HIV/AIDS' spread and impact on other health-related millennium development goals

– secondary publication

Anita Alban, MSc (econ), &
Nina Bjerglund Andersen, MSc (public health)

Correspondence: Anita Alban, EASE International, Toldbodgade 19B, 1253 Copenhagen K, Denmark.

E-mail: aa@easeint.com

Dan Med Bull 2007;54:163-6

ABSTRACT

HIV/AIDS threatens the development of countries with high HIV prevalence. This article focuses on the magnitude of the impact of HIV/AIDS on the millennium development goals (MDGs) for health. The article is based on a literature survey on the impact of HIV on child health, maternal mortality, tuberculosis (TB) and malaria. At global level 10% of child mortality is related to HIV/AIDS but the impact of HIV/AIDS on child mortality is much higher in high HIV prevalence countries being measured in the range of 27-42%. The impact on maternal mortality is difficult to estimate since the majority of pregnant women are not tested for HIV, but studies in a number of HIV high prevalence countries indicate an increasing negative impact on maternal mortality. The impact of HIV/AIDS on TB is significant. 9% of the TB cases are related to HIV/AIDS at the global level, but for the WHO African region alone, the impact of HIV/AIDS is estimated at 31%. There is evidence that HIV infections increase the risk for the progression of malaria in children and the risk of severe and complicated malaria in adults in stable malaria areas. However, the most evident effect of HIV on malaria is related to pregnant women.

It is concluded that strategies to reach the MDGs for health must include a comprehensive and coordinated approach to fight the major health problems including a more suitable resource allocation and organisation of health services taking into account the many inter-linkages between diseases.

METHODOLOGY

The article is based on published materials from the time period 2000-2006, and has been identified over two periods. The first literature searches were conducted in the beginning of 2005 followed by additional searches carried out in January 2006. To the extent possible all included materials represent primary sources, however, some sections include secondary sources. The reason for this discrepancy is that for some areas a large number of published materials are available while for others only few primary sources have been published. The materials have been identified both through searches in relevant databases and through consultations with experts in the relevant fields from the World Bank, WHO and UNICEF. The primary database used is PubMed. Additional specific searches have been carried out using the databases of international development organisations (UNDP, WHO, the World Bank, Stop-TB, UNAIDS and UN Millennium Project). To ensure that all relevant material was included and that the searches were done comprehensively, all reference sections of the identified articles were studied and the function, "related articles" in PubMed was used to identified key articles.

Search words used both as unrelated and in combination included: *HIV/AIDS, child mortality, child survival, infant mortality, under-5 mortality, maternal mortality, maternal survival, maternal health, pregnancy, tuberculosis, malaria, mortality, impaired immunity and Africa.*

The initial literature searches for HIV and child mortality and HIV and TB were along with evidence searches for HIV and poverty, HIV and child nutrition and HIV and primary education carried out for the International AIDS Vaccine Initiative (IAVI), resulting in the publication [1], which was presented at the UN 5-year follow-up conference on the millennium development goals (MDG)s in September 2005 in New York. For an analysis of the influence of HIV on poverty and national development, child nutrition and education in countries with high HIV prevalence reference is made to [1].

THE UN MILLENNIUM DEVELOPMENT GOALS

The UN MDGs agreed upon in 2000 by heads of states and governments constitute a set of goals for development in the world's poorest countries. The goals constitute a common ground for international development and consist of eight primary goals and 18 targets (Table 1). In contrast to preceding international promises, the MDGs are clearly formulated goals with a fixed deadline (2015), by which they are to be achieved [2]. Of the eight primary goals three are directly related to the health sector. These are goal number four, five and six that aims at reducing child- and maternal mortality and halting the spread of HIV/AIDS, malaria and other major diseases.

HIV AND CHILD MORTALITY, HIV AND MATERNAL MORTALITY

MDG number five is to reduce infant- and child mortality by two thirds by 2015. In this article focus is limited to only mortality among children under five years of age.

The development in child mortality in five African countries with HIV prevalence between 16.5% (Zambia) and 38.8% (Swaziland) is illustrated in Figure 1 and shows how mortality has increased in all five countries [3].

HIV/AIDS is by a group of experts estimated to be the cause of 10% of all deaths among children under five in Africa in 2002 [4]. The 10% applies, however, to the region as a whole and does not reflect the large inter-country differences. In high prevalence countries like Botswana, Zimbabwe, Swaziland and Namibia, HIV/AIDS is estimated to be the underlying cause of death among children under five in 42%, 35%, 27% and 27% of the cases respectively [5].

It is, however, important to highlight that the high proportions of child deaths due to HIV/AIDS only includes deaths directly caused by HIV/AIDS. Several studies of the difference in mortality rates among child born to HIV-negative mothers and children born to HIV-positive mothers thus show that children born to HIV-positive mothers have a three fold increased risk of dying compared to children born to HIV-negative mothers, irrespective of the child's own HIV status [6].

In addition to an increased risk of mortality for children of HIV-positive mothers, studies have shown that children are at a significantly increased risk of dying, if their mother dies. Since children of HIV-positive mothers are at increased risk of loosing their mother, due to the mother's increased risk of dying, the children's overall risk of dying increases further [7, 8]. In conclusion, children born in areas with high HIV prevalence face a significantly increased risk of dying before the age of five compared to children born in areas of low HIV-prevalence, both as a direct and indirect consequence of HIV/AIDS.

A reduction in maternal mortality by three quarters by 2015 is the objective of MDG number five. When studying the interactions between HIV/AIDS and maternal mortality it becomes apparent that the number of publications on the subject does not correspond to the magnitude of the problem. In addition, maternal mortality is known to be a difficult indicator to measure, and when measured, data is often subjected to relatively high uncertainty. Data on maternal mortality is thus primarily based on models developed on the basis of data from Demographic Health Surveys (DHS), where data on causes of death rarely is very specific, making studies of the interactions between HIV/AIDS and maternal mortality imprecise [9, 10].

The development in maternal mortality in five Sub-Saharan African countries with a HIV prevalence between 16,5% (Zambia) and

Table 1. The millennium development goals [2].

1. **Eradicate extreme poverty and hunger**
   - Reduce by half the proportion of people living on less than a dollar a day
   - Reduce by half the proportion of people who suffer from hunger
2. **Achieve universal primary education**
   - Ensure that all boys and girls complete a full course of primary schooling
3. **Promote gender equality and empower women**
   - Eliminate gender disparity in primary and secondary education preferably by 2005, and at all levels by 2015
4. **Reduce child mortality**
   - Reduce by two thirds the mortality rate among children under five
5. **Improve maternal health**
   - Reduce by three quarters the maternal mortality ratio
6. **Combat HIV/AIDS, malaria and other diseases**
   - Halt and begin to reverse the spread of HIV/AIDS
   - Halt and begin to reverse the incidence of malaria and other major diseases
7. **Ensure environmental sustainability**
   - Integrate the principles of sustainable development into country policies and programmes; reverse loss of environmental resources
   - Reduce by half the proportion of people without sustainable access to safe drinking water
   - Achieve significant improvement in lives of at least 100 million slum dwellers, by 2020
8. **Develop a global partnership for development**
   - Develop further an open, rule-based, predictable, non-discriminatory trading and financial system. Includes a commitment to good governance, development, and poverty reduction — both nationally and internationally
   - Address the special needs of the least developed countries. Includes: tariff and quota free access for least developed countries' exports; enhanced programme of debt relief for HIPCs and cancellation of official bilateral debt; and more generous ODA for countries committed to poverty reduction
   - Address the special needs of landlocked countries and small island developing states
   - Deal comprehensively with the debt problems of developing countries through national and international measures in order to make debt sustainable in the long term
   - In cooperation with developing countries, develop and implement strategies for decent and productive work for youth
   - In cooperation with pharmaceutical companies, provide access to affordable essential drugs in developing countries
   - In cooperation with the private sector, make available the benefits of new technologies, especially information and communications

38,8% (Swaziland) is illustrated in Figure 2 and shows no clear tendency of the relationship between HIV/AIDS and maternal mortality [11].

Exact estimates on the impact of HIV/AIDS on maternal mortality are difficult to make, due to the uncertainties mentioned above and due to the fact that the HIV-status of the women often is unknown. It is estimated that only about 10% of all pregnant women in Africa know their HIV-status. In addition, maternal deaths are rarely linked to HIV/AIDS in official records [12]. The evidence currently available on the subject that can provide the basis for a discussion of the impact of HIV/AIDS on maternal mortality does, however, indicate an increasing impact of HIV/AIDS on maternal mortality, especially in countries with high HIV-prevalence rate (>15%). Research form high prevalence countries such as South Africa (21%) does thus indicate that HIV/AIDS today is one of the leading obstetric causes to maternal deaths [12]. National studies from Malawi and Zimbabwe suggests that the risk of maternal death is 8-9 times higher among HIV-positive women than among HIV-negative women. In addition, the studies show that pregnancy related deaths, parallel to the increase in the number of HIV-positive pregnant women in Malawi and Zimbabwe, have increased 1.9 and 2.5 times respectively over the last ten years [13]. The impact of HIV/AIDS on maternal mortality is also illustrated in a study from South Africa from 1998, where it was shown that HIV/AIDS was the cause of 13% of all maternal deaths, making it the second largest cause of maternal deaths. A similar study, also from South Africa, from 1999-2001, confirms the increasing importance of HIV/AIDS. In that time period HIV/AIDS had increased to become the most important cause of maternal death at 17% [14]. The explanation for the increased risk of maternal death among HIV-positive women is ascribed to the women's increased vulnerability to infections and postoperative complications [12]. One of the most common causes of death for HIV-positive mothers is, however, co-infection with TB. This correlation has been reported in several studies including a study from South Africa, which found 54% of all maternal deaths caused by TB to be related to HIV-infections [15]. The same correlation of co-infection with HIV and TB is found in Zambia: Despite improved obstetric services maternal mortality has increased eightfold over the past 20 years, especially due to the increased TB related maternal mortality as a consequence of HIV-infection [16].

With a continuous accelerating HIV/AIDS epidemic in Africa, where an increasing number of especially young women are infected with HIV compared to men of the same age, HIV/AIDS contributes to the reversal of hard-gained reductions in maternal mortality [12]. The continuous increasing trend in the HIV-epidemic, especially among women in many Sub-Saharan African countries [17], is very worrisome from a perspective of maternal health. As the HIV/AIDS epidemic carries on, and more women will have been infected with HIV for a longer time, an increasing number of pregnant women with HIV/AIDS complications are foreseen. This again will lead to a significant increase in maternal mortality rates. Further, a high HIV-prevalence among young women, as is the case in Zambia and Zimbabwe, where 80% of all HIV-infected in the age group 15-24 years are women [18], will impact on both maternal mortality and child mortality, since the number of HIV-positive pregnant women, HIV-positive mothers and HIV-positive children will continue to increase. Effective strategies to bring back on track the reduction in maternal mortality will require a coherent approach and a much stronger focus on HIV/AIDS than has so far been the case.

HIV AND OTHER MAJOR INFECTIOUS DISEASES

The sixth MDG: Combat HIV/AIDS, malaria, and other diseases threatening societies includes operationalised targets for HIV: Have halted by 2015 and begun to reverse the spread of HIV/AIDS (target 7) and: Have halted by 2015 and begun to reverse the incidence of malaria and other major diseases (Target 8). HIV is an immunosuppressive illness and the spread of HIV also impacts negatively on the incidence of a range of other bacterial-based infections including

fungal infections – referred to as opportunistic infections [19]. To analyse the impact of HIV on other infectious diseases we have chosen to focus exclusively on TB and malaria.

The latest figures published by the UN Millennium Project (www.unmillenniumgoals.org) show that six out of ten countries with a high HIV prevalence rate have experienced recent increases in the incidence of TB – Botswana and Lesotho having experienced the highest increases. But even low-prevalence countries (HIV prevalence rates lower than 5%) experience increases in the incidence of TB – this tendency includes countries in Eastern Europe, for example Estonia, Russia, and Ukraine with prevalence rates at 1-2%.

The findings of increased incidence of TB support the conclusion drawn by Elzinga, Raviglione & Maher [20], who draw attention to the fact that the MDG target for TB in many countries in Sub-Saharan Africa will not be reached because of the HIV epidemic. The authors predict that TB will continue to rise in Sub-Saharan Africa and Eastern Europe (former Soviet Union states) and conclude that a full implementation of DOTS (Directly Observed Treatment Short-course) is not enough to combat the HIV driven TB epidemic in Sub-Saharan Africa. The authors express concern that reaching the sixth MDG for TB will take several decades on the African continent.

Dye and colleagues [21] continue the discussion on the possibilities of reaching the MDG target for TB in an article from 2005 and arrive at the conclusion that the problems facing Sub-Saharan Africa and Eastern Europe Regions are insurmountable before 2015 [21]. A team from WHO's Stop TB programme reaches the same understanding as Elzinga, Raviglione & Maher [20] when analysing the possibilities of decreasing the incidence, prevalence and mortality of TB before 2015. The authors support their conclusions on results from "case reports", analyses of prevalence rates, and death certificates from the WHO global database on TB. Based on their findings, the authors suggest that the DOTS strategy be implemented more aggressively in these regions and extended to include more flexible approaches and methods of procedures of co-infections and medicine resistance. If the countries in Sub-Saharan Africa and Eastern Europe were excluded from the global statistics it is assessed that the global prevalence rate of TB will be half of what is was in 1990 in 2015 – and the MDG for this component of the eighth target reached.

In 2003 Corbett and colleagues [22] calculated the magnitude of the impact of HIV on the incidence of TB and concluded that 9% of new cases of TB in 2000 were related to HIV with great variations in different regions of the world. The authors estimate that in Africa 31% of all new cases of TB are related to HIV, while in South East Asia the figure is down at 3%. Further, the authors found that in 2000 the prevalence rates of co-infections were 5% or higher in eight African countries [22].

Williams and Dye [23] argue that the risk of developing TB doubles immediately after a person is infected with HIV and points out that the risk keeps increasing as long as the person is alive. In a later study from South Africa by Sonnenberg et al this argument has been underscored [24].

The future strategy of reducing the TB epidemic in Africa is thus not only about reaching full implementation of DOTS but equally so on implementing an effective strategy to fight HIV [20].

Until recently, the correlation between HIV and malaria has not drawn considerable attention. However, a number of publications and reports have recently been released that discuss the impact of HIV on the risk and severity of malaria [25]. Although the interaction between HIV and malaria is not as apparent as the relationship between child mortality, maternal mortality and TB, recent research into this field discloses problems with co-infections between HIV and malaria in certain geographical areas where HIV is widespread and malaria stable – and even in areas where the incidence of malaria is unstable.

The effect of HIV on malaria – incidence as well as severity – is split into three categories. Firstly, there is evidence that HIV impacts on the progression of malaria for both children and adults. In areas where malaria incidence is not stable it seems that HIV infected adults are at increased risk of developing complicated and severe malaria. In areas with stable malaria researchers have found an increased risk of a-symptomatic and clinical malaria and an increased lethality among adults. In areas with stable malaria incidence, researchers have also found an increased incidence of malaria fever. The increased risk of severe malaria among HIV infected adults seems correlated to low levels of CD-4 counts, but the biological

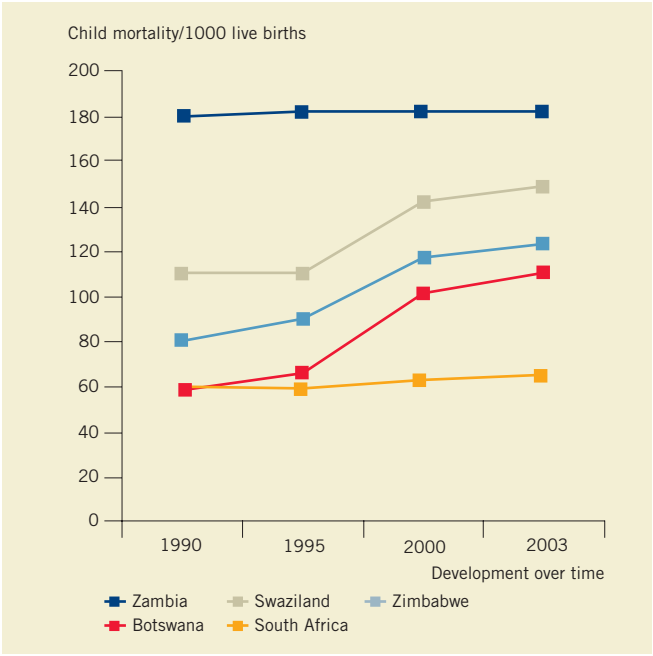

Figure 1. Child mortality – high prevalence countries. The development of child mortality (under-five mortality) in five African countries with HIV prevalence rates between 16.5% (Zambia) and 38.8% (Swaziland) [15]. The trend for all countries represented is increasing or stagnating figures of child mortality.

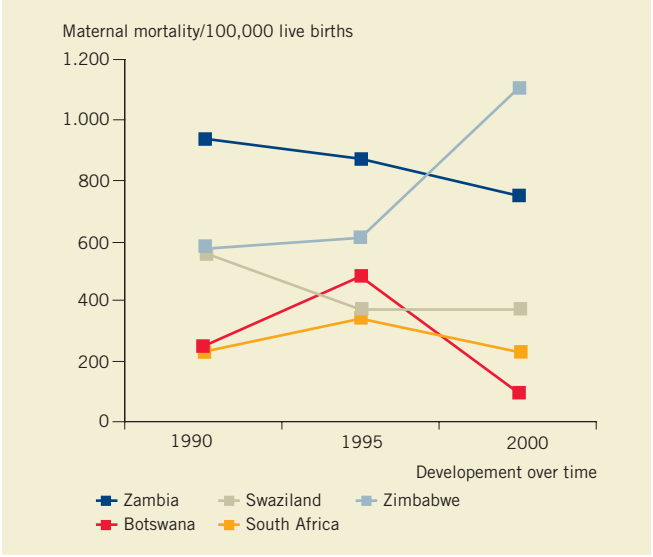

Figure 2. Maternal mortality in HIV high prevalence countries. The development in maternal mortality in the same five African countries with high HIV prevalence rate represented in figure 1. However, contradictory to the findings in figure 1, the relationship between maternal mortality and HIV cannot be established. In Botswana with a very high HIV prevalence rate of 37.3 maternal mortality decreases from 480 in 1990 to 100 only five years later, while Zimbabwe with a HIV prevalence rate at 24.6% at the end of 2005 experience a significant increase in maternal mortality from 610 to 1100 per 100000 live births.

mechanisms behind this relation/correlation are at present not explained [26].

Secondly, it has been discovered that a co-infection between HIV and malaria increases the risk of side effects when a person is being treated with anti-malaria medicines and medicines to prevent opportunistic infections. Treatment of malaria and HIV-related opportunistic infections is frequent among HIV infected pregnant women who receives both anti-malaria medicines, cotrimoxazole, to prevent opportunistic infections. The reason for increased risk of a negatively medical reaction is that both medicine regimens contain sulpha [25].

At present time the best-documented effect of HIV on malaria is related to pregnant women. It has been demonstrated that HIV infection in pregnant women impacts on their biological ability to control *Plasmodium falciparum* infections – independent of the number of pregnancies. The incidence and density of malaria parasitaemia have been found to be higher among HIV positive pregnant women than among pregnant women not infected with HIV. Pregnant women who are co-infected with HIV and malaria have a higher risk of developing anaemia and this impacts negatively on the foetus that is exposed to reduced intra-uterine growth and a low birth-weight. Anaemia among pregnant women is a recognized risk factor for increased maternal mortality. Further, pregnant women who are HIV positive respond less favourable to both prevention and treatment of malaria than women who are not HIV infected [27].

DISCUSSION

In this article we have analysed the impact of HIV on a number of indicators of other health-related MDGs: child mortality; maternal mortality; TB; and malaria. By doing so we have limited ourselves in two ways: 1) HIV and other infectious diseases is not a one-way impact – it goes both ways, and 2) the correlation is more complex than we have described since the MDGs impact on each other in chain reactions. People who are poor have a lower level of education, lower level of health status, lower level of nutritional status, are less knowledgeable about how HIV is transmitted and how to avoid infection, and poor people expose themselves more often to health risks as a social coping strategy. It has been demonstrated that low calorie and protein intake in combination with increased income inequity is strongly correlated with HIV prevalence in 44 countries in Africa [28]. When a mother dies, it impacts negatively on health-, education-, nutrition- and economic status for many orphans and leads to a welfare loss it takes generations to overcome. Further, infectious diseases, such as the "neglected tropical diseases" schistosomiasis, ascariasis and thricuriasis, also leave people physically vulnerable to HIV infection. This has let some researchers to suggest the development of a "rapid-impact package" for neglected tropical diseases to reduce the incidence of HIV, TB and malaria [29].

The result of our analysis shows that effective prevention of HIV is not only a good in itself, but for many countries with high prevalence rates, it will increase the chances of reaching or at least approaching the other MDGs as well. The present situation in many countries in sub-Saharan Africa indicates that the health-related MDGs are not being approached. What we see is a widening of the distance to the targets set by the international society. This negative development can only be reversed if the correlation and the dynamics between the different diseases are included in a joint framework apart from the vertical approaches being the state of the art. Poverty, good nutrition and formal education play an important role for such a strategy to succeed. The health system has a great responsibility in ensuring that this perspective is well understood and supported by the health care sector and an unambiguous responsibility that the correlation between different health problems are reflected in the approaches taken within health care – including the way the system is organised and the resources allocated.

This article is based on a study first published in Ugeskr Læger 2006; 168:3035-9.

References

1. Alban A, Andersen NB. Putting it together. AIDS and the millennium development goals. Post S, Taylor K, editors. September 2005. New York, USA, IAVI. Policy Discussion paper.
2. UNDP. MDG targets and indicators. www.undp.org/mdg/goallist.shtml February 2007
3. United Nations Statistics Division. Children under five mortality rate per 1,000 live births (UNICEF estimates). www.millenniumindicators.un.org/unsd/mi/mi_series_results.asp?rowId=5 /juli 2006.
4. Newell M, Brahmbhatt H, Ghys P. Child mortality in AIDS-affected countries. AIDS 2004; 18(Suppl 2):27-34.
5. Black RE, Morris SS, Bryce J. Where and why are 10 million children dying every year? Lancet 2003; 361:2226-2234.
6. Zaba B, Whitworth J, Marston M et al. HIV and mortality of mothers and children. Evidence from cohort studies in Uganda, Tanzania, and Malawi. Epidemiology 2005;16:275-280.
7. Nakiyingi J, Bracher M, Whitworth J et al. Child survival in relation to mother's HIV infection and survival: evidence from a Ugandan cohort study. AIDS 2003; 17:1827-34.
8. Zaba B, Marston M, Nakiyingi J et al. HIV and child mortality: evidence from surveillance studies in Uganda, Tanzania and Malawi. 2003. Washington DC, USAID and University of North Carolina. Measure Evaluation.
9. AbouZahr C, Wardlaw T. Maternal mortality at the end of a decade: signs of progress? Bulletin of the World Health Organisation 2001; 79(6):561-573.
10. Hill K, AbouZahr C, Wardlaw T. Estimates of maternal mortality for 1995. Bulletin of the World Health Organisation 2001;79:182-93.
11. United Nations Statistics Division. Maternal mortality ratio per 100,000 live births (WHO, UNICEF, UNFPA). www.unstats.un.org/unsd/mi/mi_series_results.asp?rowID=553/ July 2006.
12. McIntyre J. Maternal Health and HIV. Reproductive Health Matters 2005;13(25):129-35.
13. Bicego G, Boerma JT, Ronsmans C. The effect of AIDS on maternal mortality in Malawi and Zimbabwe. AIDS 2002;16:1078-81.
14. McIntyre J. Mothers infected with HIV. Brit Med Bull 2003;67:127-35.
15. Khan M, Pillay T, Moodley JM et al. Maternal mortality associated with tuberculosis-HIV-1 co-infection in Durban, South Africa. AIDS 2001; 15:1857-63.
16. Ahmed Y, Mwaba P, Chintu C et al. A study of maternal mortality at the University Teaching Hospital, Lusaka, Zambia: the emergence of tuberculosis as a major non-obstetric cause of maternal death. Int J Tuberc Lung Dis 1999;3:675-80.
17. UNAIDS. AIDS epidemic update December 2005. Geneva, Switzerland: UNAIDS and WHO.
18. UNAIDS. Global coalition on women and AIDS. Women and AIDS. Geneva, Switzerland: UNAIDS, 2004.
19. Corbett E, Steketee RW, Kuile FO et al. HIV-1/AIDS and the control of other infectious diseases in Africa. The Lancet 2002; 359:2177-2187.
20. Elzinga G, Raviglione MC, Maher D. Sale up: meetings targets in global tuberculosis control. Lancet 2004; 363:814-19.
21. Dye C, Watt CJ, Bleed DM et al. Evolution of tuberculosis control and prospects for reducing tuberculosis incidence, prevalence, and deaths globally. JAMA 2005; 293:2767-75.
22. Corbett E, Watt C, Walker N et al. The growing burden of tuberculosis: Global trends and interactions with the HIV epidemic. Arch Intern Med 2003;163:1009-21.
23. Williams BG, Dye C. Antiretroviral drugs for tuberculosis control in the era of HIV/AIDS. Science 2003;301(5639):1535-7.
24. Sonnenberg P, Glynn JR, Fielding K et al. How soon after infection with HIV does the risk of tuberculosis start to increase? A retrospective cohort study in South Africa gold miners. JID 2005;191:150-6.
25. Malaria and HIV interactions and their implications for public health policy. Geneva, Switzerland, WHO. Technical Consultation. 2004.
26. Cohen C, Karstaedt A, Frean J et al. Increased prevalence of severe malaria in HIV-infected adults in South Africa. Clin Infect Dis 2005;41: 1631-7.
27. Mount AM, Mwapasa V, Elliott SR et al. Impairment of humoral immunity to Plasmodium falciparum malaria in pregnancy by HIV infection. Lancet 2004;363:1860-7.
28. Stillwaggon E. HIV/AIDS in Africa: Fertile terrain. The Journal of Development Studies 2002;38(6):1-22.
29. Hotez PJ, Molyneux DH, Fenwick A et al. Incorporating a rapid-impact package for tropical neglected diseases with programs for HIV/AIDS, tuberculosis, and malaria. PLoS Medicine 2006;3(5):e001-e009.