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Published by Oxford University Press on behalf of the International Epidemiological Association
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International Journal of Epidemiology 2007;**36**:687–689
doi:10.1093/ije/dym118

Commentary: State of the ART modelling for HIV-infected children?

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Accepted 1 May 2007

In sub-Saharan Africa, where the principle transmission route of the human immunodeficiency virus (HIV) is heterosexual sex, it is women and children who bear the greatest burden of HIV infection. The rate of transmission per sex act from an infected man to uninfected women is ~3 times that from an infected woman to an uninfected man, resulting in an HIV prevalence ratio of 60% women to 40% men in many communities.¹ Children of HIV-infected mothers are exposed in the womb, during labour and delivery and post-natally through breastfeeding. If they become infected, disease progression is more rapid than in adults,² but potent anti-retroviral therapy (ART) also greatly reduces mortality in children living in low-income settings.³ In order to plan the provision of ART to HIV-infected children in these settings,

information on the number of children needing such treatment is required.

Estimating the need for ART

In this issue of the journal, Kirsty Little and colleagues⁴ present a model to estimate the number of vertically infected children that progress to moderate or severe disease and become eligible for ART in South Africa. The model considers antenatal prevalence, the risk of transmission before or at birth, infant feeding policies and their associated risk of transmission, use of co-trimoxazole to prevent opportunistic infections, use of ART and mortality rates at different ages by disease stage and according to treatment received. Background mortality rates are inferred from the mortality rates of non-infected children of HIV-positive mothers. Whilst the structure of the model is comprehensive, some of the parameters are estimated from a weak evidence base: the information comes from a pick-and-mix of studies, and sometimes from a different geographical area, as in the estimate of mortality of children on ART that is taken from a study in Abidjan, Ivory Coast, but is applied to South Africa.⁵ Fortunately, more data to inform such models

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are becoming available with the scale up of ART, and the monitoring and evaluation that follows these initiatives.⁶

Treatment and prevention

In 2005, the peak HIV prevalence in South Africa was in women aged 25–30, 40% of whom were infected.¹ In some places, such as Lesotho, prevalence has stabilized at 20% from 2000 onwards from which we can infer that the peak of infections must have occurred around 4 years earlier. Paradoxically, as ART is rolled out and less people die of AIDS, prevalence will continue to rise even if incidence falls. It is therefore crucial for monitoring incidence and future trends to examine what happens in the youngest age groups, children and 15 to 20-year-olds, which reflect newly acquired infections. Modelling scenarios show that treatment will never catch up with need if the current rate of incidence of HIV infection holds.⁷ Therefore, to reverse the epidemic a comprehensive package of prevention and treatment measures are required. The need for treatment is acute. Without access to ART, millions will die, but the future course of the epidemic will be determined by how successful prevention measures are, not by treatment.

Prevention of mother-to-child transmission: missing targets

In industrialized countries, testing of pregnant women is readily available, a combination of anti-retroviral drugs is given prophylactically during pregnancy and to the newborn, mothers can opt for delivery by elective caesarean and breastfeeding is replaced by formula feeds. These measures result in transmission rates <2%. In 2001, UNAIDS set global targets to reduce mother-to-child transmission by 20% by 2005.⁸ What was achieved? It is estimated that the transmission rate in the 33 countries most affected was ~30% in 2001 and is now 26%, a reduction of only 10%. The major problem is the low coverage of anti-retroviral drug prophylaxis. The target set by UNAIDS was 80% coverage, but no country had achieved this by 2005 and overall only 9% of pregnant women had access to prophylactic drugs. In sub-Saharan Africa, where 85% of HIV-infected pregnant women live, coverage in countries ranges from <1% to 54%.⁹

The lesser of two evils: breast is still best

About a third to one half of HIV-infected children acquired their infection through breastfeeding.¹⁰ In high-income countries this is prevented by replacing breastfeeding with formula feeding. However, in low-income countries with high burdens of infectious disease, breastfeeding has been ranked as the most cost-effective intervention to improve child survival and could prevent around 14% of infant deaths.¹¹ During the 2006 floods in Botswana, there was a serious outbreak of childhood diarrhoea and it was found that 93% of the children admitted to hospital were not breastfed and these children were

at much higher risk of dying than breastfed children.¹² Breast milk is nutritionally superior to formula feed, is free, readily available and protects against the diarrhoeal and respiratory diseases that are often fatal in the first year of life. The protective effect of breastfeeding will therefore outweigh the potential harm from transmission of HIV in many resource-limited settings. Of note, a recent cohort study from KwaZulu-Natal, South Africa, showed that exclusive breastfeeding for 6 months, that is, no additional fluids, water or solids, is associated with a low transmission rate (estimated at about 4% from 6 weeks to 6 months after delivery).¹³

Education, education, education

Prevention in the youngest age group is also key to controlling the epidemic. It has been pointed out that if each year birth cohort only had sex with partners born in the same year, HIV infection would die out.¹⁴ A common behaviour that drives the epidemic is older men having sex with younger women. In surveys of young people, those with secondary school education were more likely to have a comprehensive knowledge of HIV and AIDS compared with those with only primary education or no education.³ Education tends to delay the age at which young people first have sex and is associated with having fewer partners and greater condom use. For girls in particular, each year of education counts, giving them vital life skills, knowledge and opportunity. Those who complete secondary education know more about preventing HIV and what to do if they think they are infected. They have more economic options and independence, and are in a better position to make informed choices about avoiding risky behaviour, negotiating safer sex, delaying marriage and childbearing and having healthier babies.

Unite for Children, Unite against AIDS

In 2005, UNICEF, UNAIDS and other partners launched the *Unite for Children, Unite against AIDS* campaign,¹⁵ which targets four key areas:

- Prevention of mother-to-child transmission.
- Provision of anti-retroviral treatment to children.
- Education and counselling programmes.
- Support for orphans and vulnerable children.

An interesting possible use of the model described by Little *et al.*⁴ will be to evaluate the success of this campaign and its components, and the model could also be extended to include evaluation of different feeding strategies, including exclusive breastfeeding, taking into account different burdens of other infectious diseases. The monitoring and evaluating of the scale-up of treatment and prevention using such models is crucial to public health planning and the promotion of good practice.

Conflict of interest: None declared.

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