth are initially reported to the NSHPC. The NSHPC then notifies CHIPS of any children with confirmed infection, and for each of these children a baseline and prospective CHIPS questionnaire is sent to the clinic of care for completion.

Summary data to the end of March 2011¹

A total of 1,699 children were reported to CHIPS by the end of March 2011, comprising virtually all of those receiving HIV-related care in the UK and Ireland from 2006 onwards. The median age at first presentation of those born in the UK or Ireland has remained relatively constant at around 6 months although 11% did not present until ≥ 5 years. For children born abroad it increased from less than 2 years up to 1991 to 6 years in 1997-2002, 7 years in 2003-2005, and 9 years in 2006 onwards. Similarly the age distribution of the cohort has changed considerably over the years. In 1996 the median age was 5.1 years (inter-quartile range, IQR 2.9-7.6) and this increased year on year to 12.4 years (IQR 9.1-15.2) in 2010. Furthermore, the proportion of the cohort aged ≥ 10 years increased from 11% in 1996 to 70% in 2010.

The rate of hospital admissions in the cohort declined from 0.6 per child year in 2000 to 0.1 in 2009, and 108 children in CHIPS follow up were known to have died, including 6 in 2008, 8 in 2009 and 1 in 2010. Viral load response among those starting combination ART naïve improved with calendar time: 47% suppressed viral load $\leq 50\text{c/ml}^2$ at 12 months in 1997-2000, increasing to 82% for 2009 onwards. Furthermore there was some evidence for an increase in the duration of suppression for children starting ART naïve: in those suppressing viral load $\leq 400\text{c/ml}$ within the first 12 months of therapy in 2000-3 24% had rebounded $>1000\text{c/ml}$ within a year following suppression, while in 2004-2010 only 17% had rebounded during this time. The greatest improvement was in those aged ≥ 10 years, where the median time to rebound in 2000-2003 was 1.8 years, while in 2004-2010 this was 4.6 years.

¹ Numbers are based on reports received rather than children seen to the end of March 2011. 2010/11 data are subject to reporting delay and may therefore be incomplete.

² Or \leq lower limit of detection of the assay if the lower limit was >50 but $\leq 400\text{c/ml}$.

Of the 1,699 children reported to CHIPS, 1,190 were alive and in active follow-up at a CHIPS clinic, and 305 had transferred to adult care. Of the 1,190 remaining in CHIPS, just over half (51%) were female, 48% were born in the UK or Ireland, 79% were of black African ethnicity, and nearly all (97%) were known to have been infected through mother-to-child transmission. Half (53%) were being seen at clinics in London, 36% in the rest of England, 4% in Scotland, 1% in Wales, 5% in the Republic of Ireland, and <1% in Northern Ireland. A quarter (23%) had progressed to CDC stage B and another 25% to CDC stage C during follow-up. At last follow-up, 15% remained ART naïve, 4% were on mono or dual therapy, and over two-thirds (72%) were on combination therapy. Eight per cent were off all ART after having previously taken it. The median age of the 305 young people who transitioned to adult care was 17 years. Five year projections for perinatally HIV-infected children suggest that numbers will remain relatively stable overall as the annual number of new diagnoses equates with numbers transferring to adult care.

Developments 2010/11

UK and Ireland:

- CHIPS follow up forms for 2010-11 were returned for 73% of children known to be alive and in follow-up at hospitals collaborating in CHIPS.
- As last year, this year's annual feedback slides have been sent out together with the NSHPC's relevant regional slides.
- The CHIPS team has funding from the Monument Trust for a five year in-depth follow-up study of 400 young people in CHIPS and 300 HIV-uninfected controls. This new cohort is called AALPHI (Adolescents and Adults Living with Perinatal HIV cohort), and is in development this year and will hopefully start recruiting towards the end of 2011.
- CHIPS is also working with the UK Register of HIV Seroconverters to ensure continued follow-up of young people as they transfer to adult care. The UK Register is a national cohort of individuals whose time of HIV seroconversion can be reliably estimated. We hope that young people with perinatal infection will give consent to join the UK Register (at age 16+), which will provide critical data on the long-term consequences of HIV and ART in adulthood. We will be seeking an amendment to the UK Register's ethical approval later this year to allow for this change.

European Union:

- CHIPS has played a leading role in the paediatric component of the COHERE PLATO II project, which investigated the incidence of triple class virological failure in children across the EU, and factors associated with response. This work was recently published in the Lancet.
- CHIPS also contributes ongoing data to the European Pregnancy and Paediatric HIV Cohort Collaboration (EPPICC) pharmacovigilance programme, which this year was investigating the long-term safety of fosamprenavir and darunavir in children.
- CHIPS has led a EPPICC collaborative project describing the use of ART, response to treatment, and frequency of treatment interruptions and switching in infants across the EU.
- CHIPS has also contributed data to a Europe-wide EuroCoord project measuring the incidence of transmitted drug resistance, and its influence on response to combination ART in patients starting ART naïve.

Published papers and conference presentations

CHIPS data have been presented at the following national and international meetings in the last 12 months:

- 5th Annual CHIVA Conference, Cardiff, 2011
- 2nd International Workshop on HIV Paediatrics

- 15th International Workshop on HIV Observational Databases, Prague 2011.

In addition, the following papers, based wholly or partly on CHIPS data, have been published in or submitted to peer review journals:

- The Pursuing Later Treatment Options II (PLATO II) project team. Risk of triple-class virological failure in children with HIV: a retrospective cohort study. *Lancet*. 2011; **377**(9777): 1580-7.
- Wittkop L, Gunthard HF, de Wolf F, Dunn D, Cozzi-Lepri A, de Luca A, et al. Effect of transmitted drug resistance on virological and immunological response to initial combination antiretroviral therapy for HIV (EuroCoord-CHAIN joint project): a European multicohort study. *Lancet Infectious Diseases*. 2011; **11**(5): 363-71.
- Donegan KL, Walker AS, Dunn D, Judd A, Pillay D, Menson E, et al. The prevalence of darunavir associated mutations in HIV-1 infected children in the UK. *Antiviral Therapy* – under review.

Please visit our website (www.chipscohort.ac.uk) to obtain further details of talks and papers as well as downloads where available.

Work in progress and future plans

Over the coming months we plan to:

- begin collecting SOUNDEX on CHIPS forms, to help flag up duplicate reports of children
- gain ethics approval to enable young people leaving paediatric care to be followed-up in adult care through the UK Register of HIV Seroconverters
- continue to participate in the Electronic Patient Records study (PI: Caroline Sabin) to improve data collection methods for CHIPS
- continue to support commissioning needs by exploring outcome measures for paediatrics
- submit paper describing Kaletra dosing and response to treatment
- begin an analysis of the whole of the CHIPS cohort, concentrating on adolescence, second-line, mortality, and transition to adult care
- lead the analyses of data from the following Europe-wide individual patient meta-analyses:
 - fosamprenavir, darunavir and atazanavir long-term safety project
 - use of ART and response to treatment in infants in Europe
 - comparison of the incidence of triple-class virological failure in adults and children
 - effect of transmitted drug resistance on response to ART in children.

Forthcoming meetings

CHIVA runs a series of educational meetings, held bi-monthly in central London. For further information please contact Natasha Street at the MRC Clinical Trials Unit (nss@ctu.mrc.ac.uk).

Contacts for further information

Please visit our website for further information about CHIPS:

www.chipscohort.ac.uk

Alternatively, please contact Brendan Murphy, CHIPS Data Manager, MRC Clinical Trials Unit, Aviation House, 125 Kingsway, London WC2B 6NH, UK. Tel: 020 7670 4784. E mail: chips@ctu.mrc.ac.uk.

PLEASE NOTE – The MRC Clinical Trials Unit will be relocating to Aviation House, 125 Kingsway, London, WC2B 6NH on 1 July 2011 . Telephone numbers will not change.