Lepr Rev (2002) **73,** 376–385

The impact of HIV on tuberculosis control—towards concerted action

PETER GODFREY-FAUSSETT & HELEN AYLES

London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, UK

Accepted for publication 23 September 2002

Summary The well-established international control strategy for tuberculosis is based upon passive case-finding of the most infectious cases followed by effective chemotherapy with sufficient support to ensure and record a successful outcome. However, no country with a severe HIV epidemic is successfully controlling tuberculosis. HIV exerts a double blow. Not only must the health service manage a greatly increased number of patients (as many as fourfold higher in many African settings) but each individual patient needs to be managed more effectively if the control programme is to have a similar impact on transmission as it did in the pre-HIV era. In this paper, we discuss some of the effects of increased burden and stigmatization. We consider the potential of preventive therapy to reduce the impact of HIV on tuberculosis control and describe a more integrated approach to both infections that is being piloted in several sites in Southern Africa.

Introduction—the need to go beyond DOTS

The well-established international control strategy for tuberculosis, DOTS, which derives from the original Direct Observation of Treatment, Short-course, is based upon passive case-finding of the most infectious cases followed by effective chemotherapy with sufficient support to ensure and record a successful outcome.[1,2] The rationale for this approach is that it will rapidly reduce mortality and morbidity among patients with tuberculosis while minimizing the emergence of drug resistance and recurrent disease. It will also reduce transmission of infection and so, in the medium term, result in fewer and fewer cases leading to eventual elimination of tuberculosis as a public health burden.

In the absence of human immunodeficiency virus (HIV) in the community, each infected contact has around a 10% chance to progress to active disease. The tuberculosis control strategy should succeed in reducing transmission if each infectious case infects less than an average of 20 contacts, two of whom would then be expected to develop disease, and one of whom would become infectious. It is not realistic to use the number of contacts infected as a parameter of tuberculosis control programme performance. However, cure rates among new

Correspondence to: P. Godfrey-Faussett

 0305-7518/02/064053+07 $1.00

cases and case detection rates provide useful indicators that are linked to the likelihood of ongoing transmission and WHO has set targets for 85% and 70% for these, respectively.[1]

In the decades prior to the HIV epidemic, rates of tuberculosis were stable in most African countries. There was a balance between the tuberculosis control programmes and the tubercle bacillus. HIV upset this balance. Those infected with HIV have a much greater chance of developing active disease. As many as 40% may progress to active disease over their remaining years of life. These HIV-related tuberculosis patients may be somewhat less infectious. Nonetheless, if the same 20 contacts are infected with *Mycobacterium tuberculosis* and 10% are also HIV seropositive, the case reproduction number will exceed unity and an expanding epidemic will ensue (Figure 1a, b).

This epidemic situation has been seen in many counties and districts with high prevalence of both TB and HIV and can be illustrated by plotting the estimated TB incidence reported by WHO[3] against the adult HIV prevalence reported by UNAIDS[4] for all African countries (Figure 2). No country with a severe HIV epidemic is successfully controlling tuberculosis, although ecological studies do suggest that the quality of TB control programmes does have some impact on tuberculosis rates.[5]

HIV therefore exerts a double blow on health services struggling in the face of inadequate resources. Not only must the health service manage a greatly increased number of patients (as many as 4-fold higher in many African settings),[6] but each individual patient needs to be managed more effectively if the control programme is to have a similar impact on transmission as it did in the pre-HIV era.

Box 1

Impact of HIV on tuberculosis control

- Burden increased (4-fold rise in number of cases in Southern Africa where up to 75% TB cases are also HIV-seropositive).
- Stigma increased (Increased discrimination; probably impacting on health seeking behaviour).
- Diagnosis more difficult (larger differential diagnosis; X-rays less specific; microscopy less sensitive).
- Treatment interactions and adverse effects (rifampicin and anti-retroviral drugs; thiacetazone and severe skin eruptions in HIV-seropositive patients).
- Outcomes worse (WHO targets unattainable, programme dispirited).
- Health care resources inadequate to cope with 4-fold increase in patients.
- Health care staff numbers falling (HIV, poor conditions of service).

The greatest impact of HIV on tuberculosis control arises through this accelerated cycle of transmission and resulting increased burden. However, HIV is having much wider effects than the simple numbers outlined above (Box 1). In this paper, we discuss some of the effects of increased burden and stigmatization. We consider the potential of preventive therapy to reduce the impact of HIV on tuberculosis control and describe a more integrated approach to both infections that is being piloted in several sites in Southern Africa.

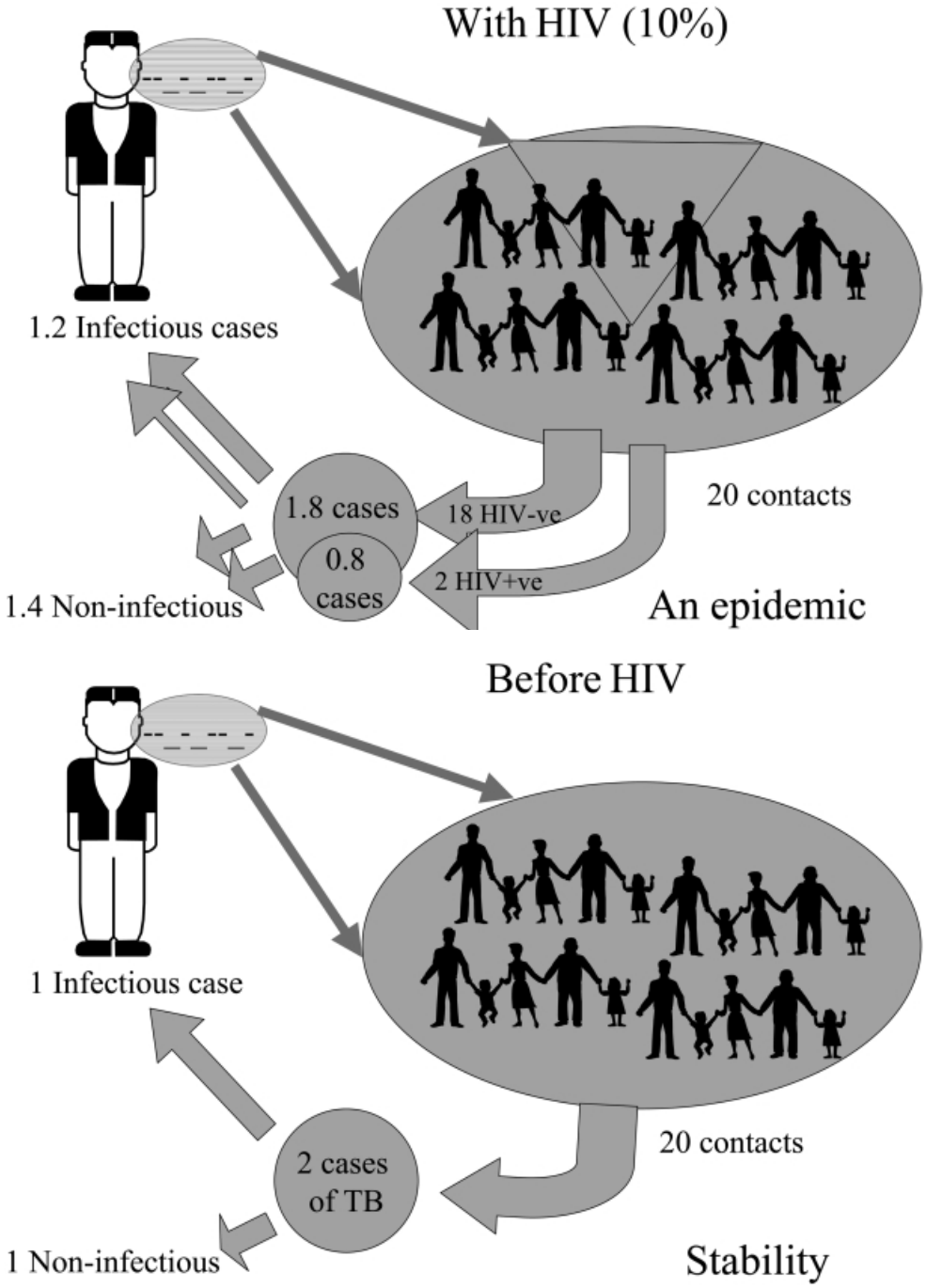

Figure 1. The cycle of tuberculosis transmission. In a stable situation before the HIV epidemic, each infectious case infects an average of 20 contacts, of whom two (10%) will develop active tuberculosis. One of these will not be infectious (extrapulmonary or non-infectious pulmonary disease). If a significant proportion of the contacts are HIV-seropositive (10% in the example shown), a larger number will progress to active tuberculosis and each infectious case will now generate more than one secondary infectious case, leading to an expanding epidemic.

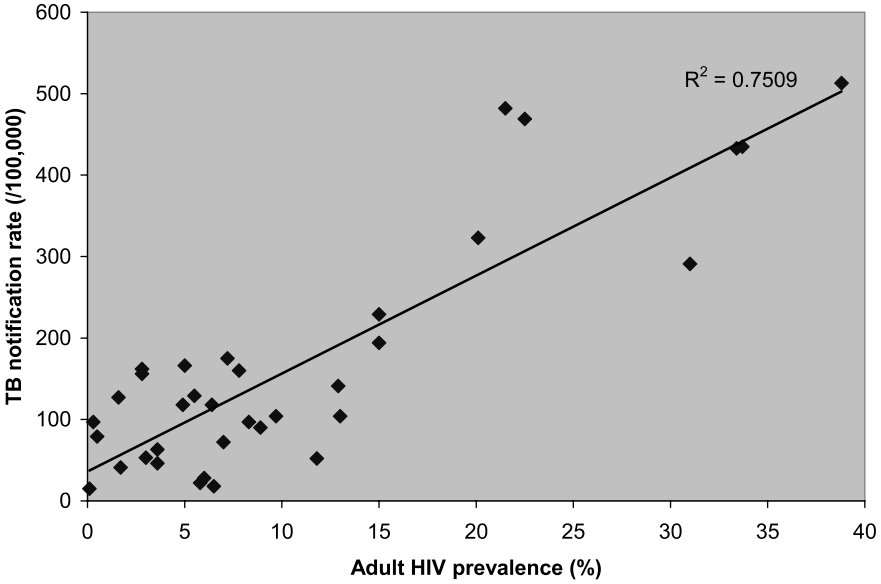

Figure 2. HIV drives the tuberculosis incidence in Africa. WHO estimates of tuberculosis incidence in African countries correlate strongly with UNAIDS estimates of adult HIV prevalence in the same countries.

Stigma, HIV and the new tuberculosis

The seroprevalence of HIV in women attending antenatal clinics in Southern Africa has risen to appalling levels of 15, 20 or even 40%, but the prevalence among tuberculosis patients has risen even higher, to levels of 50, 60 or even 80%. Such a strong association is readily apparent to everybody living in affected communities and leads to a range of beliefs that may make tuberculosis control even more difficult. People, in such communities, talk about the 'new' tuberculosis, sometimes referred to as tuberculosis 'of the bones', a vernacular term used to describe a deep seated problem from which patients do not recover and for which government tuberculosis programmes have little to offer.[7,8]

People who stand in a line to receive their tuberculosis chemotherapy are easily identified by friends and neighbours attending the same health facility and may then be assumed to be HIV seropositive. Since HIV remains highly stigmatized, the tuberculosis patient may find that their home or work situation becomes intolerable due to recrimination and discrimination.

Health care staff, too, may judge tuberculosis patients and discriminate against them. 'They treat us as if we are not human beings' said one such patient in Lusaka, Zambia. It is likely that as the stigma of HIV rubs off onto tuberculosis, case-holding and case-finding will be adversely affected.[9]

During structured in-depth interviews with 427 patients with a cough attending the urban health clinics in Lusaka, 49% strongly agreed that attending the clinic for tuberculosis tests would make people believe that they suffered from AIDS. The perception that the health services were over-burdened and likely to provide a poor service was one of the strongest predictors of delay in seeking a diagnosis.[10] This delay is likely to lead to increased transmission of tuberculosis in the community.

Health systems are not coping with the increased burden.

In the same Lusaka clinics, only 60% of those who had been coughing for more than 3 weeks or had haemoptysis were asked to submit sputum samples for examination. Two thirds of patients attending a diagnostic centre with a technician and microscope available, submitted sputum samples if asked to do so; but only one third did so if they had to find their way from a centre without laboratory facilities to a central laboratory. For patients served by this health facility, therefore, 80% of tuberculosis suspects did not have a sputum sample examined.[11]

The rising burden of cases of tuberculosis means that quality assured microscopy services will be needed at increasingly peripheral health facilities. Without expansion of training capacity, there will not be enough trained personnel to examine the samples, even if clinicians are trained to request them more appropriately.

Preventive therapy as an additional measure

Much of the additional burden of tuberculosis arises from those who are HIV-infected and develop active disease, with its risk of ongoing transmission to their families and communities. An attractive strategy for tuberculosis control is to identify such HIV-infected individuals and give them treatment for their latent tuberculous infection and prevent active disease.[12] Treatment of latent infection has been an integral part of the tuberculosis control strategy in industrialized countries for many years and has gained new prominence as a key component in the Institute of Medicine's report on the elimination of tuberculosis in the USA.[13] The principle is that a course of antituberculous drugs, less intensive than the regimen required to cure active disease, should 'sterilize' the individual by killing the dormant mycobacteria that might otherwise reactivate over the next years. Studies in the era before HIV confirmed that such treatment halved the chances of developing tuberculosis and that this protection lasted for many years.[14]

Several large randomized controlled trials were conducted in Haiti and Africa in the early 1990s, which demonstrated that preventive antituberculous therapy could reduce the incidence of tuberculosis in those who were dually infected with HIV and *M. tuberculosis*.[15–17] Further trials in the USA and Latin America showed that shorter regimens, such as two months of rifampicin and pyrazinamide, were no less effective than longer, traditional regimens using isoniazid for 6–12 months.[18,19] As a result of these trials, both (World Health Organisation (WHO) and Centres for Disease Control and Prevention (CDC) and the American Thoracic Society, introduced new guidelines promoting the use of preventive therapy in people living with HIV infection.[20,21]

In Africa, however, the efficacy of preventive therapy appears to wane rather quickly. Follow-up of one of the Zambian trial cohorts showed that beyond 30 months from starting treatment, it was no longer possible to demonstrate that either of the active treatments given (isoniazid for 6 months or rifampicin plus pyrazinamide for 3 months) was still effective.[22]

What are the possible mechanisms for the waning efficacy of preventive therapy for tuberculosis in people living with HIV?

There are two likely mechanisms for the waning effect of preventive therapy. The first is that, unlike people who are HIV-seronegative, the HIV positive subjects in the Zambian trial

did not have sufficiently robust immune systems to kill the remaining tubercle bacilli, even in the presence of antituberculous drugs. Support for such a mechanism comes from a study in Uganda, which, unlike the Zambian trials, did show longer protection in those receiving rifampicin as part of a combined preventive therapy regimen compared to those who just received isoniazid.[23]

The second mechanism that might explain the waning efficacy of preventive therapy is that following completion of preventive therapy, subjects were reinfected with *M. tuberculosis* and progressed to active tuberculosis within the short time frame of the follow-up. Such an explanation would imply that HIV positive adults were exposed to greater risks of infection with *M. tuberculosis* than would be expected from tuberculin surveys of children in the region. This explanation seems plausible given the risks of nosocomial transmission to HIV positive adults who need to visit and wait in hospitals and clinics where there are limited or no measures in place to control the spread of tuberculosis.

It is difficult to demonstrate reinfection with tuberculosis in people who have taken preventive therapy. DNA fingerprinting does allow strains of mycobacteria to be compared accurately, but the original strain that infected an individual without causing disease, will very rarely be known or be available for fingerprinting. On the other hand, HIV-seropositive individuals who have been cured of active tuberculosis have been shown to be more susceptible to reinfection and/or progression to disease than their HIV-seronegative peers.[24]

Towards a new approach

The standard approach to tuberculosis control is not sufficient in areas with a high prevalence of HIV infection. Health systems that are struggling with the burden are not responsive to the changes in perceptions and stigmatization around tuberculosis in the community. A new approach is needed that takes account of the complex social and biological interactions between tuberculosis and HIV. People with HIV in communities with a high prevalence of tuberculosis are at great risk. Yet, the majority of such individuals do not know that they are infected with HIV, and indeed, many would choose not to know arguing that little can be done for them and the weight of knowing that they were living with an incurable infection might be intolerable. Nonetheless, most people who do receive counselling and choose to find out their HIV status do not regret their decision, even if the test is positive.[25] Furthermore, the results of the Voluntary Counseling and Testing (VCT) Efficacy Study show that providing VCT services is effective in reducing risky behaviour in a way that is predicted to have a significant impact on HIV transmission.[26] Preventing HIV transmission is likely to be an effective way to reduce the burden of tuberculosis. It has been calculated that for every three cases of HIV averted, one case of tuberculosis has also been prevented.

Using this argument, the ProTEST initiative, co-ordinated by the WHO, is therefore promoting HIV testing (hence the name ProTEST), as a route into more effective care and prevention for both HIV and TB.[27,28] The aim is to create an environment in which more people will choose to be tested. Pilot sites in Southern Africa operate by increasing communication and collaboration between the various government and non-governmental service providers at a district level as well as through the provision of specific testing or clinical services where necessary.

Targeting those who choose to have an HIV test, whether they are found to be HIV negative or positive

The majority of people who access voluntary counselling and testing services are not infected with HIV, but perceive themselves to be at risk. These people need accurate information and support to help them to remain uninfected. Counselling on safer sexual behaviour, promotion of condom use and syndromic treatment of sexually transmitted infections are key services, known to reduce HIV transmission, that are either delivered at the voluntary counselling and testing sites, or are facilitated through better local referral networks.

Those who are found to be HIV seropositive need the same services, but may also need a wider range of psychosocial and medical care. From the perspective of tuberculosis control, they are at high risk of developing disease and therefore a suitable group for targeted active case finding and preventive therapy. In this way, tuberculosis can be reduced by three parallel mechanisms. First, transmission of HIV can be reduced by counselling. Secondly, transmission of tuberculosis can be reduced by earlier case-finding of those who already have active infectious disease. And thirdly, some reactivation of tuberculosis can be reduced through preventive therapy, although further research is needed to find more durable prevention, for instance by prolonging the isoniazid treatment indefinitely.

From the perspective of the person living with HIV, tuberculosis is only one of a range of risks, both medical and social. Close links with clinical services can provide care and prevention for opportunistic infections, for instance using cotrimoxazole prophylaxis for pneumocystis pneumonia,[29] and for reproductive health, such as screening for cervical dysplasia and providing family planning services. Where support groups exist, they can link people to legal and welfare services as well as provide important psychosocial support.

Where there is an expanded range of services, more people are likely to feel encouraged to come forward for HIV testing and the stigma associated with the infection will be reduced. The greatest incentive, however, to get tested will be the introduction of highly active anti-retroviral therapy (HAART). Such therapy has the power to prolong the lives of people living with HIV and to reduce the incidence of opportunistic infections among them, including significant reductions in rates of tuberculosis.[30,31] The benefits should be huge, but the constraints are also daunting. Early experience in relatively specialized centres in Africa has demonstrated that financial, health system, biomedical and personal challenges will all conspire to limit the expansion of delivery of HAART.[32] Furthermore, it is not yet clear what the impact of HAART will be on transmission of HIV at a community level. Widespread availability of HAART in London for more than 5 years has not led to a reduction in incidence of HIV infections.[33] HAART reduces the viral load in both plasma and semen[34] and so can be expected to reduce individual risks of transmission, but this benefit may be counteracted by increased survival and by changing perceptions of risk behaviour in the community.[35] Furthermore, acute HIV infection, which is associated with a high viral load and high risk of onward transmission, is rarely detected and even more rarely treated with anti-retroviral drugs. Integrating anti-retroviral treatment into the broader spectrum of care and prevention activities as outlined above should maximize the impact of measures to reduce HIV transmission as well as providing effective care for those already living with HIV.

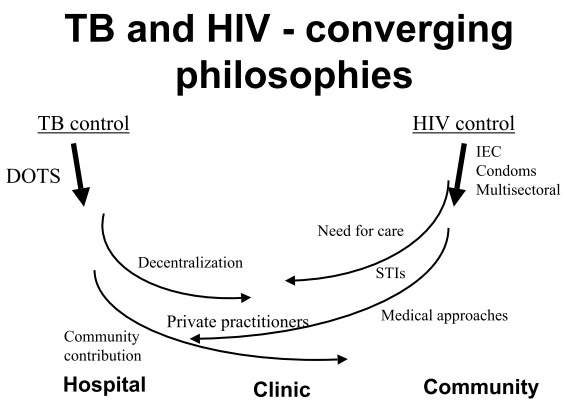

Figure 3. Converging philosophies in HIV and tuberculosis control programmes.

Concerted action

The past few years have seen a convergence of the different philosophies expounded by tuberculosis and HIV programme staff (Figure 3). Tuberculosis control was conceived as a tightly focused programme delivered largely through district hospitals. The programme had clear targets; cure 85% of new cases and detect 70% of such cases in the community. These targets could be achieved by a highly standardized set of interventions; passive case-finding with quality assured sputum microscopy as the cornerstone of diagnosis, admitting smear positive patients to tuberculosis wards and ensuring that they completed at least the two month intensive phase of their treatment as an in-patient. However, and particularly in those areas with a high prevalence of co-infection with HIV, the need to reduce overcrowding in tuberculosis wards and the need for a greater understanding of the patients' perspective have led to decentralization of both diagnosis and treatment to more peripheral levels. More and more clinics are equipped and staffed to act as diagnostic centres, while supervision of treatment has been decentralized right through to the community level.[36]

HIV programmes, by contrast, were quick to develop a broad, multi-sectoral, approach, focused on the community, that aimed at education and health promotion through many channels. The relationship between other sexually transmitted infections and HIV has led to increasing emphasis on syndromic management, usually through health centres or specialised clinics.[37] As the epidemic has matured, so the burden of care has escalated and HIV programmes are increasingly engaged with how to deliver a continuum of care that stretches from the community into the district hospital.[38] Furthermore, the power of anti-retroviral drugs to reduce morbidity and prolong life is likely to result in more engagement with the hospital team.

This convergence from community through the clinics to the hospital for HIV, and *vice versa* for tuberculosis, provides many opportunities for more concerted approaches to both infections based around the principles embedded in the ProTEST initiative.

The importance of a more concerted approach is also evident at the international level. WHO has just released its strategic framework to decrease the burden of TB/HIV 39. The fund, which was established in response to calls from the Secretary General of the UN, Koffi Annan, to respond to the HIV epidemic, was expanded to become the 'Global Fund to fight

AIDS, TB and Malaria'. The recent Commission on Macroeconomics and Health has emphasised how much could be achieved by coherent investment in health in the poorest countries of the world.[40] Sadly, despite this increase in political interest, it is clear that the funds so far pledged to the Global Fund are clearly insufficient, and neither the inaugural meeting of the African Union, nor the recent summit of the rich G8 nations was able to place the fight against HIV and related infections among their priorities for action.[41]

Conclusion

Well-coordinated district-based activities can reduce the burden of tuberculosis and HIV. The challenge is to use the new resources to demonstrate how much can be achieved and to persuade national and international purse holders to increase their investment in order to safeguard the future of our communities.

References

[1] Kochi A. The global tuberculosis situation and the new control strategy of the World Health Organization. *Tubercle*, 1991; **72:** 1–6.
[2] An expanded DOTS framework for effective tuberculosis control. *Int J Tuberc Lung Dis*, 2002; **6:** 378–388.
[3] WHO. Global Tuberculosis Control. *WHO Report 2001.* World Health Organization, Geneva, 2001.
[4] UNAIDS. Report on the Global HIV/AIDS epidemic. UNAIDS, Geneva, 2002.
[5] Cantwell MF, Binkin NJ. Impact of HIV on tuberculosis in sub-Saharan Africa: a regional perspective. *Int J Tuberc Lung Dis*, 1997; **1:** 205–214.
[6] Wilkinson D, Davies GR. The increasing burden of tuberculosis in rural South Africa–impact of the HIV epidemic. *S Afr Med J*, 1997; **87:** 447–450.
[7] Elliott AM, Hawken MP. The changing pattern of clinical tuberculosis in the AIDS era: the role for preventive therapy. *Bailliere's Clin Infect Dis*, 1997; **4:** 63–76.
[8] Farmer P. Social scientists and the new tuberculosis. *Soc Sci Med*, 1997; 44: 347–358.
[9] Ngamvithayapong J, Yanai H, Winkvist A *et al.* Feasibility of home-based and health centre-based DOT: perspectives of TB care providers and clients in an HIV-endemic area of Thailand. *Int J Tuberc Lung Dis*, 2001; **5:** 741–745.
[10] Godfrey-Faussett P, Kaunda H, Kamanga J. Why do patients with a cough delay seeking care at Lusaka Urban Health Centres? A Health Systems Research approach. *Int J Tuberc Lung Dis*, 2002; **6:** in press.
[11] Kamanga J, Kaunda H, Kambashi A. How likely are TB patients to be acurately diagnosed in urban health centres in Lusaka, Zambia? XIIth International Conference on AIDS 1998, Geneva.
[12] De Cock KM, Chaisson RE. Will DOTS do it? A reappraisal of tuberculosis control in countries with high rates of HIV infection. *Int J Tuberc Lung Dis*, 1999; **3:** 457–465.
[13] Geiter L (ed.) *Ending neglect: the elimination of tuberculosis in the United States*. National Academy Press, Washington, D.C., 2000.
[14] Comstock GW, Baum C, Snider DE Jr. Isoniazid prophylaxis among Alaskan Eskimos: a final report of the bethel isoniazid studies. *Am Rev Respir Dis*, 1979; **119:** 827–830.
[15] Mwinga A, Hosp M, Godfrey-Faussett P *et al.* Twice weekly tuberculosis preventive therapy in HIV infection in Zambia. *AIDS*, 1998; 12: 2447–2457.
[16] Pape JW, Jean SS, Ho JL *et al.* Effect of isoniazid prophylaxis on incidence of active tuberculosis and progression of HIV infection [see comments]. *Lancet*, 1993; **342:** 268–272.
[17] Whalen CC, Johnson JL, Okwera A *et al.* A trial of three regimens to prevent tuberculosis in Ugandan adults infected with the human immunodeficiency virus. Uganda-Case Western Reserve University Research Collaboration [see comments]. *N Engl J Med*, 1997; **337:** 801–808.
[18] Gordin F, Chaisson RE, Matts JP *et al.* Rifampin and pyrazinamide vs isoniazid for prevention of tuberculosis in HIV-infected persons: an international randomized trial. Terry Beirn Community Programs for Clinical Research on AIDS, the Adult AIDS Clinical Trials Group, the Pan American Health Organization, and the Centers for Disease Control and Prevention Study Group. *JAMA*, 2000; **283:** 1445–1450.
[19] Halsey NA, Coberly JS, Desormeaux J *et al.* Randomised trial of isoniazid versus rifampicin and pyrazinamide for prevention of tuberculosis in HIV-1 infection. *Lancet*, 1998; **351:** 786–792.

[20] Targeted tuberculin testing and treatment of latent tuberculosis infection. American Thoracic Society. *MMWR Recomm Rep*, 2000; **49:** 1–51.
[21] Preventive therapy against tuberculosis in people living with HIV. *Wkly Epidemiol Rec*, 1999; **74:** 385–398.
[22] Quigley MA, Mwinga A, Hosp M *et al.* Long-term effect of preventive therapy for tuberculosis in a cohort of HIV-infected Zambian adults. *AIDS*, 2001; **15:** 215–222.
[23] Johnson JL, Okwera A, Hom DL *et al.* Duration of efficacy of treatment of latent tuberculosis infection in HIV-infected adults. *AIDS*, 2001; **15:** 2137–2147.
[24] Sonnenberg P, Murray J, Glynn JR *et al.* HIV-1 and recurrence, relapse, and reinfection of tuberculosis after cure: a cohort study in South African mineworkers. *Lancet*, 2001; **358:** 1687–1693.
[25] Baggaley R, Kelly M, Weinreich S *et al.* HIV counselling and testing in Zambia: the Kara Counselling experience. *SAfAIDS News*, 1998; **6:** 2–8.
[26] Efficacy of voluntary HIV-1 counselling and testing in individuals and couples in Kenya, Tanzania, and Trinidad: a randomised trial. The Voluntary HIV-1 Counseling and Testing Efficacy Study Group. *Lancet*, 2000; **356:** 103–112.
[27] Elzinga G, Nunn P. TB and HIV: joint problems, joint solutions? *Bull World Health Org*, 2002; **80:** 469–470.
[28] Nunn P, Harries A, Godfrey-Faussett P *et al.* The research agenda for improving health policy, systems performance, and service delivery for tuberculosis control: a WHO perspective. *Bull World Health Org*, 2002; **80:** 471–476.
[29] Wiktor SZ, Sassan-Morokro M, Grant AD *et al.* Efficacy of trimethoprim-sulphamethoxazole prophylaxis to decrease morbidity and mortality in HIV-1-infected patients with tuberculosis in Abidjan, Cote d'Ivoire: a randomised controlled trial. *Lancet*, 1999; **353:** 1469–1475.
[30] Boix V, Merino E, Portilla J. Highly active antiretroviral therapy for patients with tuberculosis: the solution or the problem? *AIDS*, 2002; **16:** 1436–1437.
[31] Badri M, Wilson D, Wood R. Effect of highly active antiretroviral therapy on incidence of tuberculosis in South Africa: a cohort study. *Lancet*, 2002; **359:** 2059–2064.
[32] Weidle PJ, Malamba S, Mwebaze R *et al.* Assessment of a pilot antiretroviral drug therapy programme in Uganda: patients' response, survival, and drug resistance. *Lancet*, 2002; **360:** 34–40.
[33] Macdonald N, Evans B. Increased high risk sexual behaviour in homosexual men. There is no evidence for a decreased incidence of HIV infection. *BMJ*, 2000; **321:** 1531–1532.
[34] Taylor S, Ferguson NM, Cane PA *et al.* Dynamics of seminal plasma HIV-1 decline after antiretroviral treatment. *AIDS*, 2001; **15:** 424–426.
[35] Anderson RM, May RM, Boily MC *et al.* The spread of HIV-1 in Africa: sexual contact patterns and the predicted demographic impact of AIDS. *Nature*, 1991; **352:** 581–589.
[36] Maher D, Hausler HP, Raviglione MC *et al.* Tuberculosis care in community care organizations in sub-Saharan Africa: practice and potential. *Int J Tuberc Lung Dis*, 1997; 1: 276–283.
[37] Grosskurth H, Mosha F, Todd J *et al.* Impact of improved treatment of sexually transmitted diseases on HIV infection in rural Tanzania: randomised controlled trial. *Lancet*, 1995; **346:** 530–536.
[38] Osborne CM, van Praag E, Jackson H. Models of care for patients with HIV/AIDS. *AIDS*, 1997; **11:** S135–141.
[39] Strategic Framework to decrease the burden of TB/HIV. WHO Stop TB Department and Department of HIV/AIDS, Geneva, 2002.
[40] Mills A, Amoako KY, Kato T. Round table. The work of the Commission on Macroeconomics and Health. *Bull World Health Org*, 2002; **80:** 164–166.
[41] Kondro W. Low profile for health at Kananaskis G8 summit. *Lancet*, 2002; **360:** 61.