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Strong general health care systems: a prerequisite to reach global tuberculosis control targets†

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SUMMARY

We argue that tuberculosis control cannot reach its proposed global targets without investment in an adequate network of accessible, effective and comprehensive health services. Lessons from the past are reviewed. They underscore that passive case-detection and adequate case management is the central technical strategy for tuberculosis control. There is no compelling evidence to support active case-detection in the general population. We elaborate on why a strong health care system is a prerequisite in the framework of case-detection and treatment. The necessity to improve quality and accessibility of general health services for ensuring early detection and subsequent cure is demonstrated. It is argued why the need for strong public health care system becomes even more eminent in the light of the tuberculosis/HIV dual epidemics and of the rapid growth of unregulated private-for-profit services. We finally examine the financial gaps for tuberculosis control and discuss the need for allocating more resources to the strengthening of general health care systems. Copyright © 2003 John Wiley & Sons, Ltd.

KEY WORDS: tuberculosis control; health care system; integration; resources

INTRODUCTION

An estimated 36 million disability-adjusted life years (DALY) were lost due to tuberculosis in 2001, accounting for 2.5% of the global burden of diseases (WHO, 2002a). Escalating tuberculosis case rates over the past decade in sub-Saharan Africa and in parts of South-East Asia are largely attributable to the human

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immunodeficiency virus (HIV) epidemic (WHO, 2002b). Revised estimates of global tuberculosis/HIV epidemiology indicate that 11% (640 000) of all new tuberculosis cases in adults (15–49 years) were attributable to HIV infection in 2000 (Corbett *et al.*, 2002). The proportion was much more pronounced in Africa (31%). Tuberculosis is projected to continue rising by about 10% per year in the African countries most severely affected by HIV (Enarson, 2000).

In 1990 the Commission on Health Research for Development stated that: 'The magnitude of the tuberculosis problem is matched only by its relative neglect by the international community' (Hopewell, 2002). Two years later, a major review of health priorities in developing countries (Murray *et al.*, 1993) showed that some interventions to control tuberculosis in East Africa were extremely cost-effective in terms of cost per DALY saved. Despite conceptual and technical problems raised by the DALY method (Paalman *et al.*, 1998; Stefanini, 1999), this report had the merit of bringing this disease back on the international agenda. In the same year, WHO declared tuberculosis 'a global emergency' and started promoting the DOTS (Directly Observed Treatment, Short-course) strategy package as a key to control. This five-element package consists of: political commitment; early case-detection; standardized short course chemotherapy (including DOT—Directly Observed Therapy); uninterrupted drug supply; recording and reporting for outcome assessment (WHO, 2002b).

Ministers of health and finance from 20 countries that have 80% of the world's tuberculosis cases issued the Amsterdam Declaration in 2000, committing to accelerated action against tuberculosis (Enarson, 2002; Hopewell, 2002; Lee *et al.*, 2002). In the same year, the World Health Assembly called for creation of the global partnership 'Stop TB', encompassing the high burden countries, international technical agencies and their development partners. Global public-private partnerships (GPPPs) were launched, including most recently, the Global Fund to Fight AIDS, Tuberculosis and Malaria. These initiatives suggested a climate of trust, solidarity and goodwill at a global level. Nevertheless, fears and reservations have been expressed, including risks for the integrity of public institutions under GPPPs (Walt and Buse, 2000; Buse and Walt, 2000a,b) and potential for neglect of general health services by the global fund (Lambert and van der Stuyft, 2002). Thus, the need is to minimize risks while harnessing the potentials of these initiatives for the interests of tuberculosis control.

In spite of these encouraging developments, the number of tuberculosis cases continues to rise and only a minority of the world's population has access to high quality tuberculosis services (WHO, 2001). Furthermore, HIV and multidrug-resistant (MDR) tuberculosis have the potential to turn the disease again into the 19th century's 'captain of all these men of death' (Frieden *et al.*, 2000). Tuberculosis is projected to remain one of the 10 leading causes of disease burden even in the year 2020 (Murray and Lopez, 1997). With the current picture of tuberculosis epidemiology and control, it will take decades to reach the proposed global targets for case-detection and treatment (Blower and Daley, 2002). We will argue in this paper that tuberculosis control cannot reach its targets without investing in an adequate network of accessible, effective and comprehensive health services.

LESSONS FROM THE PAST

Tuberculosis control before chemotherapy

Tuberculosis is a very old disease and a wealth of experience with various strategies to control the disease is available. At its peak, towards the end of the 18th century (related to rapid urbanization during the industrial revolution), the tuberculosis mortality rate in England was over 500 per 100 000 person-years (Jochem and Walley, 1999). It then started to decrease to about 50 per 100 000 person-years in 1950. In Western Europe, 90% of the decline in tuberculosis incidence and mortality occurred 100 years *before* the availability of curative drugs, during which time patient management was confined to isolation in special hospitals or sanatoria.

At the end of the 19th century, tuberculosis was the leading cause of death in New York with a mortality rate of 280 per 100 000 people (Frieden *et al.*, 2000). Biggs of the New York City Department of Health proposed a systematic approach to tuberculosis control that reveals striking similarities with current recommendations: early case-detection through provision of microscopy, case management, mandatory reporting and systematic follow-up, political will and isolation to stop transmission (Frieden *et al.*, 2000). His efforts were not an unalloyed success. It took a decade to implement—even partially—the programme. Furthermore, the epidemiological impact of his work is difficult to determine, as the mortality rate from tuberculosis had already begun to decline.

It is clear that improved socio-economic conditions (and to some extent the isolation of tuberculosis patients in sanatoria) contributed more to the dramatic decline of the disease in industrialized countries than medical interventions (McKeown, 1976). The association between poverty and tuberculosis has been demonstrated over and over again. Even effective health services will be less successful in achieving tuberculosis control in a context of overall poverty.

. . . and after chemotherapy became available

The discovery of streptomycin in 1944 raised expectations of an effective weapon for rapid tuberculosis control worldwide (Raviglione and Pio, 2002). In 1947 the first tuberculosis Expert Committee of WHO met and established the Tuberculosis Section within WHO's secretariat, to assist countries in developing control programmes based on BCG vaccination and case management. Major progress resulted from the introduction of isoniazid and pyrazinamide in the 1950s. The discovery of these drugs prompted the building of a vertical control programme. This single-purpose structure was introduced using satellite tuberculosis clinics responsible for case-finding through mass radiography and bacteriological diagnosis, and tuberculosis hospitals for segregation of patients during chemotherapy.

By the late 1950s it became clear in most of the less developed countries that there was no decline of tuberculosis. Evidently, the vertical approach was not producing a durable effect on tuberculosis epidemiology (Raviglione and Pio, 2002), while researchers in India demonstrated that it is epidemiologically and economically sound to limit detection efforts to persons who seek assistance at the health service because of symptoms (Banerji and Andersen, 1963). They concluded that

development of district tuberculosis centres as an integral part of the basic health care system would not only be economical and practical, but would effectively contribute to the alleviation of suffering caused by tuberculosis. Their study along with a series of other studies supported by the Indian government, WHO and the British Medical Research Council (BMRC) in two Indian institutions (Fox *et al.*, 1999) provided the foundations for a radical move towards the integration of tuberculosis programmes into general health services. After the 1950s, vaccination efforts were questioned when it became clear that BCG had almost no beneficial effect on the transmission of tuberculosis in developing countries (Styblo and Meijer, 1976). The discovery of rifampicin led to the development of short-course chemotherapy regimens (6 months), largely as a result of the work of BMRC in the 1960s and 1970s (Fox *et al.*, 1999). The role of systematic isoniazid prophylaxis for latent tuberculosis infection has major operational limitations and has been limited to special risk groups such as household contacts and, more recently, HIV-positive individuals (Raviglione and Pio, 2002). One of the first countrywide programmes, which was permanent and based technically on direct examination of sputum smear from self-presenting patients and ambulatory treatment, was established in Tanzania in the late 1970s. By the early 1980s, the programme had resulted in high cure rates in new cases, the number of retreatment cases remained low, there was no increase of resistance and the number of specialized personnel were kept to a minimum (Nkinda *et al.*, 1984).

Thus, until today, case management—case-detection and treatment—has remained the central technical strategy for tuberculosis control. So what is to be done is 'simply' treating people who have the disease, thereby reducing the duration of illness and risk of death and decreasing further transmission. These basic principles of early case-detection and cure to control tuberculosis still hold true in the era of the HIV epidemic. However, to the extent to which the tuberculosis epidemic is fuelled by the HIV epidemic, HIV prevention is synergetic to tuberculosis control. Hence, in ideal circumstances today, all new cases of tuberculosis would consult without delay, would be immediately suspected of suffering from tuberculosis, would be diagnosed promptly, would receive correct treatment, would obtain the prescribed drugs and would take the full treatment regimen regularly until final cure (Dujardin *et al.*, 1997). This, coupled with HIV/AIDS control measures (Badri *et al.* 2002), should lead to a substantial decrease in tuberculosis transmission. Of course, real life presents the challenges of implementation, among which are the swings of the management policy pendulum between disease specific and integrated approaches to tuberculosis control (Raviglione and Pio, 2002).

CASE-DETECTION AND TREATMENT STRATEGY NEED STRONG HEALTH CARE SYSTEMS

Case-detection

Both theory (Dye, 2000) and practice (Grzybowski *et al.*, 1976) suggest that incidence and death rates could be forced down quickly if we could shorten diagnostic and treatment delays, and hence the average duration of infectiousness. By the end

of the year 2000, only 27% of the estimated total smear-positive cases world-wide were detected, and the rate of progress in case-finding between 1999 and 2000 was no faster than the average since 1994, a mean annual increment of 133 000 smear-positive cases (WHO, 2002c). Delays between onset of symptoms and diagnosis being made have been reported in both developing and industrialized countries, varying from 6.2 weeks in Australia and 12 weeks in Botswana to 16 weeks in Ghana (Lienhardt *et al.*, 2001). Thus the sad fact is that only a small proportion of all smear-positive tuberculosis patients in the world are detected and many are diagnosed and treated late.

Passive versus active case-finding

A key premise of tuberculosis control has always been that active case-finding is unnecessary, because symptoms are so severe that cases will seek early treatment soon after they develop (Newell, 2002). Active case-finding has also been associated with extremely high cost and disappointing results (Toman, 1979). The current problem of low case-detection and delays, however, has revived debates over whether it is better to identify tuberculosis cases among symptomatic people attending general health services as opposed to an approach of more active case-finding. Mathematical modelling and cost-effectiveness calculations have recently been used to argue in favour of (non-targeted) active case-finding in countries where tuberculosis programmes have demonstrated their ability to achieve good cure rates (Murray and Salomon, 1998a, 1998b). In high tuberculosis prevalence countries, the cost-effectiveness (less than US$100 per DALY averted) of repeated mass screening are thought to make these interventions extremely attractive to decision makers. Criticisms about the feasibility of the intervention are dismissed on the basis that the cost-effectiveness merits the necessary high investments. However, the modelling exercise failed to provide a sensitivity analysis on key assumptions and uncertainties (Anderson, 1998). Also, the opportunity costs of the 'high investments' on the general health services were not even considered. Therefore the conclusion of the Murray and Salomon study seems too narrow to be credible in the policy arena.

In some high risk groups, active case-detection may be highly efficient, such as prisoners and HIV-infected persons. The ProTest initiative aims to promote HIV voluntary testing as a key to a more coherent response to HIV and tuberculosis (Godfrey-Faussett *et al.*, 2002). This could contribute to the identification of a significant number of new cases where HIV-associated tuberculosis is important. Voluntary counselling and testing (VCT) could be the opportunity not only for early case-detection of tuberculosis, but also for identifying candidates for preventive therapy. If proven successful, this approach should be extended. This will require VCT to be established in general health services in order to ensure broad access and coverage, and linking it with treatment and patient support as discussed in a later section of this paper.

We are thus yet to see compelling evidence to support active case-finding of tuberculosis in general population. Apart from concerns regarding the cost and sustainability, its effectiveness in attaining not only good detection but also high cure rate is clearly questionable.

Utilization and delays

The case for tuberculosis control through general health services is clear, but one should not ignore the fact that tuberculosis patients seemingly underutilize these services. Why are those cases who come to general health services detected so late in the course of the disease? A body of literature documents how qualities and characteristics of individuals and health service delivery influence delay and utilization (Auer *et al.*, 2000; Wandwalo and Morkve, 2000; Lienhardt *et al.*, 2001; Lonnroth *et al.*, 2001; Needham *et al.*, 2001; Pronyk *et al.*, 2001; Demissie *et al.*, 2002; Rajeswari *et al.*, 2002). There are conflicting patterns across studies indicating which determinants have the most influence. However, one should look beyond qualities and characteristics of individuals as predictors of delay, as these are less amenable to change. Major opportunities to increase utilization and reduce delay arise in examining the way in which care and support is delivered (Lonnroth *et al.*, 2001). The accessibility and quality of general health services are indeed the key problem. In many parts of the developing world, especially where tuberculosis incidence is high, health services are in an appalling state. Problems include insufficient health facilities, poor physical state of facilities, lack of sufficient staff and drugs, and absence of continuing education for personnel. In rural settings, bad roads and incomplete coverage by telephone systems make transportation and communication difficult. Not surprisingly, studies of the quality of services in such settings are almost always pessimistic (Smits *et al.*, 2002).

Clearly, if we expect general health services to detect tuberculosis cases early and successfully, these services first need to be accessible: financially, geographically, culturally and in terms of opening hours. Patients in some rural areas have to travel nearly 40 km, or (much) more, to reach a health centre with microscopy facilities (Wandwalo and Morkve, 2000; Demissie *et al.*, 2002; Rajeswari *et al.*, 2002;). Most government health centres are open only during working hours and lack human, medical and financial resources. Recent data also show that in many areas the financial accessibility to tuberculosis diagnosis and treatment is still a huge problem. In Tanzania, total direct and indirect costs of tuberculosis at household level for a complete treatment period were estimated to be in the range of US$186 to US$1457 (Wyss *et al*., 2001). In Thailand, average out-of-pocket expenditures for the disease can reach more than 15% of annual household income; up to 11.8% of tuberculosis patient households have taken out bank loans and 15.9% have sold part of their property (Kamolratanakul *et al.*, 1999). A study in urban Zambia found that in seeking diagnosis, patients incurred mean total costs equivalent to 127% of their mean monthly income, while 38% blamed money shortages for their delay in seeking diagnosis (Needham *et al.*, 1998). Suggested interventions to overcome these financial barriers include reducing the number of health encounters, decreasing travel distances and strict enforcement of a free tuberculosis care policy (Needham *et al.*, 1998; Kamolratanakul *et al.*, 1999).

It has also been documented that when patients use clinics or general practitioners as their point of first contact, only a small proportion of them were appropriately managed at their initial visit (Pronyk *et al.*, 2001). This low diagnostic capacity is partly due to shortage of competent and motivated health workers, reflecting

the generally poor health service quality. This indicates the need for the availability of resources and regular supervision essential for proper quality assurance (Demissie *et al.*, 2002). Ineffectiveness of general health services in case-detection also suggests the need to review their operational diagnostic procedures. The necessity for a more effective diagnosis guideline in primary health care services has been recently addressed through the WHO practical approach to lung health strategy (PAL). The proposed approach standardises management of patients presenting with respiratory symptoms, combining tuberculosis case-detection with management of other respiratory disease (WHO, 2002d).

An unknown but probably substantial and increasing proportion of tuberculosis patients attend the private-for-profit health sector. Particularly in Asia and Latin America, the private health sector is growing rapidly while the regulatory system remains weak or absent (Uplekar *et al.*, 2001). Unfortunately the management of patients in the private-for-profit health sector is often very poor and constitutes a weak link in the referral chain, thus contributing to significant delays in many settings. More than half of tuberculosis patients who contacted a private physician in Vietnam were neither correctly diagnosed nor referred for further investigation (Lonnroth *et al.*, 2001). In India, private practitioners usually resort to symptom-based treatment, followed by x-ray examination, and very rarely request a sputum examination (Rajeswari *et al.*, 2002). The delay associated with private health sector consultation may be a result of both numerous unfruitful consultations and depletion of patients' limited financial resources (Lienhardt *et al.*, 2001). The need for improving the accessibility and quality of general health services to ensure early case-detection of tuberculosis is thus obvious.

Treatment and cure

High numbers of failed treatments lead to an increase in tuberculosis prevalence. The majority of patients who receive poor treatment survive, but remain sputum-positive and chronic transmitters of tuberculosis (Newell, 2002). Thus, once cases have been detected and diagnosed, they need to be fully treated and cured. Indeed priority should be given to efforts to guarantee proper case holding over efforts to improve case-detection (Dye *et al*., 1998). This requires both the availability of effective drugs and the adequate adherence of patients to treatment.

Poor adherence to lengthy tuberculosis treatment has always been a major issue in control of the disease. The strategy advocated by WHO to promote adherence, DOT, has sparked debates between advocates and adversaries. Taking into account recent studies (Zwarenstein *et al.*, 1998; Volmink *et al.*, 2000; Walley *et al*., 2001; Pungrassami *et al.*, 2002) we cannot avoid concluding that DOT by itself is not a panacea but may be a useful part of case management. Thus, one can argue that tuberculosis control programmes should not focus solely on DOT, or modifications of DOT, without strengthening other strategies of good patient management (Pungrassami *et al.*, 2002).

The complexity of treatment and cure has also been amplified by the HIV/AIDS epidemic and the increasing presence of private-for-profit practitioners in the developing world. Taking into account these challenges, can treatment and cure

of tuberculosis be achieved in the context of poor general health services, given a reasonable input of other resources? This calls for a few comments.

First, outcomes of treatment, in particular death rates, are related to early case-detection. The later the detection, the poorer the prognosis. The consequences of delayed case-detection might be even worse for HIV-related tuberculosis, by accelerating the decline in immunocompetence (Harries *et al.* 2001a). There are striking differences between death rates among tuberculosis control programmes. Among the 22 high burden countries, death rates for new smear-positive cases range from 1.1% in China to 11% in Mozambique (WHO, 2002c). In the city of Kinshasa, Democratic Republic of Congo (DRC), data from 1990 indicate that tuberculosis death rates were 1.98% among HIV-negative patients and 20.6% for HIV-positive patients (Perriens *et al.*, 1991). More recent data from the DRC Ministry of Health suggest that the death rate for more than 11 000 smear-positive tuberculosis patients who started treatment in 1999 was 'only' 3%, with a prevalence of HIV infection among these cases estimated between 30% and 50% (Ministère de la Santé, 2000). These were patients managed under control programmes integrated in a well functioning network of mainly private non-profit health services (non-government and religious organizations). Such a fatality figure compares rather well with a mean death rate of 4.1% for the 22 high burden countries and death rates from some settings with almost no contribution from HIV, for instance 4.6% in Bangladesh and 4.4% in Pakistan (WHO, 2002c).

Second, the care needs of a tuberculosis patient are not limited to treatment. Patients who present themselves for care do not come sorted into clear-cut diagnostic categories. They have a range of symptoms. The precise nature of the condition is not always clear and overlap is common. In Africa, it is estimated that 32% of tuberculosis cases are HIV-positive (Dye *et al.*, 1999). Especially where prevalence of HIV-associated tuberculosis is high, treatment of patients with tuberculosis can simply not be limited to treatment of tuberculosis and HIV care cannot be delivered without strong health systems (WHO, 2002e; Buve *et al.*, 2003).

A full range of HIV and tuberculosis prevention and care interventions should be available from general health services (WHO, 2002e). Ultimately, a comprehensive general health system is needed to deliver an essential package of interventions to respond to the global health care needs of tuberculosis patients.

Third, in situations where private practitioners treat more than 15% of identified cases, it will not be possible for public health services alone to attain acceptable cure rates (Newell, 2002). The corresponding figure often quoted for Asia is 60% (Uplekar *et al.*, 2001) and it is widely agreed that treatment in these private-for-profit health services is usually of very poor quality with low cure rates (Newell, 2002). Thus, there is a need for pragmatism. Patients attend the private sector and its role should be optimized. However, one cannot help wondering about the feasibility, cost, and benefits of such interventions on a large scale. Research in the field is in its infancy and only few success stories under favourable conditions of small scale pilot settings have been reported (Uplekar *et al.*, 2001). Tuberculosis is a disease of the poor, and makes them even poorer. For the time being, reliance of control programmes on the for-profit health sector should be treated with caution.

From this analysis of early case-detection and treatment, we conclude that even in the light of the tuberculosis/HIV dual epidemics and rapid growth of an unregulated private-for-profit health sector, an accessible and effective public health care system is a necessary (though not sufficient) condition to achieve targets set for tuberculosis control.

RESOURCES FOR TUBERCULOSIS CONTROL

The average annual per capita expenditure on health is US$26 in countries with under US$1200 per capita GNP including most of in Sub-Saharan Africa, (Jha *et al.*, 2002). In the 48 poorest countries, it is only US$13. Moreover, there has been a substantial reduction in public spending per capita across low-income countries. This has been accompanied by a significant shift towards private health expenditures, which appears increasingly to be substituting rather than supplementing public expenditures (Jowett, 1999). Poor households spend more on health care as a proportion of income than do richer groups (Fabricant *et al.*, 1999). The Commission on Macroeconomics and Health argued that, to improve the health of the world's poor a large and sustained increase over current levels of health care expenditure is a must (Jha *et al.*, 2002). Such funding to be shared by rich and poor countries, would need to continue for several decades and must include payment for health workers' salaries and system support. Achieving high coverage of effective interventions requires a well-functioning health system, as well as overcoming a set of financial constraints. Recent evidence has reaffirmed the devastating effect of chronic under-investment in health systems in poor countries over decades (Brugha *et al.*, 2002). Staff and drugs shortages, poorly motivated staff, and the lack of resources for conducting routine supervisory visits will inevitably be obstacles to strengthening routine diagnostic and curative services for tuberculosis.

Lessons from developed and developing countries show that financial resources are a key ingredient in controlling tuberculosis (Harries *et al.*, 2001b; Lambert and van der Stuyft, 2002; Tiruviluamala and Reichman, 2002) . Existing financing for tuberculosis control, prior to the Global Fund to Fight AIDS, Tuberculosis and Malaria has been predominantly from governments of high burden countries with relatively minor contributions (4%) from grant funding and a resource gap of up to 27% of estimated total needs (Floyd *et al.*, 2002). In absolute terms, the largest identified funding gaps are in China (US$45 million per year), Indonesia (US$10 million per year) and DRC (US$7 million per year). In relative terms, identified gaps are highest (25% to 100% of total needs) in Afghanistan, Myanmar, DRC, China, Indonesia and Uganda.

When the Global Fund to Fight AIDS, Tuberculosis and Malaria made its first round of payments to disburse nearly US$2 billion, substantial additional funding amounting to US$270 million became available, particularly for tuberculosis control in China, Indonesia and Ethiopia. But substantial gaps remain, amounting up to US$827 million, which encompass mainly resources for strengthening general health services (Floyd K. 2002. *Financing of TB Control in the 22 HBCs*. Presentation at the 33rd IUATLD World Conference on Lung Health 6–10 October 2002,

Palais des Congrès, Montreal, Canada. Unpublished). This resources gap is the most obvious barrier for developing countries to reach tuberculosis control targets.

CONCLUSION

While tuberculosis is a priority disease and improving cure rates a matter of considerable urgency in the most high prevalence countries, the current dramatic increase in political, economic and financial interests in its control should be seen as an opportunity for investing in both immediate programme needs and in the network of general health services that are necessary to make the control programme sustainable, effective and efficient.

Lessons learnt from past tuberculosis control efforts point to one major conclusion: successful tuberculosis control depends on accessible and effective public health systems. The Global Fund to Fight AIDS, Tuberculosis and Malaria, the general donor community and recipient governments are positioned to make substantial investment in controlling tuberculosis and alleviating the suffering of millions. We look forward to their significant investment in strengthening general health care systems to achieve tuberculosis control targets.

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