

Monitoring the scale-up of antiretroviral therapy programmes: methods to estimate coverage

J Ties Boerma,^a Karen A Stanecki,^b Marie-Louise Newell,^c Chewe Luo,^d Michel Beusenbergh,^a Geoff P Garnett,^e Kirsty Little,^c Jesus Garcia Calleja,^a Siobhan Crowley,^a Jim Yong Kim,^a Elizabeth Zaniewski,^b Neff Walker,^c John Stover,^f & Peter D Ghys^b

Abstract This paper reviews the data sources and methods used to estimate the number of people on, and coverage of, antiretroviral therapy (ART) programmes in low- and middle-income countries and to monitor the progress towards the “3 by 5” target set by WHO and UNAIDS. We include a review of the data sources used to estimate the coverage of ART programmes as well as the efforts made to avoid double counting and over-reporting. The methods used to estimate the number of people in need of ART are described and expanded with estimates of treatment needs for children, both for ART and for cotrimoxazole prophylaxis. An estimated 6.5 million people were in need of treatment in low- and middle-income countries by the end of 2004, including 660 000 children under age 15 years. The mid-2005 estimate of 970 000 people receiving ART in low- and middle-income countries (with an uncertainty range 840 000–1 100 000) corresponds to a coverage of 15% of people in need of treatment.

Keywords Antiretroviral therapy, Highly active; HIV infections/epidemiology/drug therapy; Data collection/methods; Needs assessment; Trimethoprim-sulfamethoxazole combination; Developing countries (*source: MeSH, NLM*).

Mots clés Thérapie antirétrovirale hautement active; Infection à VIH/épidémiologie/chimiothérapie; Collecte données/méthodes; Evaluation besoins; Triméthoprime-sulfaméthoxazole, Association; Pays en développement (*source: MeSH, INSERM*).

Palabras clave Terapia antirretroviral altamente activa; Infecciones por VIH/epidemiología/quimioterapia; Recolección de datos/métodos; Evaluación de necesidades; Combinación trimetoprim-sulfametoxazol; Países en desarrollo (*fuentes: DeCS, BIREME*).

Arabic

Bulletin of the World Health Organization 2006;84:145-150.

Voir page 149 le résumé en français. En la página 149 figura un resumen en español.

Introduction

On 1 December 2003, WHO in partnership with UNAIDS launched the “3 by 5” initiative, which aimed to mobilize the world to provide antiretroviral therapy (ART) to 3 million people in low- and middle-income countries by the end of 2005.¹ The 3 million target was based on an analysis published in 2001, which indicated that this figure would correspond to about a 50% coverage of adults in need of treatment.² At the end of 2003, an estimated 400 000 people in low- and middle-income countries were on treatment and almost half of those were living in Latin America. ART coverage in Africa and Asia was below 5%.

Estimation of health service coverage — such as the Millennium Development Goal indicators of measles vaccination and skilled birth attendant coverage — is mostly derived from population-based household sample surveys. If no such data are available, coverage has to be calculated from an estimate of the numerator (i.e., the number of people receiving or using the service) and the denominator (i.e., the estimated number of people in need of such services). Even for well-established programmes such as immunization and tuberculosis control, this method may give unsatisfactory results, because of under-reporting, over-reporting or methodological and techni-

cal problems with accurate estimation of the denominator.

Population-based surveys, however, are not a suitable data source for the estimation of ART coverage, since population prevalence is relatively low, reporting biases are likely, and there are ethical issues associated with stigma and discrimination. Estimates of the number of people on ART and the corresponding coverage are based on service statistics and estimates of the need for treatment.³ In this paper, we describe the procedures and methods used to monitor progress towards “3 by 5” and provide an estimate of treatment coverage achieved by the end of June 2005. For the first

^a The World Health Organization, CH-1211 Geneva 27, Switzerland. Correspondence to Dr Boerma (email: boeremat@who.int).

^b The Joint United Nations Programme on HIV/AIDS, Geneva, Switzerland.

^c Institute of Child Health, University College London, London, England.

^d UNICEF, New York, NY, USA.

^e Imperial College, London, England.

^f Futures Group, Glastonbury, Connecticut, CT, USA.

Ref. No. 05-025189

(Submitted: 5 July 2005 – Final revised version received: 3 November 2005 – Accepted: 7 November 2005)

time, children are included in overall estimates of the number of people in need of treatment.

Estimating the number of people on antiretroviral therapy

To estimate the number of people on treatment, we have used data from most recent report received from the Ministry of Health or WHO country office, or other sources from within countries. Usually, countries keep track of the number of sites providing ART and the number of people on treatment in those sites. At the end of each calendar year, data are requested by WHO from all 152 World Bank classified low- and middle-income countries. For the mid-2005 update, we focused on obtaining data from the countries with the largest unmet need for treatment.⁴ Overall, updates were received from 35 of 152 low- and middle-income countries, which accounted for 88% of the unmet need for antiretrovirals.

Since ART programmes are quite new and still being rolled out, many countries do not yet have standardized national patient-monitoring systems that require regular reporting of numbers of new patients on treatment, adherence rates, number of defaulters, loss to follow up and deaths. In many countries, the Ministry of Health currently obtains information about the number of people on treatment by directly contacting the sites providing treatment.

The level of detail in the data varies between countries. WHO seeks information on numbers of people who are currently on treatment — i.e., the number of people who continue to collect their drugs in line with the recommended schedule. However, some clinics and countries report cumulative data on the number of people starting treatment. The difference between the two numbers will reflect losses due to discontinuation of treatment or death. In addition, the double counting of people who change clinics and are reported as new patients will result in over-reporting. WHO also requests disaggregated data on the number of people on ART by age and sex: i.e., number of children, adult men and adult women. Currently less than one-third of countries report such detail.

Another source of uncertainty in data on the number of people on treatment results from the difficulty of measuring how many people access ART

through the private sector. Data from not-for-profit organizations may be reported in the overall public-sector figures, or they may be reported separately. Data from private companies that have programmes to provide ART for their workers with advanced HIV infection are reported separately. Insurance companies may provide additional data. People may also access antiretrovirals through local pharmacies and private clinics that do not report patient numbers via the usual channels.

The United States President's Emergency Plan for AIDS Relief (PEPFAR) and the Global Fund to fight AIDS, Tuberculosis and Malaria are major funders of ART programmes in low- and middle-income countries. PEPFAR focuses on 15 countries and provides estimates of the number of people on treatment every 6 months, with use of data compiled at the country level from reports by PEPFAR-supported clinics. These data and those provided by the Global Fund are used to cross-validate the data reported by the countries' Ministries of Health in countries. PEPFAR and the Global Fund also work together to avoid double counting of people on treatment. In December 2004, 63 000 people on treatment were thought to have benefited from both PEPFAR and Global Fund initiatives. Some authors have wrongly assumed that these 63 000 patients were counted twice in the WHO/UNAIDS estimate of 700 000 people on ART by the end of 2004.⁵ However, WHO/UNAIDS estimates are based on country summary-reports of data from treatment facilities; they are not calculated by adding up and double counting data from parallel reporting systems.

Country reports usually include data collected up to a time point 2–4 months before the middle (or end) of the year. We derive midyear estimates from simple linear projections of reported numbers, using the trend between the two most recent reported numbers as an indicator of growth. We applied this procedure to information from 35 countries that had provided new data for the first half of 2005. The monthly growth rate in the number of people on treatment takes into account drop-out due to deaths or non-adherence, when such data are available.

To express uncertainty in the estimates of people on ART, we used the following procedure. For the midyear country-reported data (public sector only or

public and private sector combined), we allowed an uncertainty margin related to the strength of the monitoring system. A margin of plus or minus 5% was allowed if site-specific numbers were reported (4 countries). For countries that reported data on the number of service delivery points only, we allowed an uncertainty margin of 10% (22 countries). And for countries for which partial or no detail available, we used an uncertainty margin of 25% (9 countries). For private sector numbers, which were separately reported in some countries, we used uncertainty ranges from plus or minus 10% (details on the sources available; 1 country), 25% (only limited detail; 2 countries) or 40% (incomplete or no detailed information available; 7 countries). We chose these ranges arbitrarily.

For countries that did not report new data from the first half of 2005, we used two scenarios to obtain a probable lower and upper uncertainty limit for the estimated number of people on ART. The lower estimate assumes no growth, which implies that the number of people initiating treatment is equal to the number of drop-outs due to non-adherence or death. The upper limit assumed the linear growth observed in 2004 had continued to mid-2005. We used the midpoint between these two scenarios as a point estimate for mid-June 2005.

Antiretroviral treatment needs in adults

UNAIDS and WHO have developed standard methods to estimate the size and course of the AIDS epidemic, which in turn generate estimates of HIV prevalence, incidence and mortality.^{6–10} These methods, as well as those used to estimate the number of people in need of treatment, were based on recommendations of the UNAIDS Reference Group on Estimates, Modelling and Projections (<http://www.epidem.org>). Briefly, it involves a multistep process that starts with the estimation of the size of the epidemic. HIV prevalence curves are generated from empirical data for each country and translated into estimates of adult HIV incidence and AIDS-mortality, and child HIV incidence, prevalence and AIDS mortality, based on assumptions about time from infection to illness and then death for adults and children and the probability of mother-to-child transmission. The methods developed have been implemented in three software

tools: the WORKBOOK,⁸ the Estimation and Projection Package (EPP)⁹ and Spectrum.¹⁰ All models estimate the size of incident cohorts for every year since the beginning of the epidemic. The past course of the epidemic will affect the proportion of people living with HIV who need treatment. For example, in a young and growing epidemic a smaller proportion of people living with HIV will need treatment than in a mature or declining epidemic. Uncertainty ranges around the estimates have also been provided.¹¹

WHO recommends that in resource-poor settings, adults and adolescents with HIV should start ART when the infection has been confirmed and there are clinical signs of advanced disease (HIV disease stage IV, irrespective of CD4 cell count; stage III with CD4 cell count less than 350 cells per μl) or laboratory evidence of severe immuno-suppression (CD4 cell count less than 200 per μl or, if not available, lymphocyte count less than 1200 μl with symptomatic disease).¹² There is little direct evidence about the time from seroconversion to clinical AIDS or any of the above treatment eligibility criteria. A study in Uganda estimated the median time from seroconversion to an AIDS diagnosis at 9.4 years; median time from seroconversion to death was estimated at 9.8 years. The actual time to the development of AIDS is probably shorter than 9.4 years as patients in the Ugandan study were only evaluated for signs and symptoms at visits that were scheduled every 3 months.¹³ Because of the scarcity of direct data on the time from seroconversion to treatment eligibility, the method for estimating the number of adults in need of treatment has been based on estimates of the time from treatment eligibility to death in the absence of ART.

Only a few studies in resource-poor settings have estimated the time from clinical and laboratory benchmarks to death, in the absence of ART, yielding an average survival time of just under 1 year for people with AIDS (median 9.8 months, range 6–19 months) and for people with CD4 cell count less than 200 per μl (median 10.9 months, range 7–38 months).¹⁴ Again, the actual times to death associated with these benchmarks is likely to be longer than those cited, since patients in these studies were only evaluated for signs and symptoms and CD4 counts at discrete visits. To try

and correct for this bias, these data have been compared to findings in the Swiss HIV Cohort Study (SHCS) in which CD4 counts were measured at regular intervals.^{14,15} In the SHCS, median CD4 cell count in patients with a CD4 count below 200 cells per μl was 100 cells per μl , while a median CD4 count of 200 cells per μl was recorded in patients with CD4 cell counts between 250 and 150 cells per μl . The SHCS data indicate that survival was 3.2 times longer in the group of patients with a median CD4 cell count of 200 cells per μl than in the group with a count below 200 cells per μl . Application of the SHCS survival-time ratio of patients with a median CD4 cell count of 200 per μl versus those with a median CD4 cell count of 100 per μl , suggests that average survival of patients with CD4 cell counts below 200 per μl in resource-poor countries is at least 2 years.¹⁴ These data, therefore, suggest that adults with advanced HIV infection who fit eligibility criteria for treatment would be expected to die of AIDS in about 2 years if they do not receive ART.

The number of adults with advanced HIV infection who are eligible for treatment is estimated as the number of people who will die in the current and next year, in the absence of ART. Spectrum software calculates the total number of adults in need of ART by adding the number of adults newly in need of ART in a given year, the number of adults who were on treatment in the previous year and survived into the current year, plus those who were in need last year, but have not yet been put on treatment. Recent analysis from studies in four continents has shown that patients in low-income countries have a somewhat lower survival time on ART than do patients in high-income countries.¹⁶ To calculate estimated needs for 2005, it was assumed that about 90% of adults on ART survive to the following year. Median time on treatment is expected to be about 6 years. For the estimates of children in need of ART, we have taken into account lower fertility in HIV-infected women and rates of contraceptive use.

Therefore, there is substantial uncertainty in the estimates of HIV prevalence, and the number of AIDS cases and deaths due to AIDS¹¹ as well as uncertainty related to the assumptions used to make estimates. Furthermore, the need for ART is underestimated as

people aged 50 years and older are not yet included in estimates because current models provide estimates of HIV prevalence only in people aged 15–49 years.

Antiretroviral and cotrimoxazole treatment needs in children

A recent study in Côte d'Ivoire demonstrated that 2-year survival of children on ART in developing countries is similar to that in developed countries, ranging from 73% to 98% for children with CD4 cells <5% and \geq 5% of total lymphocytes, respectively.¹⁷ Results from a study in Zambia showed that cotrimoxazole prophylaxis can reduce mortality in HIV-infected children older than 1 year by as much as 43%.¹⁸

For the calculation of treatment needs in children, new methods were added to the Spectrum modelling programme. Since there are no large-scale studies of disease progression in children in developing countries, we constructed a schedule of disease progression for infants and older children based on data from Zambia on mortality in HIV-infected children and the proportion of that mortality attributable to the development of moderate-to-severe disease.^{18,19} This analysis suggested that of all children with vertically-acquired HIV, the cumulative probability that they would advance to moderate-to-severe disease was about 36% in year 1, 50% by year 2, 65% by year 5 and 91% by year 10. Mortality in those with moderate-to-severe disease is very high in the first 2 years of life — 90% and 70%, respectively — and about 50% thereafter. Therefore, we modelled progression to moderate-to-severe disease and the need for ART as all those HIV-infected children who would die from AIDS within 2 years in the absence of ART.

Children in need of cotrimoxazole prophylaxis were defined as all children of unknown HIV status born to HIV-infected mothers and all children known to be HIV infected. In countries where only antibody tests are used for testing, HIV status cannot be confirmed in a child born to an HIV-infected mother until the age of about 18 months.²⁰ Therefore, in these settings children in need of cotrimoxazole are all those younger than 18 months born to HIV-infected mothers and all HIV-infected children over the age of 18 months. In

countries where early antigen detection (e.g. with polymerase chain reaction) is available, children in need of cotrimoxazole are defined as all those detected as HIV positive.

The 1-year survival rate in children on treatment was assumed to be 90% for ART, 91% for cotrimoxazole, and 94% for the combination of ART and cotrimoxazole.^{17, 18, 19}

Estimates of coverage and treatment need, June 2005

Table 1 shows the number of people on treatment (with uncertainty range) by June 2005, with estimated need for treatment and coverage. Overall, the estimated number of people on treatment has increased from 700 000 to 970 000 (range 840 000–1 100 000). The largest increase in number of people on treatment has been in sub-Saharan Africa from 310 000 to half a million over 6 months.

In low- and middle-income countries, nearly 6 million adults (i.e., people aged between 15 and 49 years) are in need of ART. Most of these people live in sub-Saharan Africa (4.1 million); 1.1 million live in Asia, and 450 000 in Latin America and the Caribbean. Overall, treatment coverage in Africa, Asia and Latin America and the Caribbean is 11%, 14% and 62%, respectively.

Globally, 660 000 children (i.e. younger than 15 years) are in need of ART, including 270 000 children aged 0–18 months (Table 2). Four million children are estimated to be in need of cotrimoxazole; early diagnosis could reduce this number to 2.1 million and

allow treatment cessation in uninfected children. The greatest need for treatment and prophylaxis in children is in sub-Saharan Africa, with 600 000 children in need of ART, and 3.5 million children in need of cotrimoxazole prophylaxis.

Discussion

Since the launch of “3 by 5” in late 2003, the number of people on ART in low- and middle-income countries has more than doubled, from 400 000 to about 1 million people at the end of June 2005. Major progress was made in sub-Saharan Africa and Asia, with treatment numbers tripling in 18 months. However, coverage is still low and the total numbers fall well below the target set by the “3 by 5” programme of 1.6 million people on treatment by the middle of 2005.

Improvements to the quality of monitoring systems are urgently needed and all countries must establish standardized patient-monitoring systems. Because of the lack of standardization, the current estimate of the number of people on treatment has a wide uncertainty range. Data on drug shipments to low- and middle-income countries reported by the pharmaceutical industry could provide an external source of validation. Information from research and development companies, collaborating under the Accelerating Access Initiative, and reports from producers of generic drugs indicate that about one million patient-equivalent-units of triple drug therapy were distributed in the first quarter of 2005.

In sub-Saharan Africa, available data still support the broader analysis on equity by gender and age presented

in the December 2004 progress report, although much more systematic reporting is required to obtain a better picture.⁴ Almost 6 out of 10 adults on treatment are women, reflecting an equitable distribution since more women than men are infected. Children are still under-represented in treatment numbers. For instance, reports from Malawi and Mozambique indicate that 5% and 7%, respectively, of those on treatment are children, yet overall, 13% of those in need of treatment in sub-Saharan Africa are children.

Despite major programmatic obstacles, including lack of early diagnosis, affordable drug formulations for young children, and trained medical staff, there is an urgent need to increase provision of ART to children. The establishment of an estimated need for treatment in children should help advocacy and programme planning for children. These estimates, as well as those made for adults, will not be perfect. The choice of the cut-off point of 2 years prior to death for the estimation of treatment needs from the models is currently considered a good match with treatment initiation criteria, but new studies on CD4 cell counts and disease progression, clinical patterns and treatment-seeking behaviour may lead to changes in the cut-off point in the future.

Just as estimates of HIV prevalence and deaths have uncertainty, so too do the estimates of treatment needs. Previous work has tried to quantify this uncertainty and it suggests that although global estimates of the number of people living with HIV are quite robust (of the order of plus and minus 10%), estimates

Table 1. Estimates of number of people on antiretroviral therapy (ART), need for treatment, and treatment coverage for June 2005 and treatment estimates for December 2004 in low- and middle-income countries, by geographic region

Region ^a	Estimated no. receiving ART, June 2005 (low–high estimate) ^{b, c, d}	Estimated no. in need of ART, 2005	ART coverage, June 2005 (%) ^e	Estimated no. receiving ART, December 2004 ^d
Sub-Saharan Africa	500 000 (425 000–575 000)	4 700 000	11	310 000
Asia ^f	155 000 (125 000–185 000)	1 100 000	8	100 000
Latin America and Caribbean	290 000 (270 000–310 000)	465 000	65	275 000
Europe and Central Asia	20 000 (18 000–22 000)	160 000	12	15 000
North Africa and Middle East	4 000 (2 000–6 000)	75 000	7	4 000
Total	970 000 (840 000–1 100 000)	6 500 000	15	700 000

^a Presented in descending order of number of people in need of ART.

^b In people younger than 50 years.

^c Figure is midpoint of the high and low estimates.

^d Numbers do not add up due to rounding.

^e The coverage estimate is based on the midpoint of the number of people receiving ART and the midpoint for estimated need for ART.

^f Excludes the Central Asian Republics.

Table 2. Estimates of children in need of antiretroviral therapy (ART) and cotrimoxazole prophylaxis, 2005

Region ^a	Children (0–14 years) in need of ART	Infants (0–18 months) in need of ART	Children (0–14 years) in need of cotrimoxazole (late diagnosis)	Children (0–14 years) in need of cotrimoxazole (early diagnosis)
Sub-Saharan Africa	600 000	240 000	3 500 000	1 900 000
Asia	38 900	22 700	309 000	137 600
Latin America and Caribbean	13 700	5 800	99 000	50 000
North Africa and Middle East	7 600	4 400	59 000	18 000
Eastern Europe and Central Asia	1 600	1 100	18 000	6 200
Total	660 000	270 000	4 000 000	2 100 000

^a Listed in descending order of number of children in need of ART.

for individual countries will vary much more depending on the quality of the data and the type of epidemic.¹¹ Countries are strongly involved in the estimation process, which is accompanied by regular consultation between countries and WHO and UNAIDS, and a biannual global effort to train country staff in the estimation methods and software.

Additional work is also needed to address limitations of the current models to estimate treatment needs. In children, the higher mortality in the first year of life compared to later in childhood needs to be taken into account, as does the effect of cotrimoxazole treatment on disease progression and mortality. In adults, methods need to be developed to estimate the need in people aged 50 years and over. Furthermore, recommendations on when to initiate treatment may

change over time and affect the need estimates.

Accurate monitoring will be an essential basis for the rapid expansion of treatment programmes in low- and middle-income countries. WHO, UNAIDS, UNICEF and partners will continue to work with countries to provide the best possible information on progress in the scale-up of treatment for both adults and children. As monitoring systems become more established, the treatment numbers will be provided with increasing certainty and greater disaggregation, and include essential information on treatment outcomes. ■

Acknowledgements

We would like to thank the many people and institutions that contribute to the regular updates of treatment data. These

include our colleagues in countries' Ministries of Health, in WHO, UNAIDS and UNICEF including their regional and country offices, and in international nongovernmental organizations. We are also grateful to our colleagues at the Global Fund and PEPFAR for their crucial assistance in harmonizing and validating the reports. We want to acknowledge the many national programme staff and collaborating institutions for data on the status of the epidemic. We also want to thank the many researchers, epidemiologists, demographers, and public health experts of the UNAIDS Reference Group on Estimates, Modelling and Projections.

Competing interests: none declared.

Résumé

Suivre l'élargissement des programmes de traitement antirétroviral : méthodes d'estimation de la couverture

Le présent article fait le point des sources de données et des méthodes utilisées pour estimer le nombre de personnes sous traitement antirétroviral et la couverture des programmes de traitement antirétroviral dans les pays à revenu faible ou intermédiaire, ainsi que pour suivre les progrès accomplis en direction de l'objectif des 3 millions de personnes sous traitement en 2005 fixé par l'OMS et l'ONUSIDA. Les sources de données utilisées pour estimer la couverture des programmes ainsi que les efforts consentis pour éviter une double comptabilisation et une notification en surnombre sont passés en revue. L'article décrit les méthodes utilisées pour estimer le nombre de personnes ayant

besoin d'un traitement antirétroviral et l'élargissement de leur domaine d'application à l'aide d'estimations des besoins d'enfants, en matière de traitement antirétroviral, comme de prophylaxie par le cotrimoxazole. On estimait à 6,5 millions le nombre de personnes ayant besoin d'un traitement dans les pays à revenu faible ou intermédiaire à fin 2004, dont 660 000 enfants de moins de 15 ans. L'estimation obtenue mi-2005 de 970 000 personnes sous traitement dans les pays à revenu faible ou intermédiaire (plage d'incertitude: 840 000-1 100 000) correspond à une couverture de 15 % des personnes à traiter.

Resumen

Seguimiento de la expansión de los programas de tratamiento antirretroviral: métodos para estimar la cobertura

Se examinan en este artículo las fuentes de datos y los métodos utilizados para estimar el número de personas abarcadas por los programas de tratamiento antirretroviral (TAR) y la cobertura de los mismos en los países de ingresos bajos y medios, así como

para vigilar los progresos hacia la meta «tres millones para 2005» establecida por la OMS y el ONUSIDA. Se incluye una revisión de las fuentes de datos utilizadas para estimar la cobertura de los programas de TAR, así como las medidas tomadas para evitar la

doble contabilidad y la sobrenotificación. Se describen los métodos empleados para estimar el número de personas necesitadas de TAR, ampliándolos para estimar las necesidades de tratamiento de la población infantil, tanto para el TAR como para la profilaxis con cotrimoxazol. Al final de 2004 necesitaban tratamiento en los países de ingresos bajos y medios unos 6,5 millones de personas,

incluidos 660 000 menores de 15 años. La estimación de que a mediados de 2005 recibían TAR unas 970 000 personas en los países de ingresos bajos y medios (margen de incertidumbre: 840 000 - 1 100 000) corresponde a una cobertura de un 15% de las personas necesitadas de tratamiento.

Arabic

References

- World Health Organization and UNAIDS. *Treating 3 million by 2005: making it happen*. Geneva: WHO; 2003.
- Schwartzlander B, Stover J, Walker N, Bollinger L, Gutierrez JP, McGreevey W, et al. Resource needs for HIV/AIDS. *Science* 2001;292:2434-6.
- World Health Organization, UNAIDS, GFATM, USAID, Measure, FHI. *National AIDS Programmes: a guide to indicators for monitoring and evaluating national antiretroviral programmes*. Geneva: WHO; 2005.
- World Health Organization and UNAIDS. "3 by 5" progress report, December 2004. WHO; 2005. Available from: <http://www.who.int/3by5/progressreport05/en/>
- Bate R. *Slippery AIDS statistics: why loose HIV numbers create false hope and bad policy*. American Enterprise Institute for Public Policy Research. Available from: http://www.aei.org/publications/pubID.22469/pub_detail.asp
- Walker N, Grassly NC, Garnett GP, Stanecki KA, Ghys PD. Estimating the global burden of HIV/AIDS: What do we really know about the HIV pandemic? *Lancet* 2004; 363:2180-5.
- UNAIDS Reference Group on Modelling and Estimation. Improved methods and assumptions for estimation of the HIV epidemic and its impact: Recommendations of the UNAIDS Reference Group and Estimates, Modelling and Projections. *AIDS* 2002; 16:W1-16.
- Walker N, Stover J, Stanecki K, Zaniewski AE, Grassly NC, Garcia-Calleja JM, et al. The workbook approach to making estimates and projecting future scenarios of HIV/AIDS in countries with low-level and concentrated epidemics. *Sex Transm Infect* 2004;80 Suppl 1:i10-13.
- Ghys PD, Brown T, Grassly NC, Garnett G, Stanecki K, Stover J, et al. The UNAIDS Estimation and Projection Package: a software package to estimate and project national HIV epidemics. *Sex Transm Infect* 2004;80 Suppl 1:i5-9.
- Stover J. Projecting the demographic consequences of adult HIV prevalence trends: the Spectrum Projection Package. *Sex Transm Infect* 2004;80 Suppl 1:i14-18.
- Grassly NC, Morgan M, Walker N, Garnett G, Stanecki KA, Stover J, et al. Uncertainty in estimates of HIV/AIDS: the estimation and application of plausibility bounds. *Sex Transm Infect* 2005;81:279-80
- World Health Organization. *Scaling up antiretroviral therapy in resource-limited settings: treatment guidelines for a public health approach*. Geneva: WHO; 2004.
- Morgan D, Mahe C, Mayanja B, Okongo JM, Lubega R, Whitworth JAG. HIV-1 infection in rural Africa: is there a difference in median time to AIDS and survival compared with that in industrialized countries? *AIDS* 2002;16:597-603.
- Schneider M, Zwahlen M, Egger M. *Natural history and mortality in HIV-positive individuals living in resource-poor settings: a literature review*. Available from: http://www.epidem.org/Publications/unaid%20HQ_03_463871%20final.pdf
- Mocroft A, Vella S, Benfield TL, Chiesi A, Miller V, Gargalianos P, et al. Changing patterns of mortality across Europe in patients infected with HIV-1. EuroSIDA Study Group. *Lancet* 1998;352:1725-30.
- Dabis F, Schechter M, Egger M, and ART-LINC/ART-CC STUDY GROUPS. Response to highly active retroviral therapy in low- and high-income countries: analysis of clinical databases from 4 Continents. Proceedings of the 12th Conference on Retroviruses and Opportunistic Infections; 2005 February 22-25; Boston, USA.
- Fassinou P, Elenga N, Rouet F, Laguide R, Kouakoussui KA, Timite M, et al. Highly active antiretroviral therapies among HIV-1-infected children in Abidjan, Côte d'Ivoire. *AIDS* 2004;18:1905-13.
- Chintu C, Bhat GJ, Walker AS, Mulenga V, Sinyinza F, Lishimpi K, et al. Cotrimoxazole as prophylaxis against opportunistic infections in HIV-infected Zambian children (CHAP): a double-blind randomised placebo-controlled trial. *Lancet* 2004;364:1865-71.
- Newell ML, Coovadia H, Cortina-Borja M, Rollins N, Gaillard P, Dabis F for the Ghent International AIDS Society working group on HIV infection in women and children. Mortality of infected and uninfected infants born to HIV-infected mothers in Africa: a pooled analysis. *Lancet* 2004;364:236-46.
- Blanche S, Rouzioux C, Moscato ML, Veber F, Mayaux MJ, Jacomet C, et al. A prospective study of infants born to women seropositive for human immunodeficiency virus type 1. HIV Infection in Newborns French Collaborative Study Group. *N Engl J Med*. 1989;320:1643-8.