The research agenda for improving health policy, systems performance, and service delivery for tuberculosis control: a WHO perspective

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Abstract The development of WHO's DOTS strategy for the control of tuberculosis (TB) in 1995 led to the expansion, adaptation and improvement of operational research in this area. From being a patchwork of small-scale studies concerned with aspects of service delivery, TB operational research shifted to larger-scale, often multicountry projects that were also concerned with health policy and the needs of health systems. The results are now being put into practice by national TB control programmes. In 1998 an ad hoc committee identified the chief factors inhibiting the expansion of DOTS: lack of political will and commitment, poor financial support for TB control, poor organization and management of health services, inadequate human resources, irregular drug supplies, the HIV epidemic, and the rise of multidrug resistance. An analysis of current operational research on TB is presented on the basis of these constraints, and examples of successful projects are outlined in the article. We discuss the prerequisites for success, the shortcomings of this WHO-supported programme, and future challenges and needs.

Keywords Tuberculosis, Pulmonary/prevention and control/drug therapy; Operations research; Health services research; Health services administration; HIV infections/prevention and control; World Health Organization (*source: MeSH, NLM*).

Mots clés Tuberculose pulmonaire/prévention et contrôle/chimiothérapie; Recherche opérationnelle; Recherche en santé publique; Administration services de soins; HIV, Infection/prévention et contrôle; Organisation mondiale de la Santé (*source: MeSH, INSERM*). **Palabras clave** Tuberculosis pulmonar/prevención y control/quimioterapia; Investigación operativa; Investigación sobre servicios de salud; Administración de los servicios de salud; Infecciones por VIH/prevención y control; Organización Mundial de la Salud (*fuente: DeCS, BIREME*).

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Introduction

Operational research offers significant gains at relatively low cost, and in a time frame of months or, at the most, a few years, but its application to tuberculosis (TB) has been relatively neglected (1). In this context, we mean operational research specifically aimed at developing interventions that result in improved policy-making, better design and implementation of health systems, and more efficient methods of service delivery. It is rooted in national and local experience, but can be applied at the global, national, or community level. Murray has given wider definitions of operational research (2). The present paper argues for greater investment in operational research and indicates some needs and opportunities for this, focusing on the approach to operational research taken by WHO following the development of its new recommended control strategy for TB, the "DOTS" strategy (3). The marketing of this strategy began in 1995 (4). Previously, WHO's efforts in applying operational research to TB control had been restricted by relatively low levels of funding to a patchwork of small-scale studies that were poorly focused and difficult to conduct in settings without a clear control strategy. Since 1996 WHO's operational research on TB has been concentrated in countries that have begun implementation of the DOTS strategy, and

has focused on global and regional issues through relatively large-scale multicentre projects.

Progress in operational research in some key areas

A rational framework is necessary to develop a research agenda and select priorities when resources are scarce. We have based our framework on a global analysis, made in 1998, of the reasons for the persistence of TB and the factors preventing its better control (5). What follows draws on the results of several meetings convened by WHO since 1990 with controllers and researchers from countries with high TB burdens. The aims were to arrive at an improved definition of the priorities for research on TB, to develop strategies for addressing them (6), and to implement programmes of work.

Lack of political will and commitment

The lack of political commitment in governments, development agencies, and donors was seen as the principal factor hindering TB control. This matter has to be dealt with primarily at the political level. However, the priority research response is the development of convincing arguments for the adoption and expansion of the DOTS strategy. Because economics is the

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driving force of the political process in most countries, national or provincial studies of the cost-effectiveness of the DOTS strategy are essential. In India, for example, a relatively straightforward analysis of this type (7) demonstrated a net annual potential gain to the economy of ca US\$ 500 million.

Arguments in favour of health interventions that alleviate poverty are increasingly deployed with a view to raising health expenditure (1). Direct evidence is often lacking, although the association of TB with poverty has been noted and debated for centuries (8). However, now that DOTS programmes have been in place for several years in various communities it should be possible to demonstrate their impact, if any, on social and economic indicators. This could be undertaken, for example, in China, where DOTS programmes cover roughly half the country. Specific studies may need to focus on disadvantaged groups such as women and ethnic minorities.

Studies of peoples' perception of the importance of TB are important, since politicians depend, to a greater or lesser extent, on support from their populations. Such work is also crucial for the design of advocacy campaigns seeking to raise awareness and stimulate political action, i.e. to achieve social mobilization. A study of the perceived priority of TB in India (9) showed that its control was severely underfunded, stigma was common, and the public were ignorant of the causes of and proper remedies for the disease.

Other fertile areas for research include analysis of the effectiveness of public health laws and regulations, and case studies of successful attempts to improve TB control.

Financial constraints

Apart from the need for greater financial resources, there is a requirement for more efficient spending and for better transparency and accountability. For the poorest countries, long-term donor support needs to be negotiated, but every country should gradually increase its financial commitment to TB control (1).

The research questions centre on the fact that financial flows to TB control are often unknown, while the financial and economic costs, potentials and lost opportunities are not well quantified. Economic and financial analyses of the costs of poor TB control and the realistic costs of improved programmes, as well as of their social and economic benefits, would greatly aid decision-making (10).

The question arises as to how TB control of high quality can be financed. As for other diseases of high priority, there are many options for financing such control, e.g. public provision through general taxation, publicly supported or private insurance schemes of various kinds, or direct payment by patients and their families (11). What is an appropriate level of public expenditure? Within the public sector, should finance be delivered via states, regions or provinces, or should it be provided directly to health districts or hospitals? What types of incentives, financial or otherwise, might improve outcomes, and at what levels? These questions cannot be answered unless it is known how much patients pay as out-of-pocket expenses or user fees, how much public or private insurance cover exists, and whether the public health system, private-for-profit practitioners or not-for-profit private institutions are providing services. If care is publicly provided in the main, is it properly balanced between salaries, equipment, consumables, maintenance and capital expenditure? Is its geographical distribution equitable? Does it favour the poorest people or is it subsidizing the middle classes?

Inadequate organization and management

The key factor in terms of organization and management is past failure by underfinanced public sectors to design effective health systems and deliver efficient services. The main needs are to improve the quality of management and to increase the number of outlets for the provision of TB control services.

Clear descriptions of the consequences of inadequate services are essential (12). In Africa the need is to design systems that reach dispersed, mainly rural, populations. Initiatives such as the Community TB Care in Africa Project (Box 1) aim to utilize the capacity of communities to support patients with TB during treatment. In Asia, and increasingly in Africa, the priority is to improve the performance of the ubiquitous private-for-profit practitioners (13). In western India, over 80% of patients with TB are diagnosed by private practitioners and most receive some or all of their care from these providers (14). Operational

Box 1. The Community Tuberculosis Care in Africa Project (36)

WHO and several partners set up this multinational care project in order to involve communities in the care of patients with tuberculosis (TB) and thereby to improve the performance of overstretched national TB programmes. Specifically, the aim was to reduce periods of hospital admission, improve case-holding, and reduce default rates by providing community support to patients during treatment until cure was achieved. This included direct observation of the initial phase of treatment

In each district the intervention included i) identifying and mobilizing a suitable community organization; ii) developing links between general health services, national TB control programmes, and the community organization; iii) training and supervising community members; iv) adapting recording and reporting systems for use in the community; v) distributing anti-TB drugs and preventing potential abuse, particularly of rifampicin; vi) extending the management responsibilities of national TB control programmes so as to harness the community contribution to care. Projects were established in Botswana, Kenya, Malawi, South Africa, Uganda, and Zambia in urban and rural settings. Study designs included prospective controlled studies and districts with historical controls. A variety of community organizations was involved, ranging from parish development committees to faith-based nongovernmental organizations. Coordination was undertaken by WHO.

In all the countries, community-based care was effective, feasible, affordable, and more cost-effective than the previous systems based on health facilities. Patients generally preferred it. Uganda rapidly adopted the approach as the national strategy for TB control, and most of the other countries are modifying their TB control strategies to include a community-based component. Additional countries not previously involved are now incorporating community-based care into their plans for national TB control.

Successful collaboration between general health services, national TB control programmes, and community health workers was found to depend on the following: i) good communication links and referral schemes; ii) good education of TB patients and their families; iii) training community health workers and health service staff; iv) a system of regular supervision by staff of national TB control programmes and general health services. The main challenges in implementing the intervention were linked to the identification of the leadership responsible for managing the change process, the development of management capacity, and the provision of sustainability.

For the future, in settings where high levels of treatment success are achieved, consideration could be given to the use of similar community approaches in the identification of suspect TB cases, with a view to increasing detection rates.

research projects are showing how private practitioners and hospitals can work together to improve service provision (15, 16). Most countries could benefit from pilot approaches such as these, provided that they are sufficiently large, sustainable, and coordinated with TB control at national or state level.

The maintenance of effective TB control while health sector reforms (e.g. decentralization, integration and privatization) are proceeding is a matter of concern to many managers of national TB control programmes (17). At this stage there is a need for descriptive work documenting experiences of the impact of health sector reform on TB control, so that a record can be built up of what does and does not work (18). There is no major reason why the control of TB should not adapt to the processes involved in health reform.

A number of important questions have received little attention. What kinds of health system and methods of service delivery can control TB in the shifting populations of very large cities in the developing world? Within the primary health care system, can the integration of TB control with the management of other lung diseases affecting adults offer increased efficiency (19)? Why is the rate of case detection so low in many countries? Answering the last question is a matter of urgency because of the epidemiological consequences of delayed diagnosis.

In Africa, TB case notifications are usually high and services are often overloaded. Patients can slip through the net because of the difficulty of providing the three sputum samples required for diagnosis (B. Squire, personal communication, 2002). Attempts to simplify diagnosis using existing tools have had only limited results and success in this area will probably have to await the arrival of novel technologies (20). However, innovative ways should be designed and tested in order to ensure that diagnosis by means of the tools available at present is as rapid and complete as possible (21).

Inadequate human resources

In most countries there are insufficient well-trained staff to provide TB control of adequate quality. For many countries there is poor documentation of the following: the numbers of staff needed, their cadre and training levels; the attrition rate, especially in areas where there is a high prevalence of human immunodeficiency virus (HIV) infection; the replacement rates required; and the sources of new staff. There has been little study of the impact of career structures and the importance of recognition, rewards, and incentives on staff retention. It is vital to know what national and international training schemes are needed to maintain staff numbers, quality and morale.

A comparison of policies and strategies adopted and carried out by various countries with different standards of TB control could be of great value. One key issue of concern is the impact of merging specific TB control programmes with more general communicable disease activities, as is happening in China and many other countries. Strategies for protecting health workers on wards and in laboratories are of major importance but far from easy to implement because resources are often limited (22, 23).

Unreliable anti-TB drug supply

Apart from the limited ability to afford anti-TB drugs, the major problems relate to ensuring regular supplies of drugs of

high quality. WHO's essential drugs programmes have been working in this area for many years and there is now an improved understanding of the processes for the procurement, storage, distribution and prescription of anti-TB drugs. STOP TB recently established the Global Drug Facility in order to improve the reliability of drug supplies for the poorest countries (24).

Priority research issues include the need to document failures of regularity or quality in the supply of drugs. Where the Global Drug Facility is supplying drugs, how does this affect TB control and how does it modify the way the system works? For example, donations made by the Global Drug Facility might conceivably be matched by equivalent withdrawals of public funds to be spent elsewhere.

The mechanisms for ensuring drug quality comprise a further priority area, especially in respect of the fixed-dose combinations that are increasingly recommended (25). Much remains to be done to assess more effective ways of delivering treatment, e.g. blister packaging with fixed-dose combinations and innovative ways of supporting patients to adhere to treatment.

Impact of HIV/AIDS

The impact that HIV has had on TB services in sub-Saharan Africa is well known (26). There is now a similar threat in Asia. The main problem is how to maintain, let alone improve, the control of TB in the face of enormous increases in caseload attributable to HIV. This is arguably the most serious challenge for the future of TB control. First, surveillance is essential in order to determine the scale of the problem and plan a response. Aside from surveys of HIV infection among key affected groups, it is essential to know the HIV infection rates in patients with TB. Second, the control of TB in settings with high HIV infection rates demands measures in addition to those of the basic DOTS strategy (27).

The principal research issues are therefore the design and testing of the optimal mix of measures needed at district level for the direct control of TB (strengthening and expansion of DOTS, and intensified case-finding, isoniazid preventive therapy (28)) and interventions to control HIV and, therefore, indirectly, TB (e.g. voluntary counselling and testing and the provision of condoms and antiretroviral therapy). The ProTEST Initiative is a multicentre study designed to show the effectiveness of a package of such interventions at district level, centred on voluntary counselling and testing. Thus far, the initiative has shown that districts can manage such an approach, that demand for voluntary counselling and testing is enormous provided the results can be obtained on the day of testing, and that isoniazid preventive therapy is feasible. Preliminary results suggest that isoniazid preventive therapy is cost-effective and that voluntary counselling and testing centres can identify and refer TB suspects. The impact of behavioural changes brought about through voluntary counselling and testing as well as final costeffectiveness assessments are expected to be known by mid-2003. Severely affected countries are already requesting an extension of ProTEST (29, 30). Isoniazid preventive therapy has been well addressed over the last 10 years but the intensification of case-finding has been little studied since the mass radiography campaigns of the early 20th century. Additional priority areas include ways of reducing the extremely high mortality among HIV-infected patients treated for TB (31)

and, particularly, further investigation of the controversial area of preventive therapy using trimethoprim–sulfamethoxazole (cotrimoxazole). The greatest hope, however, in the absence of an HIV vaccine, lies with the provision of antiretroviral therapy (32). There are various research questions relating to TB: How efficacious is antiretroviral therapy in the prevention of TB? How effective is it in the field? What are the best methods of delivery?

Impact of drug resistance

Current first-line drug regimens are inadequate for the cure of multidrug-resistant tuberculosis (MDR-TB) (33). Beyond the accurate surveillance of drug resistance the main question concerns the management of MDR-TB cost-effectively, affordably and equitably. WHO's multicentre DOTS-Plus project approaches this matter through operational research at the district level and negotiations at the global level (34, 35). A consensus has been reached on minimum standards for treatment programmes confronting multidrug resistance and huge price reductions have been negotiated with manufacturing companies (35). Pilot projects are operating in Eastern Europe, the Russian Federation, South America, and South-East Asia. It is expected that evidence-based standards for managing MDR-TB will have been finalized by 2003.

Conclusions

A few large-scale international and national projects with WHO involvement have begun to answer vital operational questions relating to TB control. In some instances these projects have started to improve the performance of control programmes. The prerequisites for success include a careful analysis of countries' needs and of the limiting factors. The existence of at least a basic DOTS-based TB programme greatly facilitates operational research. Evaluating and recording the outcome for each patient is an integral part of programme evaluation and is also an excellent research tool for assessing the outcomes of interventions. The integration of operational research with the work of control programmes, involving, where possible, the same personnel in both research and control activities, has resulted in a high output of information and analysis that can be swiftly applied to policy and practice, as has been shown in India and Malawi (Box 2).

However, set against the agenda presented here, these projects with which WHO is associated make a relatively small contribution. Moreover, notwithstanding a significant increase in the amount of operational research conducted and published through national TB control programmes and other agencies during the past decade, some priority areas of research have received scant attention. These include the lack of political commitment and the inadequacy of financial systems apart from cost-effectiveness assessments. The problem of human resources in TB control largely remains to be tackled. Most research, conducted with WHO support or by others, has focused on service delivery. The cost-effectiveness of operational research, as compared with other types of research or with other WHO activities, has not been assessed.

Further progress in operational research relating to TB requires continuous strategic analysis of impediments to

Box 2. Operational research at the national level

Malawi provides the most successful example of a national operational research programme in the field of tuberculosis (TB) control (37). Health systems research in TB control began in Malawi in 1994 with the recognition that the National Tuberculosis Control Programme was in dire straits: notifications were soaring as the incidence of HIV increased, cases were diagnosed without adequate investigation, hot spots of transmission were suspected, and cure rates were poor. With initial support from WHO, the Malawi College of Medicine and the National TB Control Programme set up research studies in order to tackle these problems. The diagnostic process and its shortcomings were analysed in detail; different screening methods for diagnosis were explored; an assessment was made of the degree to which health care personnel were adhering to the guidelines of the national programme; the association between HIV and TB treatment outcome was defined; and the prevalence of TB in hot spots such as prisons and health care institutions was measured. A programme management group was formed which developed and implemented a strategy on control and research. Operational research became an integral component of the National TB Control Programme and the research agenda was firmly linked to the objectives of its five-year development plan.

Research can be made directly relevant to TB control by making sure that the questions it poses are linked to constraints and objectives, thereby enabling its findings to influence policy and practice. For example, one study showed that over 40% of smear-positive TB patients spent at least one month with a traditional healer before attending for orthodox medical care: the national TB control programme has since trained over 3000 traditional healers in 15 districts. In another example, the incidence of TB among health care staff was found to be 3.6% per year. As a result the national TB control programme produced guidelines, for use in every hospital, that were aimed at reducing nosocomial TB transmission. This close integration of research with programme activities has attracted further funds from various donors. Future challenges include designing collaborative activities with the National AIDS Control Programme and reducing the incidence of TB despite the high prevalence of HIV infection.

control. This is the responsibility of WHO as well as its partner agencies and countries. The next steps that should be taken by WHO and/or other agencies include the following: development of a plan to ensure that sufficient qualified operational researchers are available in low-income countries; systematic assessment of training needs (field-oriented training manuals are planned by WHO); action to bridge the gulf between disease control personnel and academic researchers; generation of opportunities for operational researchers to interact with each other, especially at the regional and country levels; and provision of adequate funding.

Funding for operational research has probably increased significantly over the past five years but a shortfall remains. The successes of TB operational research should be publicized and donor agencies and national governments should be made aware of them. The Commission on Macroeconomics and Health has repeated calls for 5% of project assistance to be allocated to operational research. Operational research can answer many of the outstanding questions concerning the effective implementation of TB control, but only if it is adequately led and supported by trained and motivated staff with sufficient funding.

Conflicts of interest: none declared.

Résumé

Elargir le champ de la recherche pour améliorer la politique de santé et la prestation des services et pour rendre les systèmes de santé plus performants dans le domaine de la lutte contre la tuberculose : point de vue de l'OMS

La mise en œuvre en 1995 de la stratégie DOTS de l'OMS pour lutter contre la tuberculose a conduit à élargir, adapter et améliorer la recherche opérationnelle dans ce domaine. Partant d'une mosaïque d'études d'envergure limitée axées sur les aspects de la prestation des services, la recherche opérationnelle a évolué au profit souvent de projets multipays de plus grande envergure, englobant aussi politique de santé et besoins des systèmes de santé. Les programmes nationaux de lutte contre la tuberculose tiennent actuellement compte des résultats obtenus. En 1998, un comité spécial a défini les principaux facteurs faisant obstacle à l'élargissement de la stratégie DOTS: absence de

volonté politique et d'engagement, insuffisance des appuis financiers pour combattre la tuberculose, mauvaise organisation et gestion des services de santé, insuffisance des ressources humaines, approvisionnement en médicaments irrégulier, épidémie de VIH/SIDA et augmentation de la polypharmacorésistance. On trouvera dans le présent article une analyse de la recherche opérationnelle actuelle compte tenu de ces obstacles ainsi que des exemples de projets ayant abouti. Y sont également évoqués les préalables indispensables pour mener à bien un projet, les faiblesses du programme soutenu par l'OMS ainsi que les défis et les besoins futurs.

Resumen

Agenda de las investigaciones orientadas a mejorar las políticas sanitarias, el desempeño de los sistemas y la prestación de servicios para el control de la tuberculosis: perspectiva de la OMS

El desarrollo de la estrategia DOTS de la OMS para el control de la tuberculosis en 1995 propició la expansión, adaptación y mejora de las investigaciones operativas en ese terreno. De ser un mosaico de estudios en pequeña escala centrados en aspectos de la prestación de servicios, las investigaciones operativas sobre la tuberculosis han pasado a ser proyectos en gran escala, a menudo multipaíses, interesados también por las políticas sanitarias y las necesidades de los sistemas de salud. Los programas nacionales de lucha contra la tuberculosis están llevando ya a la práctica los resultados conseguidos. En 1998 un comité especial identificó los principales factores que entorpecen la expansión de la DOTS: falta de voluntad

y compromiso políticos, escaso apoyo financiero a la lucha contra la tuberculosis, mala organización y gestión de los servicios de salud, recursos humanos insuficientes, suministro irregular de medicamentos, epidemia de VIH y aumento de la polifarmacorresistencia. Se hace aquí un análisis de las actuales investigaciones operativas sobre la tuberculosis en relación con esas limitaciones, y se presentan sucintamente ejemplos de proyectos exitosos. Analizamos asimismo las condiciones necesarias para el éxito de esas iniciativas, las deficiencias de este programa apoyado por la OMS y los futuros retos y necesidades.

References

- Macroeconomics and health: investing in health for economic development. Report of the Commission on Macroeconomics and Health. Geneva: World Health Organization; 2001. p. 82-3.
- Murray CJL. Issues in operational, social and economic research on tuberculosis. In: Bloom B, editor. *Tuberculosis: pathogenesis, protection and control*. Washington (DC): American Society for Microbiology; 1994. p.583-622.
- Kochi A. The global tuberculosis situation and the new control strategy of the World Health Organization. *Tubercle* 1991;72:1-6.
- Report on the tuberculosis epidemic, 1995. Geneva: World Health Organization; 1995. Unpublished document WHO/TB/95.183.
- Report of the Ad Hoc Committee on the Global Tuberculosis Epidemic, London 17–19 March, 1998. Geneva: World Health Organization; 1998. Unpublished document WHO/TB/98.245.
- Global Tuberculosis Research Initiative, first meeting, 3–5 March 1998.
 Geneva: World Health Organization; 1998. Unpublished document.
- Dholakia R, Almeida J. The potential economic benefits of the DOTS strategy against TB in India. Geneva: World Health Organization; 1996. Unpublished document WHO/TB/96.218. Available from: URL: http://whqlibdoc.who.int/hq/ 1996/WHO_TB_96.218.pdf
- 8. Smith FB. *The retreat of tuberculosis 1850–1950.* London: Croom Helm; 1998.
- Bhatnagar D. Factors influencing the perceived priority of tuberculosis in India. Geneva: World Health Organization; 1997. Unpublished document WHO/ TB/97.234. Available from: URL: http://whqlibdoc.who.int/hq/1997/ WHO TB 97.234.pdf
- Macroeconomics and health: investing in health for economic development. Report of the Commission on Macroeconomics and Health. Geneva: World Health Organization; 2001. p. 157-75.
- The world health report 1999. Making a difference. Geneva: World Health Organization; 1999. p. 36-42.

- Pathania V, Almeida J, Kochi A. TB patients and private for profit health care providers in India. Geneva: World Health Organization; 1997. Unpublished document WHO/TB/97.223. Available from: URL: http://whqlibdoc.who.int/ hq/1997/WHO_TB_97.223.pdf
- 13. Uplekar M, Pathania V, Raviglione M. Private practitioners and public health; weak links in tuberculosis control. *Lancet* 2001;358:912-6.
- Uplekar M, Juvekar S, Morankar S, Rangan S, Nunn P. Tuberculosis patients and practitioners in private clinics in India. *International Journal of Lung Disease* and Tuberculosis 1998;2:324-9.
- Murthy KJ, Yazdani A, Hreshikesh P. Private-public mix: a workable method in implementation of DOTS. *International Journal of Lung Disease and Tuberculosis* 1999;3(9 Suppl 1):S87.
- Research for action: understanding and controlling tuberculosis in India. New Delhi: World Health Organization Regional Office for South-East Asia; 2000.
- Weil DEC. Advancing tuberculosis control within reforming health systems. International Journal of Lung Disease and Tuberculosis 2000;4:597-605.
- Bosman MCJ. Health sector reform and tuberculosis control: the case of Zambia. *International Journal of Lung Disease and Tuberculosis* 2000; 4:606-14
- Scherpbier R, Hanson C, Raviglione M, editors. Report. Adult Lung Health Initiative. Basis for the development of algorithms for assessment, classification and treatment of respiratory illness in school-age children, youths and adults in developing countries. Recommendations of the Consultation, Geneva, 4–15 May 1998. Geneva: World Health Organization; 1998. Unpublished document WHO/TB/98.257.
- Perkins MD. New diagnostic tools for tuberculosis. International Journal of Tuberculosis and Lung Disease 2000;4(12 Suppl 2):S182-8.

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- Harries AD, Kamenya A, Namarika D, Msolomba IW, Salaniponi FM, Nyangulu DS, et al. Delays in diagnosis and treatment of smear-positive tuberculosis and the incidence of tuberculosis in hospital nurses, Blantyre, Malawi.
 Transactions of the Royal Society of Tropical Medicine and Hygiene
 1997;91:15-7.
- Harries AD, Maher D, Nunn P. Practical and affordable measures for the protection of health care workers from tuberculosis in low-income countries: a discussion and next steps. *Bulletin of the World Health Organization* 1997:75:477-89.
- Nyirenda T, Mundy CJ, Harries AD, Banerjee A, Salaniponi FM. Safety in laboratories carrying out sputum smear microscopy: a dilemma for resourcepoor countries. *International Journal of Lung Disease and Tuberculosis* 1998: 2:690-3
- Global Drug Facility: an initiative of the Global Partnership to Stop TB. Geneva: World Health Organization, STOP TB Partnership; 2001. Available from: URL: http://stoptb.org/GDF/default.asp
- Blomberg B, Evans P, Phanouvong S, Nunn P. Report of an informal consultation on 4-drug fixed dose combinations compliant with the WHO model list of essential drugs. Geneva: World Health Organization; 2001. Unpublished document WHO/TDR/TB.02.1.
- 26. Raviglione MC, Harries AD, Msiska R, Wilkinson D, Nunn PP. Tuberculosis and HIV: current status in Africa. *AIDS* 1997;11 Suppl B:S115-23.
- De Cock K, Chaisson R. Will DOTS do it? A reappraisal of tuberculosis control in countries with high rates of HIV infection. *International Journal of Lung Disease and Tuberculosis* 1999;3:457-65.
- Policy statement on preventive therapy against tuberculosis in people living with HIV: report of a meeting held in Geneva, 18–20 February 1998. Geneva: World Health Organization; 1998. Unpublished document WHO/TB/98.225. Available from: URL: http://whqlibdoc.who.int/hq/1998/WHO_TB_98.255.pdf

- Maher D, Floyd K, Raviglione M. A strategic framework to decrease the burden of TB/H/V. Geneva: World Health Organization; 2002. Unpublished document WHO/CDS/TB 2002.296.
- 30. Hargreaves N, Adatu-Engwau F, Chebet K, Elzinga G, Fujiwara P, Gelmon L, et al. *WHO STOP TB and HIV/AIDS Department guidelines for phased implementation of collaborative TB and HIV activities.* In preparation.
- Harries AD, Hargreaves N, Kemp J, Jindani A, Enarson D, Maher D, et al. Deaths from tuberculosis in sub-Saharan African countries with a high prevalence of HIV-1. Lancet 2001;357:1519-23.
- 32. Harries AD, Nyangulu D, Hargreaves N, Kaluwa O, Salaniponi F. Preventing antiretroviral anarchy in sub-Saharan Africa. *Lancet* 2001;358:1819-20.
- Espinal M, Kim S, Suarez P, Kam K, Khomenko G, Migliori G, et al. Standard short-course chemotherapy for drug-resistant tuberculosis: treatment outcomes in six countries. *JAMA* 2000;283:2537-45.
- 34. Gupta R, Kim J, Espinal M, Caudron J, Pecoul B, Farmer P, et al. Responding to market failures in tuberculosis control. *Science* 2001;293:1049-51.
- Suàrez P, Floyd K, Portocarrero J, Alarcón E, Rapiti E, Ramos G, et al. Feasibility and cost-effectiveness of second-line drug treatment for chronic tuberculosis patients: a national cohort study in Peru. *Lancet* 2002. In press.
- Harries A, Kenyon T, Maher D, Floyd K, Nyarko E, Nkhoma W. Community TB care in Africa: a collaborative project coordinated by WHO. Report on a "lessons learned" meeting in Harare, Zimbabwe, 27-29 September 2000.
 Geneva: World Health Organization; 2001. Unpublished document WHO/CDS/TB/2001.291.
- Salaniponi F, Harries AD, Nyirenda T, Banerjee A, Boeree M, Nyangulu D, et al. Putting research into policy and practice: the experience of the Malawi National Tuberculosis Programme. Geneva: World Health Organization; 1999. Unpublished document WHO/CDS/CPC/TB 99.268.