DOC 2.05-16.1

INTERNATIONAL STANDARDS FOR TUBERCULOSIS CARE

Seventh Draft

7 September, 2005

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Introduction

Purpose: The purpose of the *International Standards for Tuberculosis Care* is to describe a widely accepted level of care, defined in terms of specific actions, that all practitioners, public and private, should follow in dealing with patients who have, or are suspected of having, tuberculosis. The Standards are intended to facilitate the engagement of all care providers in delivering high quality care for patients of all ages, including those with smear-positive, smear-negative, and extra-pulmonary tuberculosis, tuberculosis caused by drug-resistant organisms, and tuberculosis combined with HIV infection. A high standard of care is essential to restore the health of individuals with tuberculosis, to prevent the disease in their families and others with whom they come into contact, and to protect the health of communities.[1] Substandard care will result in poor patient outcomes, continued infectiousness with transmission of the infection to family and other community members, and, perhaps, generation and propagation of drug resistance. Care that does not reach the defined level would be considered substandard and not acceptable.

A standard differs from a guideline in that it does not provide specific guidance on disease management but, rather, presents a principle or set of principles and actions based on the principles that can be applied in nearly all situations. These principles and actions provide a platform on which care can be founded. In addition, a standard can be used as an indicator of the overall adequacy of disease management against which individual or collective practices can be measured, whereas, guidelines are intended to assist providers in making informed decisions about appropriate health interventions.[2]

The basic principles of care for persons with, or suspected of having, tuberculosis are the same worldwide: a diagnosis should be established promptly and accurately; standardized treatment regimens of proven efficacy should be used together with appropriate treatment support and supervision; the response to treatment should be monitored; and the essential public health responsibilities must be carried out. Prompt, accurate diagnosis and effective treatment are not only essential for good patient care, they are the key elements in the public health response to tuberculosis and are the cornerstone of tuberculosis control. Thus, all providers who undertake evaluation and treatment of patients with tuberculosis must recognize that, not only are they delivering care to an individual, they are assuming an important public health function that also entails a high level of responsibility to the community, as well as to the individual patient. Adherence to these Standards will enable these responsibilities to be fulfilled.

Audience: The Standards are addressed to all health care providers, private and public, who care for persons with proven tuberculosis or with symptoms and signs suggestive of tuberculosis. In general, providers in national tuberculosis programs that follow existing international guidelines are in compliance with the Standards. However, in many instances (as described under Rationale) non-program clinicians (both private and other state sector) do not have the guidance and systematic evaluation of outcomes provided by control programs and, commonly, would not be in compliance with the Standards. Thus, although program providers are not exempt from adherence to the Standards, the emphasis is on the non-program providers as the target audience.

In addition to health care providers, both patients and communities are part of the intended audience. Patients are increasingly aware of and expect that their care will measure up to a high standard. Having generally agreed upon standards will empower patients to evaluate the quality of care they are being provided. Good care for individuals with tuberculosis is also in the best interest of the community. Community contributions to tuberculosis care and control are increasingly important in raising public awareness of the disease, providing treatment support, reducing the stigma associated with having tuberculosis, and demanding that health care providers in the community adhere to a high standard of tuberculosis care.[3] The community should expect that standards of care will be provided and that, within the community, care for tuberculosis will be up to the accepted standard.

Scope: Three categories of activities are addressed by the Standards: diagnosis, treatment, and public health responsibilities of all providers. Specific prevention approaches, laboratory performance, and personnel standards are not addressed. The Standards are intended to be consistent with, and complementary to, local and national tuberculosis control policies that are consistent with World Health Organization recommendations: they are not intended to replace local guidelines and were written to accommodate local differences in practice. They focus on the contribution that good clinical care of individual patients with or suspected of having tuberculosis makes to population-based tuberculosis control. In reducing the suffering and economic losses from tuberculosis, a balanced approach emphasizing both individual patient care and public health principles of disease control is essential.

To meet the requirements of the Standards, approaches and strategies, determined by local circumstances and practices and developed in collaboration with local and national public health authorities, will be necessary. Moreover, there are many situations in which the level of care can, and should, go beyond what is specified in these standards. Local conditions, practices, and resources also will determine the degree to which this is the case.

The Standards do not address the extremely important concern with overall access to care. Obviously, if there is no care available, the quality of care is not relevant. Additionally, there are many factors that impede access even when care is available: poverty, gender, and geography are prominent among the factors that interfere with persons availing themselves to care. Also, however, if the residents of a given area perceive that the quality of care provided by the local facility(ies) is substandard, they will not seek care there. This perception of quality is a component of access that adherence to these standards will address.[1]

Also not addressed by the Standards is the necessity of having a sound, effective government tuberculosis control program. The requirements of such programs are described in a number of international recommendations from the World Health Organization (WHO) and the International Union Against Tuberculosis and Lung Disease (IUATLD). Having an effective control program at the national or local level with linkages to non-program providers enables bidirectional communication of information including case notification, consultation, patient referral, and in some instances, provision of drugs or services such as treatment supervision/support for private patients. In addition the program may be the only provider of laboratory services that enables the diagnostic standards to me met.

Rationale: Although in the past decade there has been substantial progress in the development and implementation of the strategies necessary for effective global tuberculosis control, the disease remains an enormous and growing global health problem.[4-7] One-third of the world's population is infected with *Mycobacterium tuberculosis*, mostly in developing countries where 95% of cases occur.[5] In 2003, there were an estimated 8.8 million new cases of tuberculosis, of which 3.9 million were sputum smear-positive and, thus, highly infectious.[6] Alarmingly, the number of tuberculosis cases that occur in the world each year is still growing, although the rate of increase is slowing.[6] In the African region of the World Health Organization (WHO) the tuberculosis case rate continues to increase, both because of the epidemic of HIV infection in sub Saharan countries and the poor or absent primary care services throughout the region.[4,6] In Eastern Europe after a decade of increases, case rates have only recently reached a plateau, the increases being attributed to the collapse of the public health infrastructure, increased poverty, and other socio-economic factors complicated further by the high prevalence of drug resistant tuberculosis.[4,7] In many other countries tuberculosis case rates are either stagnant or decreasing more slowly than should be expected because of incomplete application of effective care and control measures. At least in part, the failure to bring about a more rapid reduction in tuberculosis incidence relates to a failure to fully engage non-tuberculosis control program providers in the provision of high quality care that would contribute to tuberculosis control.

It is now widely recognized that many providers are involved in the diagnosis and treatment of tuberculosis.[8-11] Traditional healers, general practitioners, specialist physicians, nurses, clinical officers, academic physicians, unqualified practitioners, physicians in private practice, practitioners of alternative medicine, and community organizations, among others, all play roles in tuberculosis care and, therefore, in tuberculosis control. In addition, other public providers such as those working in prisons, army hospitals, or in general public hospitals and facilities regularly evaluate persons suspected of having tuberculosis and treat patients who have the disease.

Little is known about the quality of care delivered by non-program providers, but evidence from studies conducted in many different parts of the world show great variability in the quality of tuberculosis care and poor quality care continues to plague global tuberculosis control efforts.[1] Findings of a recent global situation assessment by the WHO suggested that delays in diagnosis were common.[10] The delay was more often in receiving a diagnosis rather than in seeking care, although both elements are important.[12] This survey and other studies also show that clinicians, in particular those who work in the private health care sector, often deviate from standard, internationally recommended, tuberculosis management practices.[9,10] These deviations include under-use of sputum microscopy for diagnosis, generally associated with over-reliance on radiography, and use of inappropriate drug regimens with incorrect combinations of drugs and mistakes in both drug dosage and duration of treatment, and failure to supervise and assure adherence to treatment.[9,10,13-19] Anecdotal evidence also suggests that there is over-reliance on poorly validated or inappropriate diagnostic tests such as serologic assays, often in preference to conventional bacteriological evaluations.

Together, these findings highlight flaws in the health care system that lead to substandard tuberculosis care for populations that, often, are most vulnerable to the disease and are least able to bear the consequences of such systemic failures. Any person anywhere in the world who is unable to access quality health care should be considered vulnerable to tuberculosis and its consequences.[1] Likewise, any community with no or inadequate access to appropriate diagnostic and treatment services for tuberculosis is a vulnerable community.[1] The initiative aimed at developing *International Standards for Tuberculosis Care* i is an attempt to reduce vulnerability of individuals and communities to tuberculosis by promoting high quality care for persons with, or suspected of having, tuberculosis.

Companion and Reference Documents: The standards in this document should be seen as being complimentary to two other important companion documents. The first, *Patients Charter of the Tuberculosis Community* that specifies the rights and responsibilities of patients, is being developed in tandem with this document. Second, the International Council of Nurses has developed a set of standards, *TB/MDR-TB Nursing Standards* (www.icn.ch/tb/standards.htm) that define in detail the critical roles and responsibilities of nurses in the care and control of tuberculosis.

As a single-source reference for many of the practices for tuberculosis care, we would refer the reader to "*Toman's Tuberculosis: Case Detection, Treatment, and Monitoring*. (second edition)"[20]

Standards for Diagnosis

Standard 1. **All persons with otherwise unexplained productive cough lasting two-three weeks or more should be evaluated for tuberculosis.**

Standard 2. **For all patients (adults, adolescents, and children who are capable of producing sputum) suspected of having pulmonary tuberculosis, at least two and, preferably, three sputum specimens should be obtained for microscopic examination.**

Standard 3. **For all patients (adults, adolescents, and children) suspected of having extra-pulmonary tuberculosis, appropriate specimens from the suspected sites of involvement should be obtained for microscopy and, where facilities and resources are available, for culture and histopathological examination.**

Standard 4. **All persons with chest radiographic findings suggestive of tuberculosis should have sputum specimens submitted for microbiological examination.**

Standard 5. **The diagnosis of sputum smear-negative pulmonary tuberculosis should be based on the following criteria: at least three negative sputum smears (including at least one early morning specimen); chest radiography findings consistent with tuberculosis; and lack of response to a trial of broad-spectrum antimicrobial agents (NOTE: Because the fluoroquinolones are active against *Mycobacterium tuberculosis* and, thus, may cause transient improvement, they should be avoided.). For such patients if facilities for culture are available, sputum cultures should be obtained. In persons with known or suspected HIV infection the diagnostic evaluation should be expedited.**

Standard 6. **The diagnosis of intrathoracic (i.e. pulmonary, pleural, and lymph node [mediastinal and/or hilar]) tuberculosis in symptomatic children with negative sputum smears is based on the finding of chest radiographic abnormalities consistent with tuberculosis, and either a history of exposure to an infectious case or evidence of tuberculosis infection (positive tuberculin skin test or interferon gamma release assay). For such patients, if facilities for culture are available, sputum specimens should be obtained (by expectoration, gastric washings, or induced sputum) for culture.**

Standards for Treatment

Standard 7. **Any care provider treating a patient for tuberculosis is assuming a public health function that includes not only prescribing an appropriate regimen but also ensuring adherence to the regimen until treatment is completed.**

Standard 8. **All patients (including those with HIV infection) who have not been treated previously should receive an internationally accepted first line treatment regimen using drugs of known bioavailability. The initial phase should consist of two months of isoniazid, rifampicin, pyrazinamide and ethambutol.[*] The preferred continuation phase consists of isoniazid and rifampicin given for 4 months. Isoniazid and ethambutol given for 6 months is an alternative continuation phase regimen but is associated with a higher rate of failure and relapse, especially in patients with HIV infection.**

The doses of antituberculosis drugs used should conform to international recommendations.

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[*] Ethambutol may be omitted in the initial phase of treatment for adults and children who have negative sputum smears, do not have extensive pulmonary tuberculosis or severe forms of extra-pulmonary disease and who are known to be HIV negative.

Standard 9. **To foster and assess adherence, a patient-centered, gender-sensitive, age-specific approach to treatment support, based on the patient's needs and mutual respect between the patient and the provider should be developed for all patients. The patient - centered approach should draw on the full range of recommend interventions and available support services and should include patient counseling and education. A central element of the patient-centered strategy is direct observation of medication ingestion (directly observed therapy-DOT) by a treatment supporter who is acceptable and accountable to the patient and to the health system.**

Standard 10. **All patients should be monitored for response to therapy, best judged in patients with pulmonary tuberculosis by follow-up sputum microscopy (two specimens) at least at the time of completion of the initial phase of treatment (two – three months), at five months, and at the end of treatment. Patients who have positive smears during the 5th month of treatment should be considered as treatment failures and have therapy modified appropriately (see standards 14 and 15). In patients with extra-pulmonary tuberculosis and in children, the response to treatment is best assessed clinically. Follow-up radiographic examinations are usually unnecessary and may be misleading.**

Standard 11. **A written record of all medications given, bacteriologic response, and adverse reactions should be maintained for all patients.**

Standard 12. **In areas with a high prevalence rate of HIV in the general population where tuberculosis and HIV are likely to co-exist, HIV counseling and testing is indicated for all tuberculosis patients as part of their routine management. In areas with lower prevalence rates of HIV, HIV counseling and testing is indicated for tuberculosis patients with symptoms and/or signs of HIV-related conditions, and in tuberculosis patients having a history suggestive of high risk of HIV exposure.**

Standard 13. **Patients with tuberculosis and HIV infection who are not receiving antiretroviral therapy should receive the same tuberculosis treatment regimen as those who do not have HIV infection. All patients with tuberculosis and HIV infection should be evaluated to determine when they should receive antiretroviral therapy. Appropriate arrangements for access to antiretroviral drugs should be made for patients who meet indications for treatment. Given the complexity of co-administration of antituberculosis treatment and antiretroviral therapy, consultation with a physician who is expert in this area is recommended before initiation of concurrent treatment for tuberculosis and HIV infection, regardless of which disease appeared first. However, initiation of treatment for tuberculosis should not be delayed**.

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Standard 14. **An assessment of the likelihood of drug resistance, based on history of prior treatment, exposure to a possible source case having drug resistant organisms, and the community prevalence of drug resistance, should be obtained for all patients. Patients who fail treatment and chronic cases should always be assessed for possible drug resistance. For patients in whom drug resistance is considered to be likely, culture and drug susceptibility testing for isoniazid, rifampin, and ethambutol should be performed promptly.**

Standard 15. **Patients with MDR tuberculosis should be treated with specialized regimens containing second-line anti-tuberculosis drugs. At least four drugs to which the organisms are known or presumed to be susceptible should be used and treatment should be given for at least 18 months. Patient centered measures are required to ensure adherence. Consultation with a provider experienced in treatment of patients with MDR tuberculosis should be obtained.**

Standards for Public Health Responsibilities

Standard 16. **All providers of care for patients with tuberculosis should ensure that close contacts (especially children under 5 years of age and persons with HIV infection) to patients with infectious tuberculosis are evaluated and managed in line with international recommendations. Children under 5 years of age and persons with HIV infection who have been in contact with an infectious case should be evaluated for both latent infection with *M. tuberculosis* and for active tuberculosis.**

Standard 17. **All providers must report both new and retreatment tuberculosis cases and their treatment outcomes to local public health authorities, in conformance with applicable legal requirements and policies.**

Research and Review Needs

As part of the process of developing the *International Standards for Tuberculosis Care*, several key areas that require additional research and further evaluation were identified (Table 6). Systematic reviews and research studies (some of which are underway currently) in these areas are critical to generate evidence to support rational and evidence-based care and control of tuberculosis. Research in these operational and clinical areas serves to complement the ongoing efforts that are focused on developing new tools for tuberculosis control - new diagnostics,[114] drugs,[115] and vaccines.[116]

Table 6. Priority areas for research and evaluation

Focus of research	Specific questions
Diagnosis and case finding	1. What is the sensitivity and specificity of various thresholds for chronic cough (e.g. 2 versus 3 weeks) as screening tests for tuberculosis? How do local conditions such as the prevalence of tuberculosis, HIV infection, asthma and COPD influence the threshold? 2. What is the optimal diagnostic algorithm for establishing a diagnosis in smear negative patients? 3. What is the best strategy for the diagnosis of smear-negative tuberculosis in persons with HIV infection? 4. What are the operational implications of HIV testing for persons suspected of having tuberculosis? 5. What is the role of therapeutic antibiotic trials in the diagnosis of smear-negative tuberculosis? 6. What is the impact of widespread use of fluoroquinolones on the utility of therapeutic antibiotic trials in the management of smear-negative

	tuberculosis? 7. What is the optimal diagnostic algorithm for children with suspected tuberculosis? 8. What is the value and role of sputum concentration in improving the accuracy and yield of smear microscopy? 9. What is the optimal cut-point for declaring a smear examination positive? 10. What is the role, feasibility, and applicability of fluorescent microscopy in routine field conditions? 11. Is there a role for intensified case finding in high HIV endemic settings? 12. What is the contribution of routine use of culture in tuberculosis care and control? 13. Is there a role for rapid culture methods in tuberculosis control programs? 14. What factors lead to delays in establishing a diagnosis of tuberculosis? 15. What is the impact of engaging ex- (or current) TB patients and/or patient organizations in active case finding? 16. What is the relevance of second line drug susceptibility test results in determining individualized retreatment regimens?

Treatment, monitoring, and support	1. What interventions are effective in improving patient (adults and children) adherence to anti-tuberculosis therapy? 2. What is the efficacy of direct observation of treatment (DOT) vs. other measures to improve adherence to treatment? 3. Who are the most effective persons to observe treatment (treatment supporters)? 4. What is the optimal duration of anti-tuberculosis therapy for patients who are HIV-positive?

	5. What interventions help in reducing mortality among tuberculosis patients co-infected with HIV? 6. What is the effectiveness of standardized vs. individualized treatment regimens in the management of mono-resistant and MDR tuberculosis? 7. What are the optimal drug doses and duration of treatment for children? 8. What is the impact of engaging ex-(or current) TB patients and/or patient organizations in improving adherence?
Public health and operational research	1. What is the effect of the DOTS strategy on tuberculosis transmission in populations with high rates of MDR tuberculosis? 2. What is the impact of HIV infection on the effectiveness of DOTS programs? 3. What interventions or measures are helpful in improving tuberculosis management practices in private practitioners? 4. What is the impact of treatment of latent tuberculosis infection on tuberculosis burden in high HIV prevalence settings? 5. What is the impact of engaging ex-(or current) patients and/or patient organizations in improving tuberculosis control programs in regions with insufficient human resources?