

## QUALITY IMPROVEMENT REPORT

## Maximising opportunities for increased antiretroviral treatment in children in an existing HIV programme in rural South Africa

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**Problem** Infants and young children infected with HIV as a result of mother to child transmission are not being identified or started with antiretroviral treatment (ART) in line with HIV guidelines in resource limited settings.

**Design** Retrospective analysis of data from a paediatric cohort before and after an intervention strategy.

**Setting** Rural public HIV treatment programme in the province of KwaZulu-Natal, South Africa.

**Key measures for improvement** Increase in the number of HIV infected infants and children who start HIV treatment each year; increase in the proportion of children starting ART with less immune suppression, shown by higher CD4 counts and less advanced World Health Organization clinical stages for HIV.

**Strategies for change** Late 2008: training in paediatric HIV for all staff in contact with mothers and children; campaigns for increased HIV testing at immunisation and clinics; routine testing of children with tuberculosis and malnutrition for HIV, and HIV testing of all children admitted to hospital. The establishment of a family HIV clinic in late 2007.

**Effects of change** The number of children (1 year to ≤15 years) starting ART each year increased from 43 in 2004 to 254 in 2011; the corresponding number of infants (<1 year) starting treatment increased from 2 to 59. A trend towards increasing CD4 counts at the start of treatment was found.

**Lessons learnt** It is possible to improve the identification of HIV infected children and ensure a prompt start on ART where needed with relatively simple measures and limited implications for staffing and budgets.

The setting is an HIV treatment and care programme in Hlabisa, a rural sub-district of the province of KwaZulu-Natal, South Africa. In 2011, the population of Hlabisa was about 220 000 people, of whom an estimated 37.8% (83 160) were children aged 1 year to ≤15 years and 2.4% (5280) infants aged <1 year. The area has a high burden of both HIV and tuberculosis,<sup>1 2</sup> with an estimated overall HIV prevalence in 2010 of 23% among adults, with no evidence of a substantive decline in HIV incidence.<sup>3</sup> In 2011 there were about 5000 deliveries, of which an estimated 2000 were to HIV positive women (Africa Centre Surveillance, www.africacentre.com). The notification rate of adult tuberculosis in Hlabisa more than doubled between 2003 and 2008, from an estimated 707 per 100 000 a year to 1700 per 100 000; 75% of those adults were HIV positive.

Since 2004 the Africa Centre for Health and Population Studies (www.africacentre.com), funded by the Wellcome Trust, has partnered with the local Department of Health in implementing and running a comprehensive HIV programme in Hlabisa.<sup>4</sup> From inception, additional funding was provided by PEPFAR, the United States' President's Emergency Plan for AIDS Relief, to support activities includ-

ing monitoring and evaluation, staff training, and management of the programme. The programme was initially based at the local 250-bed hospital but rapidly decentralised, with clients accessing HIV services at their nearest clinic, along with other primary care services, including antenatal services, child growth, immunisation clinics, tuberculosis services, and management of undernutrition. Attendance at clinics for antenatal and child health monitoring in Hlabisa is high, with over 95% of pregnant women attending for at least one antenatal visit<sup>5</sup> and primary vaccination in the first 6 months of life being achieved in over 80% of children.<sup>6</sup> The programme is led by nurses and counsellors, with doctors (mostly without postgraduate specialisation) visiting clinics to start antiretroviral treatment (ART) and manage clinical problems during follow-up. Most clinics are typical of small facilities in rural South Africa, with limited physical space and shortages of healthcare workers. One or two HIV counsellors and one to four primary healthcare nurses covering all services are allocated to each clinic, with a ratio of 795 HIV positive patients receiving ART per nurse, and 386 per counsellor (Till Barnighausen, personal communication, 2012). Numbers of people starting ART have increased substantially since the start of the programme, from 1800 at the end of 2006 to over 17 000 at the end of 2011, 73% of whom were female and 10% of whom were children aged <15 years.

The clinics in the programme follow national and provincial guidelines (reflecting international World Health Organization recommendations<sup>7</sup>) for starting and continuing treatment in HIV positive children. Healthcare and medications, including antiretroviral drugs, are free for children in South Africa and are provided by the government. Testing for HIV in pregnancy is on an "opt-in" basis, with high rates of testing (>90%); HIV testing using polymerase chain reaction at age 6 weeks is recommended for all infants born to HIV infected mothers, with results available two weeks later. Children aged >18 months not previously tested or with clinical signs or symptoms suggestive of HIV are tested using HIV antibodies with immediate results. Antiretroviral drugs are started on the basis of a combination of clinical and immunological criteria, dependent on age. The South African guidelines for paediatric HIV treatment were updated in 2010<sup>8</sup> in response to revised WHO recommendations,<sup>9</sup> including HIV treatment of all HIV infected infants (aged <12 months) irrespective of their clinical or immunological status.

In South Africa the estimated number of children starting ART each year has risen from 4200 in 2004 to 152 000 in 2011. However, assessing the proportion of eligible children who have started ART is challenging in this setting. Coverage of HIV treatment in children in South Africa has been estimated in ongoing work by Johnson and colleagues at the Centre for Infectious Disease Epidemiology and Research,

**Table 1 | Children (aged  $\leq 15$  years) starting antiretroviral treatment (ART) each year, 2004-11**

Year	No of children			Proportion of all children (out of total No in programme) (%)	Estimated mother to child transmission rate at age 6 weeks (%)	Estimated No of new paediatric cases of HIV infections*
	Aged <1 year	Aged 1- $\leq 15$ years	Total			
Jun 2004 to Sep 2005	2	43	45	9	14†	280
Oct 2005 to Sep 2006	1	99	100	8	14	280
Oct 2006 to Sep 2007	6	161	167	8	12‡	240
Oct 2007 to Sep 2008	20	251	271	8	8§	160
Oct 2008 to Sep 2009	61	414	475	13	6	120
Oct 2009 to Sep 2010	59	287	346	9	4¶	80
Oct 2010 to Sep 2011	59	254	313	7	3**	60

\*Out of total of 2000 HIV positive women.

†Data from a large mother to child transmission programme in Hlabisa sub-district.<sup>23</sup>

‡Increasing numbers of HIV positive women with low CD4 counts started ART between 2004 and 2006, resulting in an estimated decrease in the rate of mother to child transmission of HIV.

§New guidelines were introduced in February 2008, including provision of zidovudine to all pregnant women not already receiving ART from 28 weeks' gestation. By this period the ART programme was well established for adults, with no waiting times for treatment, and most women with CD4 counts <200 cells/ $\mu$ L had started ART for life.

¶Estimated further decrease in the rate of mother to child transmission of HIV as more women with low CD4 counts had started ART for life, and the guidelines rolled out in February 2008 had been fully implemented across the Hlabisa sub-district.

\*\*In August 2010 new guidelines for prevention of mother to child transmission were introduced, including: zidovudine for all pregnant women not already receiving ART from 14 weeks' gestation; all pregnant women with CD4 counts <350 cells/ $\mu$ L (rather than <200 cells/ $\mu$ L) to start ART for life; and all infants aged <1 year to start ART.

University of Cape Town.<sup>10</sup> Their models (rather than data collected from treatment sites) are available for national trends and indicate that increasing numbers of children have started ART since 2004. However, these modelled estimates cannot be split down to provincial or local level, and rural areas are probably lagging behind urban centres.

### Problem

Worldwide, in 2008 an estimated 430 000 children became infected with HIV (mostly via mother to child transmission), of whom 90% live in sub-Saharan Africa.<sup>11</sup> Without treatment children progress rapidly to disease, with about 20% of perinatally infected infants dying within the first year of life, and 50% by their second birthday.<sup>12</sup> However, early ART leads to increased survival, improved morbidity, and immunological benefits.<sup>13-15</sup>

Despite the roll-out of prevention of mother to child transmission programmes and increasing availability of HIV testing with polymerase chain reaction to identify perinatally infected infants at age 4-8 weeks, follow-up of infants remains inadequate in resource limited settings.<sup>16-17</sup> Problems cited include "vertical" systems in primary healthcare facilities and lack of integration of prevention of mother to child transmission programmes with other maternal and child health initiatives, such as immunisation and growth monitoring; missed opportunities to identify HIV positive children postnatally; poor turnaround time of results owing to lack of capacity in laboratories and transport problems from rural areas; and lack of training of primary healthcare staff to recognise and refer potentially HIV positive children, particularly older children, who have little routine contact with the health facilities. Although guidelines exist, putting these into practice in already overburdened health systems remains an enormous challenge. As a result, outside research settings many children die before diagnosis, and those who progress more slowly are diagnosed relatively late, usually presenting with illness at an advanced stage of disease.<sup>18-20</sup>

We have previously reported on the first four years (2004-08) of our decentralised nurse and counsellor driven HIV treatment programme in rural South Africa, in which 477 children had started receiving ART, of whom very few were

aged <1 year.<sup>21</sup> Using local facility and population based data and a deterministic model, we also calculated the number of children in need of treatment<sup>22</sup> and estimated that by the end of 2007 only two thirds of children who were in need of treatment and were still alive had started ART; this represents a huge unmet need.

We recognised that many opportunities were missed in the existing system to identify infants and children who were HIV positive, and we postulated that this was the result of problems in the health system rather than lack of resources, unclear guidelines, or unwillingness of parents to bring their children to clinics for testing. Here we describe initiatives introduced in late 2008 to improve early detection of HIV positive infants, to increase diagnosis of older children who missed being identified in infancy, and the impact of these strategies on the number and characteristics of children starting ART.

### Key measures for improvement

Our aim was to identify perinatally infected HIV positive children as early as possible and start ART as appropriate; to diagnose older HIV positive children who had missed being tested as infants; to start ART in children before they were clinically unwell; and to ensure sustainability of these improvements.

Key outcomes measured were:

- Number of HIV positive infants (children aged <12 months) starting ART
- Number of HIV positive children aged 1 to  $\leq 15$  years starting ART
- Proportion of children starting ART with higher CD4 counts or CD4% values (indicating less immune suppression) and at WHO stages 1-2 rather than stages 3-4 (indicating better health).

As discussed above, providing an accurate denominator for children eligible for ART, and thus being able to report on the proportion of eligible children receiving HIV treatment, poses a problem in our setting. It relies on accurate numbers of HIV infected pregnant women (and thus accurate numbers of HIV exposed infants) and on accurate numbers of HIV exposed infants known to be HIV infected in utero and during delivery. We have good estimates of the proportion

Table 2 | Clinical markers in infants and children starting antiretroviral treatment, by age group and period in which treatment started

Age group and period in which treatment started	CD4%		CD4 count		WHO stage 3 or 4†	
	Median (interquartile range)	No (%) with count missing	Median (interquartile range)	No (%) with count missing	No (%)	No (%) with count missing
<b>Infants (&lt;1 year), n=208</b>						
Jun 2004 to Sep 2006, * n=3	15 (12-19)	1 (33)	733 (403-1063)	1 (33)	0	2 (66)
Oct 2006 to Sep 2007, n=6	14 (10-21)	1 (17)	702 (492-1070)	1 (17)	5 (83)	0
Oct 2007 to Sep 2008, n=20	13 (11-20)	8 (40)	721 (485-1131)	8 (40)	16 (80)	0
Oct 2008 to Sep 2009, n=61	20 (16-28)	16 (26)	1454 (464-1454)	16 (26)	49 (80)	4 (7)
Oct 2009 to Sep 2010, n=59	23 (14-33)	15 (25)	836 (256-1595)	15 (25)	24 (41)	13 (22)
Oct 2010 to Sep 2011, n=59	20 (11-31)	26 (44)	1063 (378-1586)	26 (44)	25 (42)	14 (24)
<b>Children 1 to 5 years, n=613</b>						
Jun 2004 to Sep 2006, n=39	14 (9-16)	10 (26)	508 (187-1796)	7 (18)	—	—
Oct 2006 to Sep 2007, n=61	12.5 (7.5-16)	5 (8)	454 (283-832)	4 (7)	—	—
Oct 2007 to Sep 2008, n=105	15 (11-20)	16 (15)	524 (322-737)	16 (15)	—	—
Oct 2008 to Sep 2009, n=193	16 (12-22)	20 (10)	635 (406-1003)	20 (10)	—	—
Oct 2009 to Sep 2010, n=118	19 (14-24)	14 (12)	690 (409-1104)	14 (12)	—	—
Oct 2010 to Sep 2011, n=97	18 (11-24)	20 (21)	618 (263-1004)	19 (20)	—	—
<b>Children &gt;5 to ≤15 years, n=896</b>						
Jun 2004 to Sep 2006, n=103	9 (5-15)	16 (16)	184 (92-360)	13 (13)	—	—
Oct 2006 to Sep 2007, n=100	10 (5-14)	12 (12)	188 (101-299.5)	8 (8)	—	—
Oct 2007 to Sep 2008, n=146	11 (6-16)	11 (8)	175 (82-384)	9 (6)	—	—
Oct 2008 to Sep 2009, n=221	13 (7-20)	15 (7)	293.5 (154.5-487)	13 (6)	—	—
Oct 2009 to Sep 2010, n=169	14 (9-23)	12 (7)	276 (137-464)	9 (5)	—	—
Oct 2010 to Sep 2011, n=157	14.5 (6-20)	35 (22)	219 (112-435)	34 (22)	—	—
<b>Children 1 to ≤15 years, n=1509</b>						
Jun 2004 to Sep 2006, n=142	—	—	—	—	89 (63)	15 (11)
Oct 2006 to Sep 2007, n=161	—	—	—	—	114 (71)	17 (11)
Oct 2007 to Sep 2008, n=251	—	—	—	—	198 (79)	20 (8)
Oct 2008 to Sep 2009, n=414	—	—	—	—	337 (81)	24 (6)
Oct 2009 to Sep 2010, n=287	—	—	—	—	189 (66)	38 (13)
Oct 2010 to Sep 2011, n=254	—	—	—	—	127 (50)	63 (25)

\*The period Jun 2004 to Sep 2006 is longer than the others because of small numbers of infants.

†Data not currently available separately for age groups 1 to 5 and >5 to ≤15.

of pregnant women who are HIV infected from anonymous surveillance at the Africa Centre and from the Department of Health. However, we do not know the exact number of HIV exposed infants who are HIV infected as some may not have been tested for HIV and others may have died before having the opportunity to be tested for HIV. Therefore, our denominator for eligible children remains an estimate based on several assumptions (table 1), and we provide our first two key outcomes as numbers rather than proportions.

### Process of gathering information

Baseline clinical and laboratory data of all children starting ART in the HIV programme are collected from paper based records stored at clinics and entered into a secure, electronic database hosted at the Africa Centre. We analysed data from all children in the programme from June 2004 to September 2008 before implementing our intervention, and from October 2008 to September 2011 after introducing the improvement strategies. Characteristics at the start of ART included age and sex, CD4 count and CD4%, WHO clinical HIV stage, “weight for age” z score, and haemoglobin and albumin (both predictors of mortality). All analyses were performed in Stata (version 11.0).

Since the programme’s inception, all drugs and healthcare have been provided free of charge in the primary healthcare clinics and health workers have had access to clear guidelines for managing HIV positive children. After the

initial roll-out of the programme there have been no waiting lists for patients needing ART. A prevention of mother to child transmission programme had been operating in the Hlabisa area since 2001, with provision for all pregnant HIV positive women to receive appropriate management at their nearest local clinic. Before 2010 women received single dose nevirapine in labour; this was changed in August 2010 to: (a) combination ART for life for women with CD4 counts of ≤350 cells/μL, and (b) for the remaining women, zidovudine monotherapy from early pregnancy plus single dose nevirapine and a dose of emtricitabine plus tenofovir in labour and oral daily nevirapine for their infants for at least six weeks.

### Analysis and interpretation

In the first four years of the programme (June 2004 to September 2008) we identified two problems:

- Few of the children starting ART were aged <1 year (table 1)
- Children starting ART had low CD4%, low CD4 counts, high WHO clinical stages (suggesting immune compromise at start of treatment), and CD4 counts well below the eligibility criteria for treatment (table 2).

Therefore, we examined the cascade of HIV care from pregnancy to early childhood to identify why so few infants were starting ART despite our estimates of expected need.<sup>22</sup> As clinic waiting times and the cost of antiretroviral drugs

## Measures taken in late 2008 to improve early identification of young children with HIV and ensure treatment of all eligible children

### One day training for lay HIV counsellors

- This included the following topics:
  - Immunological eligibility criteria for starting ART in children. Counsellors received charts of the CD4 counts and CD4% cut-offs for starting ART and practised reading laboratory reports to work out if children of different ages were eligible
  - Clinical eligibility criteria for starting ART in children. Counsellors received charts of the WHO HIV clinical stages for children; clinical scenarios were presented, and counsellors practised “staging” the children. Although staging is done by nurses and doctors, this exercise emphasised to counsellors the importance of staging children clinically and not relying only on immunological eligibility criteria. This is particularly important for children with tuberculosis, who are WHO clinical stage 3 but often have CD4 counts above the immunological threshold for treatment.
- The one day training was repeated annually, with special emphasis in 2010, when the guidelines changed to include giving ART to all infants, irrespective of immunological or clinical criteria. The counsellors received printed leaflets containing the new guidelines, and all the clinics received leaflets for their notice boards and consulting rooms.

### Documentation of HIV status for all children

- At all training sessions staff were trained on the importance of ensuring that an HIV status was recorded on the clinic card of all young children (which was held by the mother). If the status was missing on the card of any HIV exposed child being seen in primary healthcare, the nurses referred the child immediately to a counsellor for testing (polymerase chain reaction if aged <18 months; rapid test if aged ≥18 months).

### HIV testing during immunisation campaigns

- Annual primary healthcare campaigns in KwaZulu-Natal are organised by the Department of Health and provide opportunities for children who have missed immunisations or scheduled vitamin A supplements to receive these. The campaigns focus on the targeted task and do not consider other child health matters. Nurses and counsellors were trained to use this opportunity to check the HIV status of HIV exposed children and to ensure that HIV positive children had been referred to the HIV treatment programme. We chose immunisations and vitamin A supplements for the campaigns as these health interventions are usually targeted at children under age 5 years, are conducted at least annually, and thus provide an excellent opportunity to “catch” children whose HIV diagnosis had been missed previously.

### Clinical staging for all HIV positive children

- After the training mentioned above, the counsellors were instructed to refer all HIV positive children to the clinic nurse or doctor for clinical staging without waiting (potentially for two weeks) for the results of CD4 counts. All counsellors received this instruction at every annual training meeting; the counsellor supervisor who visited the clinics to conduct inhouse training reinforced this.

### Referral of all sick HIV exposed children for medical assessment

- HIV exposed children were considered a vulnerable group. Nurses and counsellors were instructed to refer all children with clinical features suggestive of HIV whose mothers were HIV positive, for immediate medical assessment (for example, for failure to thrive, oral thrush beyond the neonatal period, persistent diarrhoea, chronically discharging ears). The WHO’s Integrated Management of Childhood Illness (IMCI) strategy is a method of assessing and managing sick children in resource limited settings with a shortage of medical staff. The South African adaptation of the IMCI guidelines includes a section on identifying HIV in children and includes a list of signs and symptoms. The adapted IMCI guidelines were included in the one day training for counsellors and a similar one day training for nurses. Many of the nurses had been trained in IMCI, and this section of the course was re-emphasised.<sup>24 25</sup>

### Link with tuberculosis and malnutrition programmes

- Tuberculosis and malnutrition are associated with HIV, so linking with these services and the HIV treatment programme is important. The link with the tuberculosis service was part of an initiative that encompassed both adult and paediatric tuberculosis services.<sup>26</sup> Anyone in Hlabisa with tuberculosis had an HIV test (or confirmation of a previous HIV test) as part of their management. This was documented on the paediatric tuberculosis “initiation” card that is given to all children starting tuberculosis treatment in the province. Any child with an unknown HIV status was referred immediately for HIV testing and the subsequent result written on the child’s card.
- Nurses from all the clinics and the dietitian from the sub-district received specific training on malnutrition. Nurses were instructed to refer any children with malnutrition and an unknown HIV status to the counsellors for testing.

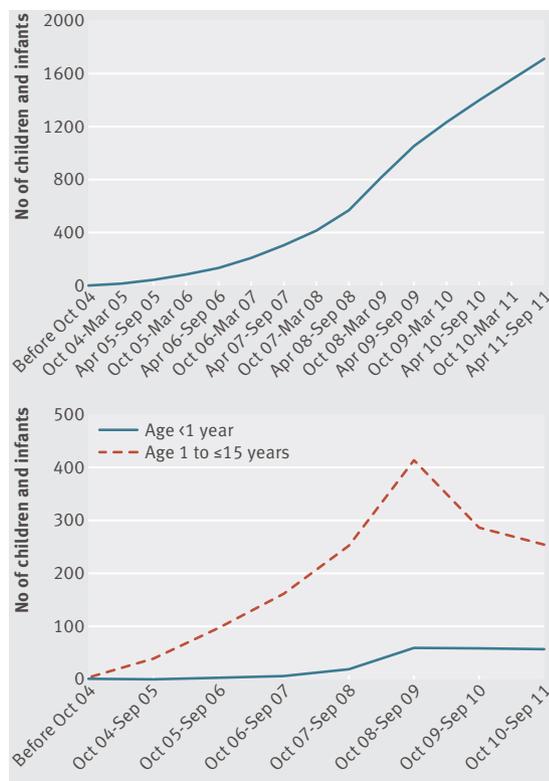
### HIV testing for children in hospital

- Hospital admissions for malnutrition, tuberculosis, pneumonia, or chronic diarrhoea provide a good opportunity to identify children with undiagnosed HIV. Hospital staff conducted HIV testing in the children’s ward of Hlabisa Hospital, and documented HIV status for each child on admission in the case file. Results were retrieved from the laboratory for children who had been tested (with, for example, polymerase chain reaction) but whose result was not documented on their clinic card and whose mothers were unaware of the result. Children who had not been tested for HIV were tested in the ward, with appropriate consent.

### Feedback of progress to clinic staff

- Feedback to the clinic staff took various forms:
  - Annual programme meetings: feedback on numbers of children who began ART (data similar to those in table 2) was presented to counsellors and nurses
  - Monthly monitoring and evaluation meetings: feedback to clinic staff on monthly and cumulative data on numbers of children and infants starting ART
  - Regular programme meetings: presentation of statistics stratified by clinic (meetings were attended by all programme staff).

Top panel: Cumulative number of children and infants starting antiretroviral treatment (ART): June 2004 to September 2011. Bottom panel: Annual numbers of children and infants receiving ART June 2004 to September 2011



presented no barrier, we thought the problem probably resulted from missed opportunities to test and diagnose young children with HIV, rather than HIV positive children not receiving treatment; this thinking was in line with findings from other sites in sub-Saharan Africa.<sup>16 17</sup>

### Strategy for change

We implemented a series of measures from late 2008 to improve early identification of HIV positive infants and fast track them for treatment, and to ensure that older children had a definitive HIV test result recorded on their health card and were receiving treatment if eligible (box). We employed no additional staff, conducted all training in-house, and used no external laboratory services.

Additionally, in late 2007 one of the authors (RMB) established a weekly multidisciplinary family clinic at the busiest government clinic in the Hlabisa sub-district. It was established primarily as an HIV clinic, but other paediatric problems are also managed at the clinic, and children presenting with diseases such as tuberculosis and malnutrition can also be tested for HIV. Referrals from other clinics in the area are accepted, ART can be started immediately if necessary, discharges from hospital are followed up, and the child acts as an index case to ensure that other members of the family, particularly siblings, are tested for HIV and receive appropriate care.

### Effects of change

We compared data from the period before the intervention strategies with those from September 2008 onwards. The number of children (aged 1 to ≤15 years) starting ART each year increased from 43 in 2004 to 254 in 2011, with the largest increases from September 2008 onwards. The number of infants (aged <1 year) starting treatment each

year increased from 2 to 59 over the same period (table 1). Of all 1134 children and infants starting ART from September 2008 onwards, 70 (6%) started ART at the hospital, the rest at the primary healthcare clinics. Obtaining an accurate denominator for the number of children eligible for treatment is problematic and relies on the number of HIV exposed infants who are estimated to be infected, rather than the number of infants actually testing HIV positive. This is because HIV infected but untreated infants are at risk of dying in the first month of life before there has been an opportunity to test them. Table 1 gives the estimated number of new cases of HIV infection annually in infants and the number of children who started ART.

The figure (top panel) shows the cumulative number of children and infants starting ART, with sharp increases observed from early 2008 onwards. Similar annual increases were observed in children and infants, especially in the one year period immediately after the interventions were introduced (fig 1 (bottom panel)). Thereafter the number of infants starting ART has stabilised at around 50 a year. With the changes in the prevention of mother to child transmission regimen for pregnant women, the mother to child transmission rate in infants at age 6 weeks has fallen from 14% in the early years of the prevention programme (2001-06)<sup>23</sup> to 3% in 2011. With an estimated 2000 deliveries to HIV positive women annually in the Hlabisa sub-district, fewer than 60 infants annually would be expected to be vertically infected with HIV from 2011 onwards. The number of children aged 1 year to ≤15 years starting ART peaked in 2008-09 and then declined, which we assume is a result of a large number of older children being identified with HIV during the early months of the intervention, and subsequently children being picked up at a younger age. In year 7 (October 2010 to September 2011) 59 infants started ART, with an estimated 60 new paediatric HIV infections over the same period.

Most of the infants and children, both before and after the quality improvement interventions, were in WHO clinical stage 3 or 4 when they started ART, mainly owing to diagnosis with comorbid pulmonary tuberculosis (stage 3) or severe acute malnutrition (stage 4) (table 2). One of the intervention strategies was to provide HIV testing for all children admitted to the local hospital, and all those presenting to clinics with tuberculosis or malnutrition; this “mopping up” of older sick children will have accounted for many of those in WHO stage 3 or 4, and from 2009 to 2011 a trend emerged towards starting treatment in less advanced disease in children aged 1 year to ≤15 years (table 2). We cannot comment on any such trends in infants as the changing guidelines in 2010<sup>8</sup> meant that all infants were eligible for HIV treatment irrespective of their clinical or immunological stage. This is corroborated by the trend of higher CD4 counts and CD4% seen in the later years of the programme, particularly in those aged 1-5 years, suggesting that children were being identified when they were in better health (table 2).

### Next steps

Our results show that in a rural health district it is possible to improve identification of children needing ART and improve early diagnosis of HIV positive infants with

relatively simple measures and limited implications for staffing and budgets. Guidelines are in place, but vertical health programmes present barriers to ensuring holistic assessment of children, including early HIV diagnosis. This applies particularly to children attending tuberculosis services and presenting with malnutrition and to infants attending immunisation and growth clinics. All these points of care represent opportunities to determine the HIV status of a child and refer them for treatment and care. One of the key elements of our initiatives has been regular feedback of results to clinic and programme staff, often ignored in settings where monitoring and evaluation are under-resourced or poorly conducted.

Our findings show that most children still presented in WHO clinical stage 3 or 4, which probably reflects the high prevalence of tuberculosis in the area. However, we found suggestions of a trend towards treatment starting at lower WHO clinical stages and higher CD4 counts; this trend may be linked to earlier diagnosis of HIV.

With the introduction of new regimens for prevention of mother to child transmission (including expanded eligibility criteria for ART for pregnant women) and immediate ART for all infants aged under 1 year with confirmed HIV status, there is now the real possibility to eradicate mother to child transmission of HIV and to identify and treat the few children who are HIV positive within the first three months of life.

In February 2013 the management of the Hlabisa HIV programme changed. The funding to South Africa by the US emergency AIDS plan PEPFAR, always intended for a limited time period, was substantially reduced, and the programme is now managed wholly by the local Department of Health. Systems are now well established to continue this optimal treatment and care of HIV infected children in Hlabisa: the Department of Health staff are trained, integration with the paediatric tuberculosis services is in place, and the programme has followed a decentralised model from inception.

We will continue to monitor the prevention of mother to child transmission programme and the follow-up of HIV exposed infants in Hlabisa, and we are aiming to achieve virtual eradication of mother to child HIV transmission over the next five years and to start ART in all HIV positive infants in the first four months of life. Our findings should be encouraging to other rural areas of sub-Saharan Africa with equally high HIV prevalence and limited resources.

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**Competing interests:** All authors have completed the ICMJE uniform disclosure form at [www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf) (available on request from the corresponding author) and declare: The Africa Centre for Health and Population Studies is supported by a core grant from the Wellcome Trust (050524). The Hlabisa HIV Treatment and Care Programme is made possible through the US Agency for International Development (USAID) and the President's Emergency Plan (PEPFAR) under the terms of Award No 674-A-00-08-00001-00. The opinions expressed herein are those of the authors and do not necessarily reflect the views of USAID or the US government. The funders played no part in the analysis or writing of this manuscript. We declare no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

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- Houlihan CF, Mutevedzi PC, Lessells RJ, Cooke GS, Tanser FC, Newell ML. The tuberculosis challenge in a rural South African HIV programme. *BMC Infect Dis* 2010;10:23.
- Welz T, Hosegood V, Jaffar S, Batzing-Feigenbaum J, Herbst K, Newell ML. Continued very high prevalence of HIV infection in rural KwaZulu-Natal, South Africa: a population-based longitudinal study. *AIDS* 2007;21:1467-72.
- Tanser F, Barnighausen T, Grapsa E, Newell ML. Effect of ART coverage on rate of new HIV infections in a hyper-endemic, rural population: South Africa. *Conference on Retroviruses and Opportunistic Infections*. Seattle, US, 2012. [www.retroconference.org/2012b/Abstracts/45379.htm](http://www.retroconference.org/2012b/Abstracts/45379.htm).
- Houlihan CF, Bland RM, Mutevedzi PC, Lessells RJ, Ndirangu J, Thulare H, et al. Cohort profile: Hlabisa HIV treatment and care programme. *Int J Epidemiol* 2010;40:318-26.
- Wilkinson D, Cutts F, Ntuli N, Abdool Karim SS. Maternal and child health indicators in a rural South African health district. *S Afr Med J* 1997;87:456-9.
- Ndirangu J, Barnighausen T, Tanser F, Tint K, Newell ML. Levels of childhood vaccination coverage and the impact of maternal HIV status on child vaccination status in rural KwaZulu-Natal, South Africa. *Trop Med Int Health* 2009;14:1383-93.
- World Health Organization. Antiretroviral therapy of HIV infection in infants and children in resource limited settings: towards universal access. 2006. [www.who.int/hiv/pub/guidelines/WHOpaediatric.pdf](http://www.who.int/hiv/pub/guidelines/WHOpaediatric.pdf).
- National Department of Health, South Africa. Guidelines for the management of HIV in children. 2nd ed. 2010. [www.hivfshs.org/document/2010/08/19/guidelines-for-the-management-of-hiv-in-children-2nd-edition-2010](http://www.hivfshs.org/document/2010/08/19/guidelines-for-the-management-of-hiv-in-children-2nd-edition-2010).
- World Health Organization. Antiretroviral therapy for HIV infection in infants and children: towards universal access. Recommendations for a public health approach: 2010 revision. [www.who.int/hiv/pub/paediatric/infants2010/en/](http://www.who.int/hiv/pub/paediatric/infants2010/en/).
- Johnson L. Access to antiretroviral treatment in South Africa, 2004-11. *Southern African Journal of HIV Medicine* 2012;13(1).
- Joint United Nations Programme on HIV/AIDS. AIDS epidemic update 2009. [http://data.unaids.org/pub/Report/2009/JC1700\\_Epi\\_Update\\_2009\\_en.pdf](http://data.unaids.org/pub/Report/2009/JC1700_Epi_Update_2009_en.pdf).
- Newell ML, Coovadia H, Cortina-Borja M, Rollins N, Gaillard P, Dabis F. Mortality of infected and uninfected infants born to HIV-infected mothers in Africa: a pooled analysis. *Lancet* 2004;364:1236-43.
- Newell ML, Patel D, Goetghebuer T, Thorne C. CD4 cell response to antiretroviral therapy in children with vertically acquired HIV infection: is it associated with age at initiation? *J Infect Dis* 2006;193:954-62.
- Prendergast A, Mphatswe W, Tudor-Williams G, Rakgotho M, Pillay V, Thobakgale C, et al. Early virological suppression with three-class antiretroviral therapy in HIV-infected African infants. *AIDS* 2008;22:1333-43.
- Violari A, Cotton MF, Gibb DM, Babiker AG, Steyn J, Madhi SA, et al. Early antiretroviral therapy and mortality among HIV-infected infants. *N Engl J Med* 2008;359:2233-44.
- Ginsburg AS, Hoblitzelle CW, Sriprapatana TL, Wilfert CM. Provision of care following prevention of mother-to-child HIV transmission services in resource-limited settings. *AIDS* 2007;21:2529-32.
- Rollins N, Little K, Mzolo S, Horwood C, Newell ML. Surveillance of mother-to-child transmission prevention programmes at immunization clinics: the case for universal screening. *AIDS* 2007;21:1341-7.
- KIDS-ART-LINC Collaboration. Low risk of death, but substantial program attrition, in pediatric HIV treatment cohorts in Sub-Saharan Africa. *J Acquir Immune Defic Syndr* 2008;49:523-31.
- Bolton-Moore C, Mubiana-Mbewe M, Cantrell RA, Chintu N, Stringer EM, Chi BH, et al. Clinical outcomes and CD4 cell response in children receiving antiretroviral therapy at primary health care facilities in Zambia. *JAMA* 2007;298:1888-99.
- Kiboneka A, Wangisi J, Nabiryo C, Tembe J, Kusemererwa S, Olupot-Olupot P, et al. Clinical and immunological outcomes of a national paediatric cohort receiving combination antiretroviral therapy in Uganda. *AIDS* 2008;22:2493-9.
- Janssen N, Ndirangu J, Newell ML, Bland RM. Successful paediatric HIV treatment in rural primary care in Africa. *Arch Dis Child* 2010;95:414-21.
- Cooke GS, Little K, Bland RM, Thulare H, Newell ML. Need for paediatric HIV treatment within primary health care in rural South Africa. *PLoS ONE* 2009;4:e7101.
- Rollins NC, Coovadia HM, Bland RM, Coutsooudis A, Bennis ML, Patel D, et al. Pregnancy outcomes in HIV-infected and uninfected women in rural and urban South Africa. *J Acquir Immune Defic Syndr* 2007;44:321-8.
- Horwood C, Liebeschuetz S, Blaauw D, Cassol S, Qazi S. Diagnosis of paediatric HIV infection in a primary health care setting with a clinical algorithm. *Bull World Health Organ* 2003;81:858-66.
- Horwood C, Voce A, Vermaak K, Rollins N, Qazi S. Experiences of training and implementation of integrated management of childhood illness (IMCI) in South Africa: a qualitative evaluation of the IMCI case management training course. *BMC Pediatr* 2009;9:62.
- Coovadia H, Bland R. From Alma-Ata to Agincourt: primary health care in AIDS. *Lancet* 2008;372:866-8.

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