Researchers estimate lives lost due to delay in antiretroviral drug use for HIV/AIDS in South Africa

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Boston, MA – More than 330,000 lives were lost to HIV/AIDS in South Africa from 2000 and 2005 because a feasible and timely antiretroviral (ARV) treatment program was not implemented, assert researchers from the Harvard School of Public Health (HSPH) in a study published online by the *Journal of Acquired Immune Deficiency Syndromes* (JAIDS) (http://www.jaids.com/). In addition, an estimated 35,000 babies were born with HIV during that same period in the country because a feasible mother-to-child transmission prophylaxis program using nevirapine (an anti-AIDS drug) was not implemented, the authors write.

The paper estimates the consequences of the HIV/AIDS policies followed by the South African government for a five-year period when neighboring countries ramped up their HIV-prevention programs. The paper may have broader implications for the evaluation of consequences of public health programs.

Dr. Pride Chigwedere, MD, SD, lead author of the paper, and colleagues estimated what they described as the ARV benefits lost that were attributable to government policies restricting or delaying the use of ARV treatment in South Africa. For comparison, the authors used Botswana and Namibia, neighboring countries facing epidemics of similar scale and dynamics and with similar resources per capita. Dr. Chigwedere led the analysis while earning his doctoral degree in immunology and infectious diseases from HSPH, graduating in June

2008. He came to HSPH from Zimbabwe, where he was a practicing physician treating AIDS patients.

South Africa is one of the countries most severely affected by the AIDS epidemic. The authors cite UNAIDS data that the prevalence of HIV/AIDS in the adult population is 18.8 percent, with approximately 5.5 million persons infected with HIV. Under the leadership of Thabo Mbeki, who was president of South Africa during the period examined in the paper, the government restricted use of donated nevirapine and blocked funds for more than a year from the Global Fund to Fight AIDS, Tuberculosis, and Malaria awarded to the South African province KwaZulu Natal, the authors recount. President Mbeki formally resigned in September 2008.

The authors estimated the lost benefits of ARV drug use for two groups: AIDS patients and children born to HIV-infected mothers. The research team framed those lost benefits as "person-years," meaning the number of years of life lost due to premature death from HIV/AIDS. The team chose a limited time period for examination to estimate only the ARV benefits already lost and to avoid speculation about the future direction of ARV policies in South Africa.

For background, the pharmaceutical company Boehringer Ingelheim announced in July 2000 that it would offer nevirapine free of charge for five years for the prevention of mother-to-child transmission of HIV-1 in developing economies. South Africa restricted the availability of nevirapine to two pilot sites per province until December 2002, said Dr. Chigwedere. The country's government launched a national program for the prevention of mother-to-child transmission in August 2003 and a national ARV treatment program in 2004. By 2005, the authors estimated, there was 23% ARV treatment coverage and less than 30% prevention of mother-to-child transmission coverage in South Africa. By comparison, neighboring Botswana began a program for the prevention

of mother-to-child transmission in 1999 and a national ARV treatment program in 2001. Using WHO "3x5" initiative data, the authors estimated that there was 85% ARV treatment coverage in Botswana and 71% in Namibia by 2005. Both Botswana and Namibia achieved >70% prevention of mother-to-child transmission coverage by 2005.

To estimate the lost benefits, the research team compared the actual number of persons who received ARVs for treatment or for prevention of mother-to-child transmission between 2000 and 2005 with what was reasonably feasible in the country during that period. They then multiplied the difference by the average efficacy of ARV treatment or prevention of mother-to-child transmission prophylaxis. To read a summary of the methodology, see text at bottom of press release.

"The analysis is robust," said Dr. Chigwedere. "We used a transparent and accessible calculation, publicly available data, and, where we made assumptions, we explained their basis. We purposely chose very conservative assumptions and performed sensitivity analyses to test whether the results would qualitatively change if a different assumption were used."

In conclusion, the authors write: "Access to appropriate public health practice is often determined by a small number of political leaders. In the case of South Africa, many lives were lost because of a failure to accept the use of available ARVs to prevent and treat HIV/AIDS in a timely manner."

"Estimating the Lost Benefits of Antiretroviral Drug Use in South Africa," JAIDS, online October 16, 2008. Print publication expected December 1, 2008. Pride Chigwedere, MD, George R. Seage III, ScD, MPH, Sofia Gruskin, JD, MIA, Tun-Hou Lee, ScD, and M. Essex, DVM, PhD.

Calculation of Person-Years Lost/AIDS Patients

The authors first estimated the number of persons who were eligible to receive ARV treatment by obtaining the number of deaths from AIDS in South Africa for the period 2000? from UNAIDS. Patients with AIDS who died without getting treatment lost the entire average benefit of ARV therapy. Data regarding individuals who received ARV therapy in South Africa between 2000 and 2005 were obtained from the UNAIDS and WHO "3 by 5" records (23% in 2005, less than 10% in 2004, 3% in 2003, and less than 3% for preceding years). The authors propose that South Africa could have started an ARV treatment program in 2000, covering not more than 5% of persons who needed therapy but ramping up the coverage as drugs became less expensive and more international resources became available to 50% coverage by 2005. This estimate is lower that the coverage achieved by both Botswana and Namibia. Then they estimated the average life-years that ARV therapy adds to patients with AIDS in Africa, based on primary studies, a meta-analysis, and a comparison with developed countries. The authors calculated that 2.2 million person-years were lost in South Africa from 2000 to 2005 by not implementing a feasible and timely ARV treatment program.

Calculation of Person-Years Lost/Mother-to-Child Transmission Prevention Failure

The authors estimated the number of children infected with HIV through vertical transmission, using data from the Actuarial Society of South Africa AIDS and Demographic Model and reducing that number to account for HIV prevalence in South Africa with population growth in mind. They estimated mother-to-child transmission prevention coverage using data from the PMTCT Task Team in South Africa and the Health Systems Trust. The research team assumed that it was feasible for South Africa to start a mother-to-child transmission prevention program in

2000, given that nevirapine was available for free, and estimated a ramping up to about 55% coverage by 2005. This estimate is less than the coverage achieved by both Namibia and Botswana. They used the HIV Network for Prevention Trials 012 trial, which showed that single-dose nevirapine decreased transmission by 47% compared with oral ZDV in a breastfeeding population. To estimate the person-years lost per case of HIV transmitted, the authors assumed a life expectancy of 48 years and then subtracted the average survival of an HIV-infected baby without ARV treatment. The authors estimated that 1.6 million person-years were lost in South Africa from 2000 to 2005 by not implementing a mother-to-child transmission prophylaxis program using nevirapine.

Source: Harvard School of Public Health