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Tuberculosis (TB)Progress toward Millennium Development Goals (MDGS) and DOTS in Who Eastern Mediterranean Region (EMR)

Khoaja M. Khaled

TUBERCULOSIS (TB) PROGRESS TOWARD MILLENNIUM DEVELOPMENT GOALS (MDGS) AND DOTS IN WHO EASTERN MEDITERRANEAN REGION (EMR)

By

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M.D., KABUL MEDICAL INSTITUTE

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TABLE OF CONTENTS

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LIST OF ACRONYMS

AFB	Acid-fast bacillus
AIDS	Acquired Immune Deficiency Syndrome
BCG	Bacillus Calmette-Guerin
DALYS	Disability Adjusted Life Years
DOT	Directly observed therapy
DOTS	Directly Observed Therapy, Short-course
DST	Drug susceptibility testing
EMR	Eastern Mediterranean Region
FDCs	Fixed-dose drug combinations
GLC	Green Light Committee
HIV	Human Immunodeficiency Virus
IRB	Institutional Review Board
LTBI	Latent TB infection
MDGs	Millennium Development Goals
MDR-TB	Multidrug-resistant Tuberculosis
NTPs	National TB control programs
PAL	Practical approach to lung health
PPD	Purified protein derivatives
QFT-G	QuantiFERON-TB Gold test
TST	Tuberculin skin tests
WHA	World Health Assembly
XDR-TB	Extensive drug-resistant Tuberculosis

LIST OF TABLES

LIST OF FIGURES

LIST OF APPENDICES

ABSTRACT

Khaled Aryanfar

Tuberculosis (TB) progress toward Millennium Development Goals (MDGs) and Directly Observed Therapy, Short-course (DOTS) in WHO Eastern Mediterranean Region (EMR)

(Under direction of Frances McCarty, PhD)

Background: Tuberculosis (TB) is an airborne infection. Though effective anti-TB drugs have been available for more than 50 years, over one-third of the world's population is exposed to TB bacterium; deaths due to TB infection occur at high frequency every day worldwide. Today, drug-resistant TB, TB/HIV co-morbidity and poor health infrastructure are major challenges worldwide, particularly in less developed countries.

Objectives: The primary objective of the study was to assess the progress of TB control programs in twenty-two Eastern Mediterranean Region countries toward Millennium Development Goals (MDGs) including implementation of the Directly Observed Treatment, Short-course (DOTS). Also, the study was designed to explore TB/HIV co-morbidity and to assess some factors potentially associated with TB progress in the region.

Methods: Secondary data, obtained from the World Health Organization, World Bank, and World Resource Institute on line databases were used. Paired samples t-test and bivariate correlation were conducted.

Results: Between 1990 and 2005, TB incidence had decreased 9%, TB prevalence had decreased 37% (statistically significant) and TB mortality had decreased 28%; nevertheless, MDG targets were not met. TB/HIV co-morbidity increased in the region especially in HIV-high burden countries. Though DOTS population coverage was increased to 94% in 2005, DOTS new smear-positive case detection rate was 61% (target 70%) and DOTS treatment success was 80% (target 85%). Thus, the 1991 Stop TB Partnership targets were not met.

Conclusions: In spite of the progress of TB control programs in the EMR, MDGs and DOTs targets of 2005 were not obtained. Further efforts such as allocation of more resources, strengthening of TB surveillance systems, extension of drug-resistant TB and TB/HIV collaborative programs, and TB research are required to achieve MDGs by 2015 and to fully implement the new Stop TB Strategy in the region.

INDEX WORDS: TB burden, TB/HIV co-morbidity, and Eastern Mediterranean Region

CHAPTER I
INTRODUCTION

Tuberculosis (TB) is an airborne infectious disease that is preventable and curable. Though effective drugs to treat and cure the disease have been available for more than 50 years, over one-third of world's population has been exposed to TB bacterium, and new infections occur at a rate of one person per second, indeed, someone with TB is dying every 15 seconds in the world. Left untreated, a person with active TB will infect an average of 10 to 15 other people every year. Not everyone infected develops the full blown disease; asymptomatic, latent TB infection is most common. However, one in ten latent infections will progress to active TB, which, if left untreated, kills more than half of its victims. In 2005, mortality and morbidity statistics included 14.6 million chronic TB cases, 8.9 million new cases and 1.6 million deaths, mostly in developing countries. If TB disease is detected early and fully treated, people with the disease quickly become non-infectious and eventually cured. Multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB), HIV-associated TB, and poor health infrastructure are major challenges worldwide (1-6).

The goals of TB control programs are to reduce mortality, morbidity and transmission of the disease, while preventing drug resistance, until it no longer poses a threat to public health. TB control programs also aim to reduce human suffering and the social and economic burden families and communities have to bear as a consequence of the disease. The persistence of TB has been due chiefly to the neglect of TB control by

governments, poorly managed TB control programs, poverty, population growth and migration, and a significant rise of TB cases in HIV endemic areas. To address the situation, a global strategy called Directly Observed Therapy, Short-course (DOTS) was introduced in 1991. DOTS has been implemented in joint TB/HIV programs with cost-effective results and a treatment success rate of 72% (7-10). Furthermore, at the United Nations Millennium Summit in 2000, world leaders agreed to set of time bound and measurable goals and targets combating poverty, hunger, disease, illiteracy, environmental degradation and discrimination against women, called Millennium Development Goals (MDGs). One of them, specifically MDG 6, target 8 says, "Halting TB prevalence and death to half by 2015 and begin to reverse the incidence of TB." (11).

The Global Plan to Stop TB 2006-2015, launched in 2006, was initiated to reduce TB burden through contributions of both developing and developed countries. We can achieve MDGs if the Global Plan to Stop TB is effectively implemented. Successful implementation could tremendously decrease prevalence and death rate of TB, Multi-drug resistant TB (MDR-TB), and TB/HIV co-infection (11).

TB is an important public health problem in the Eastern Mediterranean Region (EMR). Every year the disease kills about 136,000 people and affects approximately 630,000 more. These numbers maybe fueled by political and economic instability, migration and displacement, HIV/AIDS, poverty, malnutrition, poor health infrastructure, and drug-resistant strains (12-17). The DOTS strategy was introduced in the Eastern Mediterranean region in the mid-1990s. Most countries in the region have DOTS. In 2005, the regional DOTS coverage was close to 90% and the regional average treatment

success rate was about 84%.Though TB burden (incidence, prevalence and death rates) decreased "between 1980 to 2005", there are still many challenges to address in the region. The regional case detection rate is expected to be only 45% by the end of 2005. Case detection in the two high-burden countries of the region – Pakistan and Afghanistan – is still quite low at 17% and 18%, respectively. Key components of DOTS, particularly case-finding and surveillance are of low quality. Coverage of drug resistance TB and HIV –TB co infection surveillance is low as well. In sum, much effort is needed to achieve MDGs through implementation of the Global Plan to Stop TB and DOTS (12, 13, 15, 17-20).

Study Objectives and Research Questions

The study objectives are to identify and describe the progress and barriers of TB control programs in 22 EMR countries toward MDGs and 1991 National Health Assembly (NHA) targets for DOTS. The study also explores TB prevention programs in different countries based on different variables such as political stability, population density, literacy, GDP, income, health service coverage, healthcare force, health expenditure, HIV prevalence, immunization coverage, sanitation, and nutrition. The specific questions are:

- Has the Eastern Mediterranean region made progress towards achieving MDGs and DOTS?
- How is TB/HIV co-morbidity in the region?
- Does the achievement of EMR countries differ in terms of infrastructure variables?

- What are some of the data gaps, challenges and accomplishments to be used as lessons for future interventions?

Study significance

The present research is coincident with the endpoint of the 1991 NHA targets for DOTS and the midpoint towards achieving MDGs in 2005. Therefore, this study attempted to conduct an assessment of the TB situation and TB control programs in the Eastern Mediterranean region. The findings of the study can be used by WHO, EMRO, relevant ministries of public health and the public health community. Furthermore, this study will provide some general and data-based recommendations on the feasibility of adopting or enhancing existing TB control strategies for the region.

CHAPTER II

REVIEW OF THE LITERATURE

The literature review was written based on information from about 60 articles and abstracts, and reports, figures and web pages (about 99 references) obtained via Pubmed, Global, Google, WHO, StopTB, Wekimedia, CDC, and revolutionhealth websites.

Tuberculosis (TB) is a common and deadly infectious disease caused by Mycobacterium, mainly *Mycobacterium tuberculosis (MTB)*. Tuberculosis most commonly attacks the lungs (Pulmonary TB), but can affect any parts of the body such as the central nervous system, the lymphatic system, the circulatory system, the genitourinary system, bones, joints and even the skin. Some types of Mycobacterium such as *Mycobacterium Bovis*, *Mycobacterium Africanum*, *Mycobacterium Canetti*, and *Mycobacterium Microti* can also cause tuberculosis, but these species do not usually infect healthy adults. Though effective drugs to treat and cure the disease have been available for more than 50 years, over one-third of world's population has been exposed to TB bacterium. New infections occur at a rate of one person per second, and someone with TB is dying every 15 seconds in the world. Left untreated, a person with active TB will infect an average of 10 to 15 other people every year. Not everyone infected develops the full blown disease; asymptomatic, latent TB infection is most common. However, one in ten latent infections will progress to active TB, which, if left untreated, kills more than half of its victims. In 2004, mortality and morbidity statistics included

14.6 million chronic TB cases, 8.9 million new cases and 1.6 million deaths, mostly in developing countries (1-6).

Tuberculosis has plagued human beings for millennia. Signs of tubercular damage have been found in Egyptian mummies and in bones dating back at least 5,000 years (5, 6). Today, despite advances in treatment, TB is a global pandemic, fueled by the spread of HIV/AIDS, poverty, poor health infrastructure and the emergence of drug-resistant strains of the bacterium that causes the disease. "Between 2000 to 2004", about 20% of TB cases were resistant to standard treatment, and approximately 2% resistant to second-line drugs. The World Health Organization (WHO) declared TB a global health emergency in 1993, and the Stop TB Partnership developed a Global Plan to stop TB, aiming to save 14 million lives "between 2006 and 2015"(1-6).

MTB and TB transmission

Mycobacterium tuberculosis (MTB) is an aerobic bacterium that divides every 16 to 20 hours, an extremely slow rate compared with other bacteria, which usually divide in less than an hour. For example, *E.coli*, one of the fastest-growing bacteria divides every 20 minutes. MTB is classified as a *Gram-positive* bacterium, since it has a cell wall but lacks a phospholipid outer membrane. However, if a Gram stain is performed, MTB either stains very weakly *Gram-positive* or does not retain dye due to the high lipid and mycolic acid content of its cell wall. MTB is a small rod-like bacillus that can withstand weak disinfectant and survive in a dry state for weeks. In nature, it can only grow within the cells of a host organism, but MTB can be cultured *in vitro*. Scientists can identify MTB under a regular microscope, using certain histological techniques on expectorate

samples from phlegm. MTB is classified as an *acid-fast bacillus* (AFB), since it retains certain stains after being treated with acidic solution. *Ziel-Neelsen* stain is the most common staining technique, which dyes AFBs a bright red that stands out clearly against a blue background. Other ways to visualize AFBs include an *auramine-rhodamine* stain and *fluorescent microscopy* (6).

When people with active pulmonary TB cough, sneeze, speak, kiss or spit, they expel infectious aerosol droplets 0.5 to 5 µm in diameter. For instance, a single sneeze can release up to 40,000 droplets. Since the infectious dose of TB is low, inhalation of only a single bacterium can cause a new TB infection. People with prolonged, frequent, or intense contact are at particularly high risk of becoming infected, with an estimated 22% infection rate. A person with active but untreated TB can infect 10-15 other people per year. Others at risk include people who live in TB endemic areas, residents and employees of high risk congregate settings, medically underserved and low income population, children exposed to adults in high risk categories, and immunocompromised people. In sum, transmission can only occur from people with active—not latent—TB. The probability of transmission from one person to another depends upon the number of infectious droplets expelled by a carrier, the effectiveness of ventilation, the duration of exposure, and the virulence of the M. tuberculosis strain, so the chain of transmission can therefore be broken by isolating patients with active disease and starting effective anti-TB therapy. After two weeks of such treatment, people with non-resistant active TB generally cease to be contagious. Rarely, a pregnant woman with an active TB disease may pass the bacteria to her fetus (1-6).

Pathogenesis

It is estimated about 90% of infected people with MTB have asymptomatic, latent TB infection (LTBI), and only 10% of LTBI will progress to active TB. However, if untreated, the death rate for these active TB cases is more than 50%. TB infection begins when the mycobacterium reaches the pulmonary alveoli, where they invade and replicate within alveolar macrophages. The primary site of infection in the lungs is called the Ghon focus. Bacteria are picked up by dendrite cells, which do not allow replication, although these cells can transport the bacilli to local (mediastinal) lymph nodes. MTB further spreads through the bloodstream to the more distant tissues and organs, where secondary TB lesions can develop in lung apices, peripheral lymph nodes, kidneys, brain, and bones. All parts of the body can be affected by the disease, though it rarely affects the heart, skeletal muscles, pancreas and thyroid. Tuberculosis is classified as one of the granulomatous inflammatory conditions. Macrophages, T lymphocytes, B lymphocytes and fibroblasts are among the cells that aggregate to form a granuloma, with lymphocytes surrounding the infected macrophages. The granuloma functions not only to prevent dissemination of the mycobacterium, but also provides a local environment for communication of cells of the immune system. Within the granuloma, T lymphocytes (CD4+) secrete cytokines such as interferon gamma, which activates macrophages to destroy the bacteria with which they are infected. T lymphocytes (CD8+) can also directly kill infected cells. Importantly, bacteria are not always eliminated within the granuloma, but can become dormant, resulting in a latent infection.

Another feature of the granulomas of human tuberculosis is the development of cell death, or necrosis, in the center of tubercles. To the naked eye this has the texture of soft white cheese and was termed caseous necrosis. If TB bacteria gain entry to the bloodstream from an area of damaged tissue they spread through the body and set up many foci of infection, all appearing as tiny white tubercles in the tissues. This severe form of TB disease is most common in infants and the elderly and is called miliary (disseminated) tuberculosis. Patients with disseminated TB have a fatality rate of approximately 20%, even with intensive treatment. Tissue destruction and necrosis are balanced by healing and fibrosis. Affected tissue is replaced by scarring and cavities filled with cheese-like white necrotic material. During active disease, some of these cavities are joined to the air passages, or bronchi and this material can be coughed up. The material contains living bacteria and can therefore pass on infection. Treatment with appropriate antibiotics kills bacteria and allows healing to take place. Upon cure, affected areas are eventually replaced by scar tissue (5, 6).

Clinical features

As mentioned previously, TB spreads through airborne droplets when a person with the infection coughs, talks, sings or sneezes. In general, a person needs prolonged exposure to an active TB patient before becoming infected by TB. Even then, symptoms of the disease may not develop, or may develop many years later. Doctors make a distinction between LTBI and active TB:

Latent TB Infection (LTBI): In most people who breathe in TB bacteria and become infected, the body is able to fight the bacteria to stop them from growing. The bacteria

become inactive, but they remain alive in the body and can become active later. People with LTBI have no symptoms, are not contagious, and usually have a positive skin test reaction or QuantiFERON-TB Gold test (QFT-G). They may develop active TB disease if they do not receive treatment for LTBI (1, 2, 5, and 6).

Active TB: TB bacteria become active if the immune system cannot stop them from growing. The active bacteria begin to multiply in the body and cause active TB disease. The bacteria attack the body and destroy tissue. If this occurs in the lungs, the bacteria can actually create a hole in the lung. Some people develop active TB disease soon after becoming infected, before their immune system can fight the TB bacteria. Other people may get sick later, when their immune system becomes weak for another reason. Babies, young children, people infected with HIV, people with conditions such as substance abuse, diabetes mellitus, silicosis, cancer, Leukemia, Hodgkin's disease, severe kidney disease, low body weight, etc can develop the disease rapidly. Symptoms of TB depend on where in the body the TB bacteria are growing. TB bacteria usually grow in the lungs. TB in the lungs may cause symptoms such as a cough lasting three or more weeks that may produce discolored or bloody sputum, unintended weight loss, fatigue, slight fever, night sweats, chills, loss of appetite, and pain with breathing or coughing (pleurisy) (1, 2, 5, 6).

Tuberculosis also can target almost any part of the body, including joints, bones, urinary tract, central nervous system, muscles, bone marrow and lymphatic system. When TB occurs outside the lungs, signs and symptoms vary, depending on the organs involved. For example, tuberculosis of the spine may result in back pain, and tuberculosis

that affects the kidneys might cause blood in urine. Tuberculosis can also spread through the entire body, simultaneously attacking many organ systems. Left untreated TB can cause some life- threatening complications and death (1, 2, 5, and 6).

Pulmonary TB can cause permanent lung damage when it is not diagnosed and treated early. Untreated active disease can also spread to other parts of the body where it can lead to serious or life-threatening complications. TB that infects the bone, for example, can cause severe pain, abscesses and joint destruction (5).

Meningeal TB, which occurs when TB infects the brain and central nervous system, and miliary TB, which occurs when TB bacteria spread throughout the entire body, are particularly dangerous forms of the disease. Children are especially susceptible to both meningeal TB and miliary TB (5). Recurrent TB is the most serious complication, which occurs after the initial infection and the development of drug-resistant strains of the disease (5)

Diagnosis

TB can be a difficult disease to diagnose, due mainly to the difficulty in culturing of this slow-growing organism in the laboratory. A complete medical evaluation for TB must include a medical history, a chest X-ray, and a physical examination. It may also include tuberculin skin test, serological test, microbiological smears and cultures (5, 6).

Tuberculin test: The most commonly used diagnostic tool for TB is a simple skin test. Although there are two methods, doctors consider the Mantoux test the more accurate.

The Mantoux skin test consists of an intradermal injection of exactly one tenth of a milliliter (mL) of purified protein derivatives (PPD) of MTB tuberculin in the forearm. Within 48 to 72 hours, a health care professional will check the arm for a local reaction to the injected material. Depending on the response, the test is diagnosed as positive - usually shown by a hard, raised bump at the injection site (5-15 mm). This means the person is likely to have TB infection. The Mantoux test is not perfect – it is possible to have either a false-positive or false-negative test. A false-positive test occurs when a person is infected with a mycobacterium other than the one that causes TB, or if a person has ever been vaccinated with Bacillus Calmette-Guerin (BCG), a TB vaccine which is widely used in countries with high TB infection rates. False negative results occur in conditions such as severely weakened immune system, vaccinations with live viruses such as Measles and Small pox, improper testing, overwhelming TB disease, and recent TB infection which takes eight to ten weeks for the body to react after infection (5, 6).

Recent TB tests: As a replacement for the Mantoux test, several other tests are being developed. QuantiFERON-TB Gold (QFT) is a blood test that measures the patient's immune reactivity to the TB bacteria and is useful for initial and serial testing of persons with an increased risk of latent or active tuberculosis infection. Results of this test may be available in as soon as one day. Guidelines for the use of QuantiFERON-TB Gold were released by the CDC in December 2005. However, the test is not yet widely available. Researchers in October 2006 also reported encouraging results from another test under investigation for use primarily in developing countries. It's called the microscopic-observation drug-susceptibility (MODS) assay and relies on sputum samples

to detect the presence of TB bacteria. MODS produces accurate results in as little as seven days. Additionally, the test can identify drug-resistant strains of the TB bacteria. If the results of a TB test are positive, then further tests can be conducted to help determine whether you have active TB disease (5, 6).

Chest X-ray: When a person has a positive skin test, the doctor is likely to order a chest X-ray. In some cases, this may show white spots where the immune system has walled off TB bacteria. In others, it may reveal a nodule or cavities in the lungs caused by active TB (5).

Culture tests: If a chest X-ray shows signs of TB or a urine sample indicates infection, the doctor may take a sample of stomach secretions or sputum - the mucus that comes up when the person coughs. The samples are tested for TB bacteria, and the doctor can have the results of special smears in a matter of hours. Although it takes longer, samples may also be sent to a laboratory where they are examined under a microscope as well as placed on a special medium that encourages the growth of bacteria (culture). The bacteria that appear are then tested to see if they respond to the medications commonly used to treat TB. The doctor uses the results of the culture tests to prescribe the most effective medications for the patient (5).

TB diagnosis in children: It is harder to diagnose TB in children than in adults – they are far less likely than adults to have signs and symptoms of the disease, even when they are quite sick. Children also may swallow sputum, rather than coughing it out, making it harder to take culture samples. Infants and young children may have no reactions to the

skin test. For these reasons, presence of an adult who tests positive may be used to help diagnose TB in a child (5).

TB Diagnosis in people with HIV/AIDS: Diagnosing TB in HIV-positive people can be challenging, in part because signs and symptoms of HIV/AIDS are often similar to those of TB. What is more, people with HIV may not react to a standard TB skin test, and X-rays, sputum tests and other exams may fail to show evidence of early TB infection (5).

Treatment

Until the mid-20th century, people with tuberculosis were routinely cared for in sanitariums - often for years - where the clear, cold air, abundant food and enforced rest were believed to heal the lungs and halt the wasting, characteristic of the disease. Often, the treatment not only helped cure TB, but also prevented its spread. Today, medications are the cornerstone of tuberculosis treatment. However, the therapy is lengthy. Normally, a TB patient takes antibiotics for six to 12 months to completely destroy the bacteria. The exact drugs and length of treatment depends on the age, overall health, the results of susceptibility tests, and whether the parson has latent or active TB (5).

LTBI treatment: After confirming LTBI by TB tests, chemotherapy or preventive drug therapy is recommended to destroy dormant bacteria that might become active in the future. The standard treatment is a daily dose of isoniazid (INH) for six to nine months. Long-term use can cause side effects, including the life-threatening liver disease, hepatitis. Also taking medication such as acetaminophen, aspirin, and alcohol greatly increase risk of liver damage during treatment (5, 6).

Active TB treatment: The standard "short" course treatment for active TB is isoniazid, rifampicin, pyrazinamide, and ethambutol for two months, then isoniazid and rifampicin alone for additional four months. The patient is considered cured at six months (although there is still a relapse rate of 2 to 3%). If the organism is known to be fully sensitive, then treatment is with isoniazid, rifampicin, and pyrazinamide for two months, followed by isoniazid and rifampicin for four months. Ethambutol needs to be not used[1, 2]. There are six classes of second-line drugs (SLDs) used for the treatment of TB. A drug is classified as second-line instead of first-line for one of the following reasons: it may be less effective than the first-line drugs (e.g., p-aminosalicylic acid), it may have toxic side-effects (e.g., cycloserine), or it may be unavailable in many developing countries (e.g., fluoroquinolones). The six classes of SLDs are as follows:

- aminoglycosides: e.g., amikacin (AK), kanamycin
- polypeptides: e.g., capreomycin, viomycin, enviomycin
- fluoroquinolones: e.g., ciprofloxacin (CIP), moxifloxacin (MXF)

[1] Standard abbreviations: All first-line anti-TB drug names have a standard three-letter and a single-letter abbreviation: such as streptomycin is STM or S, isoniazid is INH or H, rifampicin is RMP or R, ethambutol is EMB or E, pyrazinamide is PZA or Z. The US commonly uses abbreviations and names that are not internationally recognized: rifampicin is called rifampin and abbreviated RIF; streptomycin is commonly abbreviated SM (6).

[2] Drug regimens: A prefix denotes the number of months the treatment should be given for; a subscript denotes intermittent dosing (so 3 means three times a week) and no subscript means daily dosing. Most regimens have an initial high-intensity phase, followed by a continuation phase (also called a consolidation phase or eradication phase); the high-intensity phase is given first, then the continuation phase, the two phases divided by a slash. So, 2HREZ/4 HR3 means isoniazid, rifampicin, ethambutol, pyranzinamide daily for two months, followed by four months of isoniazid and rifampicin given three times a week (6).

- thioamides: e.g. ethionamide, prothionamide
- cycloserine (the only antibiotic in its class)
- p-aminosalicylic acid (PAS or P).

Other drugs that may be useful, but are not on the WHO list of SLDs: rifabutin; macrolides: e.g., clarithromycin (CLR); linezolid (LZD); thioacetazone (T); thioridazine; arginine; vitamin D; R207910. These drugs may be considered "third-line drugs" and are listed here either because they are seldom effective (e.g., clarithromycin) or because their efficacy has not been proven (e.g., linezolid, R207910). Rifabutin is effective, but is not included on the WHO list as in most developing countries, it is impractically expensive (5, 6).

TB is treated with combination therapy 2HREZ/4HR3 [2] (except LTBI or chemoprophylaxis), because regimens that use only single drugs result in the rapid development of resistance and treatment failure. The rationale for using multiple drugs to treat TB is based on simple probability. A patient with extensive pulmonary TB has approximately 10^{12} bacteria in his/her body, and therefore will probably be harboring approximately 10^5 EMB-resistant bacteria, 10^4 STM-resistant bacteria, 10^4 INH-resistant bacteria and 10^2 RMP-resistant bacteria. Resistance mutations appear spontaneously and independently, so the chances of the patient harboring a bacterium that is spontaneously resistant to both INH and RMP is 1 in 10^6, and the chances of the patient harboring a bacterium that is spontaneously resistant to all four drugs is 1 in 10^{11}. There are other theoretical reasons for supporting combination therapy. The different drugs in the regimen have different modes of action: INH and EMB are bacteriostatic (they stop the

bacteria replicating, but do not kill them); RMP is bactericidal (it actually kills bacteria) (6).

Completing treatment is essential because TB bacteria grow slowly; treatment for an active infection is lengthy - usually six to 12 months. After a few weeks, the patient may not be contagious and may start to feel better, but it is essential that he/she finishes the full course of therapy and takes the medications exactly as prescribed by the doctor. Stopping treatment too soon or skipping doses can create drug-resistant strains of the disease that are more dangerous and difficult to treat. Drug-resistant strains that are not treated can quickly become fatal, especially in people with impaired immune systems. In an effort to help people stick with their treatment regimen, some doctors and clinics use a program called directly observed therapy (DOT). In this approach, a nurse or other health care professional administers the medication so that the TB patient does not have to remember to take it on his/her own (5).

Treatment side effects of TB drugs are not common, but can be serious when they do occur. TB medications can be highly toxic to the liver. When taking these medications, side effects such as nausea, vomiting, loss of appetite, jaundice, fever, abdominal tenderness or soreness, and blurred vision or colorblindness will generally appear (5).

Drug-resistant TB treatment: Multidrug-resistant TB (MDR-TB) is any strain of TB that cannot be treated by the two most powerful TB drugs, isoniazid and rifampin. Extensive drug-resistant TB (XDR-TB) is a newly developed strain of TB that is resistant to the

same treatments that MDR-TB is, and additionally XDR-TB is resistant to three or more of the second-line TB drugs. Both strains develop as a result of partial or incomplete treatment - either people skip doses, or do not finish their entire course of medication, or because they are given the wrong treatment regimen. This gives bacteria time to undergo mutations that can resist treatment with first-line TB drugs. MDR-TB can be treated, but it requires at least two years of therapy with second-line medications that can be highly toxic. Even with treatment, many people with MDR-TB may not survive. And even when treatment is successful, people with this form of TB may need surgery to remove areas of persistent infection or repair lung damage. Treating these resistant forms of TB is far more costly than treating nonresistant TB, making therapy unaffordable in many parts of the world. Because these resistant infections are spreading and could potentially make all TB incurable, some experts believe that ineffective treatment is ultimately worse than no treatment at all (5).

HIV/AIDS co-infected TB patient treatment: Treating TB people who are co-infected with HIV/AIDs is a particular challenge. HIV-positive people are especially likely to develop MDR-TB and to rapidly progress from latent to active infection. What is more, the most powerful AIDS drugs - protease inhibitors - interact with rifampin and other drugs used to treat TB, reducing the effectiveness of both types of medications. To avoid interactions, people living with both HIV and TB may stop taking protease inhibitors while they complete a short course of TB therapy that includes rifampin. Otherwise, they may be treated with a TB regimen in which rifampin is replaced with another drug that is less likely to interfere with HIV/AIDS medications. In such cases, doctors carefully

monitor the response to therapy, and the duration and type of regimen may change over time. Without treatment, most people living with both HIV and TB will die, often in a matter of months. In such cases, the primary cause of death is TB, not HIV/AIDS (5).

Prevention

There are two parallel approaches to prevent and control TB. First, people with TB and their contacts should be identified and then treated (secondary or tertiary prevention). Identification of infections often involves testing high-risk groups for TB. Second, children should be vaccinated to protect them from TB (primary prevention). Unfortunately, no vaccine is available to provide reliable protection for adults. However, in tropical areas where the incidence of atypical mycobacterium is high, exposure to non-TB mycobacterium gives some protection against TB (5, 6).

Experts also advise an annual skin test for people who have HIV or any other immunocompromised disease, live or work in a prison or nursing home, health facilities, or have a substantially increased risk of exposure to the disease (5). If the test was positive for latent TB, chemotherapy with isoniazid can reduce the risk of developing active TB in the future (5).

Bacille Calmette-Guérin (BCG) is a vaccine against TB that is prepared from a strain of the attenuated (weakened) live bovine tuberculosis bacillus, *Mycobacterium bovis*, that has lost its *virulence*[3] in humans by being specially cultured in an artificial

[3] Virulence: The disease-producing power of a microorganism; infectiousness **6.** Wikimedia. Tuberculosis. http://en.wikipedia.org/wiki/Tuberculosis..

medium for years. The bacilli have retained enough strong *antigenicity* to become a somewhat effective vaccine for the prevention of human TB. Many countries with high prevalence of TB use BCG vaccine as part of their TB control programs, especially for infants. This was the first vaccine for TB, developed at the *Pasteur Institute in France* "between 1905 and 1921". However, mass vaccination with BCG did not start until after World War II. The protective efficacy of BCG for preventing serious forms of TB (e.g. meningitis) in children is greater than 80%; its protective efficacy for preventing pulmonary TB in adolescents and adults is variable, ranging from 0 to 80%. However, as previously stated, vaccination with BCG also causes a false-positive result on a Mantoux skin test . Therefore, it is not recommended for general use in the United States. Researchers are working on developing more effective TB vaccines (5, 6).

Adherence to medication is the most important step to protect the patient and others from of TB. As previously described, when the patient stops treatment early or skip doses, TB bacteria have a chance to develop mutations resistant to the most potent TB drugs. The resulting drug-resistant strains are much more deadly, expensive and difficult to treat (5).

Quarantine of the patient can be beneficial. Keeping the patient isolated, covering the mouth of the patient during the first 2-3weeks, and safe disposal of materials contaminated with the patient sputum may lessen the risk of transmission (5).

Public health significance:

TB Epidemiology

TB is still a major cause of death worldwide, but data has shown that the global epidemic is on the threshold of decline. According to the World Health Organization (WHO), nearly two billion people—one–third of the world's population—have been exposed to the tuberculosis pathogen.

Annually, about eight million people become ill with TB, and two million people die from the disease, worldwide. In 2005, around 14.6 million people had active TB disease with nine million new cases, 7.4 million of them in Asia and sub-Saharan Africa. A total of 1.6 million people died of TB, including 195 000 patients infected with HIV. Between 1980 and 2005, 90 million TB patients were registered in national surveillance systems and reported to WHO, also more than 26 million were notified by DOTS programs since 1995. This vast body of surveillance data suggested the global TB incidence rate peaked sometime between 2000-2005, although the total number of new cases is still rising each year. Data shows the global TB epidemic is now on the threshold of decline (21).TB prevalence and death rates have probably been falling globally for several years. In 2005, the TB incidence rate was stable or in decline in across WHO regions[4], and had reached a peak worldwide. However, the total number of new TB cases was still rising slowly, because the case-load continued to grow in the African, Eastern Mediterranean and South-East Asia regions. The estimated annual incidence rate varies from 356 per 100,000 in Africa to 41 per 100,000 in the Americas (5, 6, and 21).

[4] WHO six regions are; African region (AFR), the Region of Americas (AMR), the Eastern Mediterranean Region (EMR), the European Region (EUR), the South East Asia region (SEAR), and the Western Pacific Region (WPR) (3).

Tuberculosis is the world's greatest infectious killer of women of reproductive age and the leading cause of death among people with HIV/AIDS. In 2004, the country with the highest repeated incidence of TB was South Africa, with 718 cases per 100,000 people. India has the largest number of infections, with over 1.8 million cases. In developed countries, tuberculosis is less common and is mainly an urban disease. In the United Kingdom, TB incidences range from 40 per 100,000 in London to less than 5 per 100,000 in the rural South West of England; the national average is 13 per 100,000.In the United States, the overall tuberculosis case rate was 4.9 per 100,000 persons in 2004.The incidence of TB also varies with age. In Africa, TB primarily affects adolescents and young adults. However, in countries where TB has gone from high to low incidence, such as the United States, TB is mainly a disease of older people (5, 6, and 21).

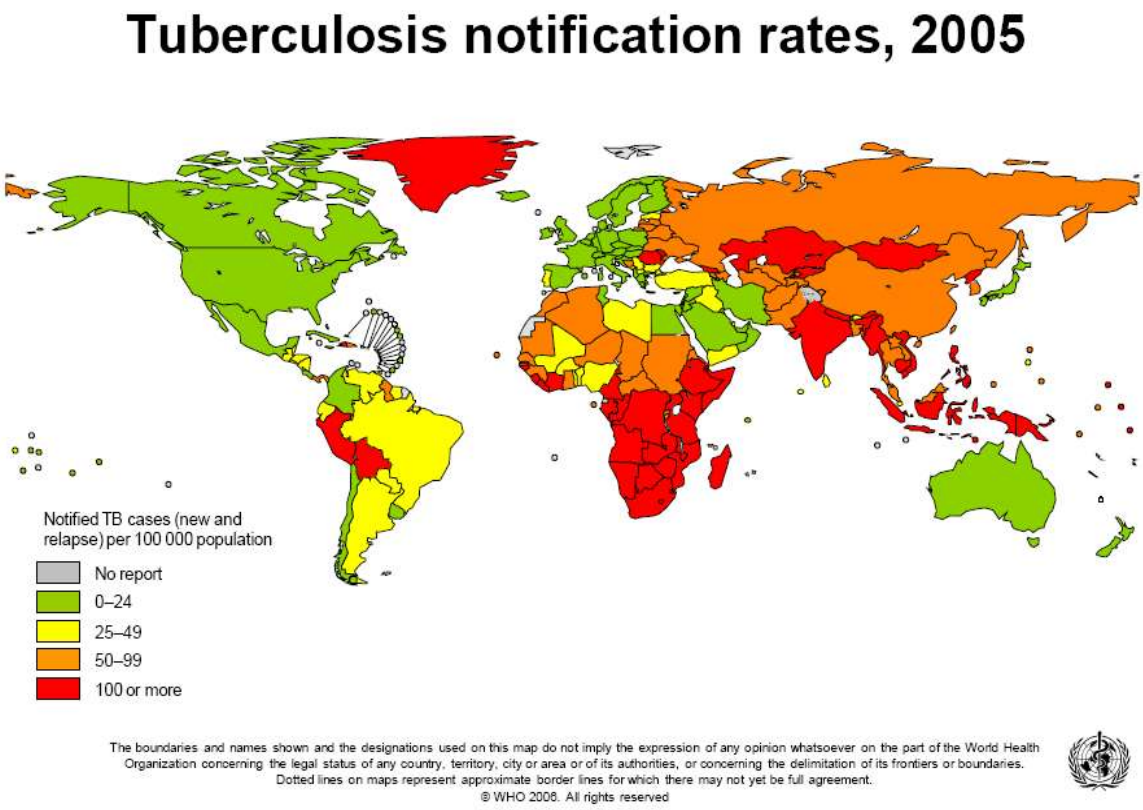

Figure 1. Tuberculosis notification rates, 2005 (22)

Twenty -two countries have been recognized as high burden countries, which account for approximately 80% of the estimated number of new TB cases (all forms) arising worldwide each year. These 22 countries are not necessarily those with the highest incidence rates per capita; many of the latter are medium-sized African countries with a high rate of TB/HIV co-infection and they are under focus of intensified efforts of DOTS expansion (21). Further information can be found in Figures 14, 21-26 in the appendixes.

TB Risk Factors

A number of factors have contributed to the global TB crisis, but the leading cause is the spread of HIV, the virus that causes AIDS. Tuberculosis and HIV have a deadly relationship - each fuels the progress of the other. Infection with HIV suppresses the immune system, making it difficult for the body to control TB bacteria. As a result, people with HIV are many times more likely to progress from dormant to active disease than are people who are not HIV-positive. TB is one of the leading causes of death among people living with AIDS - not only because they are more susceptible to TB, but also because TB can increase the rate at which the AIDS virus replicates. One of the first indications of HIV infection may be the sudden onset of TB - often in a site outside the lungs (extra-pulmonary TB) (5).

Anyone of any age, race or nationality can contract TB, but certain factors increase the risk of the disease (5).Weak immunity can increase the individual risk of catching TB. When the immune system is healthy, macrophages can often successfully wall off TB bacteria, but the body cannot mount an effective defense if the resistance is low. A number of factors can weaken the immune system such as HIV/AIDS, diabetes, the lung disease silicosis, receiving treatment with corticosteroids, arthritis medications, substance abuse and long-term drug or alcohol use (23-26).

TB can occur at any point in the course of progression of an HIV infection. The risk of developing TB rises sharply with worsening immune status.HIV promotes the rapid progression of LTBI to active disease and is the most powerful known risk factor for the activation of LTBI. Compared with an individual who is not infected with HIV, a person infected with HIV has a 10 times increased risk of developing TB. TB is among

the leading killers of people with HIV, and up to 50% of people with HIV or AIDS develop TB. In some regions of Africa, up to 77% of TB patients also have HIV. Worldwide, more than 21 million people are co-infected with TB and HIV, and 70% are concentrated in Africa. A large number of these people will develop active TB if they do not receive treatment. Co-infection is even starting influence the gender distribution of TB in many African countries; as HIV prevalence among young African women rises, they are also increasingly bearing the burden of TB (27-30).

By the end of 2000, about 11.5 million HIV-infected people worldwide were co-infected with M. tuberculosis. Seventy percent of co-infected people were in sub-Saharan Africa, 20% in South-East Asia, 1% in Eastern Mediterranean, 1% in Europe, 4% in Western Pacific and 4% in Latin America and the Caribbean approximately (31). Further information is included in Figure 21 in the appendix.

TB is also associated with poverty. The majority of the poor in the world are likely to have TB as result of contributing factors such as lack of basic health services, poor nutrition and inadequate living conditions. In turn, illness and death from TB reinforces and deepens poverty in many communities. For example, studies in India have shown that the prevalence of TB is between two and four times higher among groups with low income and no schooling. Overcrowded conditions, poor nutrition and inadequate sanitation increase the probability of being infected and developing active TB. Once they are ill, those who have limited access to health services are less likely to be diagnosed and treated for TB. The greater the numbers of people with active TB in a community, the more likely others are to become infected. This becomes a vicious circle

in poor communities where TB flourishes. Therefore, it is no surprise at present; over 90% of TB cases and 90% of deaths from TB occur in developing countries. A key challenge for TB control today is finding those people who have limited access to effective TB treatment and curing them. Expanding innovative approaches such as linking the public and private sectors in the treatment and referral of such cases will be critical in reducing TB deaths among the poor. The problem is compounded because people living in poverty and in unstable political situations often move or migrate and therefore may not complete their treatment, leading to drug-resistant forms of the disease (32-41).

Crowded living conditions also contribute to the spread of TB. TB spreads most easily in cramped, crowded, poorly ventilated spaces. Incidence rates in prisons, juvenile detention centers and homeless shelters are higher than that in the general population. TB bacteria also can flourish in nursing homes because older adults often have immune systems weakened by illness or aging (42-47).

Strains of TB that are resistant to conventional drugs have been documented in every country. Drug-resistant TB is caused by inconsistent, impartial or inappropriate treatment. People infected with drug-resistant TB, are highly contagious and transmit the drug-resistant strain of TB to others. As a result, it is on the increase in developing and transitional countries. Hotspots for multi-drug resistant TB are Estonia, Latvia and certain regions in Russia and China. It is estimated that drug-resistant TB accounted for 3.2% of the world's new cases in 2000. Multi-drug resistant TB is more expensive and difficult to treat. Before recent negotiations with pharmaceutical companies, it was over one hundred

times more expensive to treat than conventional TB, with long-term treatment up to two years with second line anti TB drugs which are highly toxic (48-60). Further information is included in Figures 23-24 in the appendixes.

Malnutrition or poor diet and food low in calories, puts a person at greater risk of TB and it may impair survival in TB patients. It is thought that chronic lack of appetite can be one of the causes of malnutrition associated with TB and therefore maybe a potential independent risk factor for latent TB. Latent TB infected people with poor appetite develop active TB rapidly, and then these patients have poor treatment outcome. Studies have shown that supplementation with a multivitamin, including Zn, during treatment of pulmonary TB may reduce mortality in those co-infected with HIV.Furthermore, malnutrition and intestinal parasites cause immunosuppression, which in turn may cause false-negative tuberculin skin tests (TST) and failure to identify TB infection (61-72).

Although more men than women are diagnosed with TB and die from it in most of the world, TB is nevertheless a leading infectious cause of death among women. Annually, about three-quarters of a million women die of TB, and over three million contact the disease, accounting for about 17 million Disability Adjusted Life Years (DALY). TB is a leading cause of death among women of reproductive age and is estimated to cause more deaths among this group than all causes of maternal mortality. As tuberculosis affects women mainly in their economically and reproductively active years, the impact of the disease is also strongly felt by their children and families. Mortality, incidence, and DALY indicators do not reflect this hidden burden of social

impact. One of the reasons is women are less likely than men to be tested and treated for TB. In addition, as greater numbers of women become infected with HIV, more are also becoming sick with TB (73, 74). However, studies in AFG, a country with one of the highest mortality rates (about 1600 per 100.000 population), have found about 66% of TB detected cases were women. This maybe due to low access to basic health services, poverty, malnutrition, and low access to sanitation (99).

Over 250 000 children die every year of TB. Children are particularly vulnerable to TB infection because of frequent household contact. Children also suffer when their parents are infected. Every year in India alone, more than 300 000 children leave school on account of their parental TB (73, 74).Cases of TB in children usually represent between 10% and 20% of all TB cases. The frequency of childhood TB in a given population depends on the number of infectious cases, the closeness of contact with an infectious case, the age of children when exposed to TB, and the age structure of the population. Children rarely have sputum smear-positive TB and so it is unlikely they are a powerful source of transmission. TB in children is mainly due to failure of TB control in adults, the failure to cure infectious cases (patients with sputum smear-positive PTB). Good treatment of TB in childhood will result in the following: a) improved well-being through decreased morbidity and mortality; b) improved credibility and reputation of the NTP; and c) less chance for children to have TB reactivation with cavitation[5] in later life (31).

[5] Cavitation: The formation of cavities in a body tissue or an organ, especially those formed in the lung as a result of tuberculosis.

Political stability is a term used to describe the socio-political climate or condition of a country. It means absence of violence, absence of civil unrest, absence of guerrilla warfare, governmental longevity, and the absence of structural change, legitimacy, and effective decision making. Political and economic stability are important in implementing public health programs and achieving its goals, particularly TB control programs. Political and economic instability exacerbate other factors such as poverty, hunger, immigration, displacement, malnutrition, and HIV/AIDS prevalence, which each fuels TB epidemics. Sub-Saharan Africa and some other instable countries with high burden of HIV-TB co-infection are good examples of instable countries (14, 75-83).

The association between smoking and TB has been investigated for several decades. Both passive and active exposure to tobacco smoke has shown to be associated with TB infection and with the transition from being infected to developing active TB disease. There may be several reasons for the association between smoking and TB. Smoking may decrease immune response or damage the protective effect of tiny hair-like structures called cilia in the airways, resulting in increased TB risk. It has been shown that ever smokers are more likely to have cough, dyspnea, chest radiograph appearances of upper zone involvement, cavity and miliary appearance, and positive sputum culture, but are less likely to have isolated extra-pulmonary involvement than non-smokers. Smoking has been found to be associated with both relapse of TB and TB mortality. There appears to be enough evidence to conclude that smoking is causally associated with TB disease. Patients with TB need and should receive counseling and assistance in stopping smoking. A meta-analysis study reported smokers, compared to nonsmokers,

were 73 percent more likely to become infected with TB and more than twice as likely to develop active TB. Overall, smokers are 40 to 60 percent more likely than nonsmokers to develop active TB after being infected with TB bacteria (84-90).

Global TB Control Programs

The goals of TB control programs are to reduce mortality, morbidity and transmission of the disease, while preventing drug resistance, until it no longer poses a threat to public health. The programs also aim to reduce human suffering, including the social and economic burden families and communities have to bear as a consequence. The forty-fourth World Health Assembly (1991) set the targets for global TB control to be achieved by the year 2000. The target was to cure 85% of the identified TB cases and to detect overall 70% of such cases. In view of the slow progress in many high burden countries, the target date was revised to 2005. Enabling achievement of high cure rates for all, and especially infectious TB cases, remains the highest priority. Besides helping to rapidly reduce transmission, TB programs achieving high cure rates are likely to attract the great majority of existing cases. Giving priority to case finding before ensuring access to high quality care for diagnosed cases could compound the TB problem by producing chronic cases and MDR-TB. Improved and expanded case detection activities should follow sustained achievement of high cure rates (8).

Countries are expected to achieve the global targets by integration of TB activities into general health services, introduction of guidelines for health care providers on proper management of respiratory diseases, incorporation of community health workers and volunteers for service delivery, involvement of private and other non-governmental

health providers and adaptation of DOTS implementation to suit local settings and situations. This should result in reduction of TB morbidity, mortality and disease transmission leading to a gradual decline in the epidemiological burden of the disease (8).

Directly Observed Therapy, Short-course (DOTS)

The forty-fourth World Health Assembly (1991) recognized the growing importance of TB as a public health problem and the potential for cost-effective control using currently available tools. This led to a reassessment of ongoing TB control efforts. The persistence of TB has been due chiefly to the neglect of TB control by governments, poorly managed TB control programs, poverty, population growth and migration, and a significant rise of TB cases in HIV endemic areas. To help address the situation, a new framework for effective TB control was then developed and a global strategy called DOTS was introduced. DOTS – the internationally approved TB control strategy – has been implemented together with TB/HIV programs, which has had cost-effective results and high treatment success rate .DOTS is also an excellent model for delivering antiretroviral (ARV) therapy to HIV infected people. Because nearly three-fourths of TB patients are co-infected with HIV in high-burden countries, TB services form important entry points for scaling up access to ARVs (7-10).

The five elements of the DOTS strategy, considered essential for global TB control are (7-10):

a) Political commitment with increased and sustained financing. Clear and sustained political commitment by national government is crucial to ensure sustained, comprehensive tuberculosis control activities. This political commitment helps to

implement DOTS and the Stop TB Strategy effectively and to foster national and international partnerships, which should be linked to long-term strategic action plans prepared by NTPs. Strategic action plans should address technical and financial requirements and promote accountability for results at all levels of the health system; they should include TB-related and other relevant indicators, and – where appropriate – political commitment should be backed up by national legislation. Local partnerships with many potential contributors will help improve TB care in terms of access, equity and quality. As current resources are inadequate, so further effort is required to mobilize additional resources from domestic as well as international sources, with a progressive increase in domestic funding. The global financing and partnership resources now available for poverty reduction, health systems improvement and disease control offer new opportunities for TB control programs. Even with adequate financing, critical deficiencies in human resources in the health sector will impede progress in many low- and middle-income countries, especially in Africa. Therefore, Political commitment is required to support the overall structural and financial changes needed to improve the availability, distribution and motivation of competent health workers. Special efforts, including good strategic planning, will be needed to ensure the availability of adequate and competent human resources for health care in general and TB care in particular (7-10).

b) Case detection through quality-assured bacteriology. Bacteriology remains the recommended method of TB case detection, first using sputum smear microscopy and then culture and drug susceptibility testing (DST) (80). A wide network of properly equipped laboratories with trained personnel is necessary to ensure access to quality-

assured sputum smear microscopy. This is likely to require additional investments in the laboratory network in many countries. In addition, every country should have a well-resourced and fully functioning national reference laboratory. The laboratory network should be based on some principles such as; adoption based on international standards, decentralization of diagnostic services, and communication at various level of network and quality management. Culture and DST (80) services should be introduced in a phased manner, at appropriate referral levels of the health system. Their functions should include diagnosis of sputum smear-negative TB, diagnosis of TB among HIV-positive adults and children, diagnosis and monitoring of response to treatment of MDR-TB, and testing related to periodic surveys of the prevalence of drug resistance. Maintaining the quality of the laboratory network depends on regular training, supervision and support, and motivation of laboratory staff. Existing public and private laboratories should be used wisely (7-10).

c) Standardized treatment, with supervision and patient support. Standardized short-course chemotherapy, using regimens of six to eight months are recommended, for at least all confirmed smear positive cases. Good case management includes directly observed therapy during the intensive phase for new sputum smear-positive cases, the continuation phase of rifampicin-containing regimens and the whole re-treatment regimen. The mainstay of TB control is organizing and administering standardized treatment across a country for adult and pediatric TB cases – sputum smear-positive, smear-negative, and extra-pulmonary. WHO guidelines on patient categorization and management should be followed. These guidelines emphasize use of the most effective standardized, short-course regimens, and of fixed-dose drug combinations (FDCs) to

facilitate adherence to treatment and to reduce the risk of the development of drug resistance. Separate WHO guidelines are also available for management of patients with drug-resistant TB. Services for TB care should identify and address factors that may make patients interrupt or stop treatment. Supervised treatment, which may have to include direct observation of therapy (DOT), helps patients to take their drugs regularly and complete treatment, thus achieving cure and preventing the development of drug resistance. Supervision must be carried out in a context-specific and patient-sensitive manner, and is meant to ensure adherence on the part both of providers (in giving proper care and support) and of patients (in taking regular treatment). Depending on the local conditions, supervision may be undertaken at a health facility, in the workplace, in the community, or at home. It should be provided by a treatment partner or treatment supporter who is acceptable to the patient and is trained and supervised by health services. Patient and peer support groups can help to promote adherence to treatment. Selected patient groups, for example prisoners, drug users, and some people with mental health disorders, may need intensive support including DOT. Locally appropriate measures should be undertaken to identify and address physical, financial, social and cultural barriers – as well as health system – barriers to accessing TB treatment services. Particular attention should be given to the poorest and most vulnerable population groups. Examples of actions that may be appropriate include expanding treatment outlets in the poorest rural and urban settings, involving providers who practice close to where patients live, ensuring the services are free or heavily subsidized, offering psychological and legal support, addressing gender issues, improving staff attitudes, and undertaking advocacy and communication activities (7-10).

d) An effective drug supply and management system. An uninterrupted and sustained supply of quality-assured anti-TB drugs is essential to control TB. A reliable system of procurement and distribution of essential anti-TB drugs to health facilities should be in place. The TB recording and reporting system is designed to provide the information needed to plan, procure, distribute and maintain adequate stocks of drugs. Anti-TB drugs should be available free of charge to TB patients. Treatment has benefits that extend to society as a whole (cure prevents transmission to others). Legislation related to drug regulation should be in place, and use of anti-TB drugs by providers should be strictly monitored. The use of FDCs of proven bioavailability and of innovative packaging such as patient kits can help to improve drug supply logistics as well as drug administration, promote adherence to treatment and prevent development of drug resistance. The Global Drug Facility and the Green Light Committee (GLC) offer countries with limited capacity the benefit of access to quality-assured TB drugs at reduced prices and also facilitate access to training on drug management (7-10).

e) A monitoring and evaluation system with impact measurement. A standardized recording and reporting system is vital for TB control program. This consists of standardized recording of individual patient data, including information on case detection and treatment outcomes, which are then used to compile treatment outcome reports in cohorts of patients. These data, when compiled and analyzed, can be used at the facility level to monitor treatment outcomes, at the district level to identify local problems as they arise, at provincial or national level to ensure consistently high-quality TB control across geographical areas, and nationally and internationally to evaluate the performance of each country. In addition, regular supervision should be carried out to verify the

quality of information and to address performance problems. To enhance recording and reporting, additional diagnostic information including sputum culture, DST and HIV test results are needed. These data can be used to guide patient management in both developed and developing countries. TB program managers also need to monitor records and reports from public and private care providers not directly linked to the NTP. Special attention must be paid to ensure the confidentiality of patient information. Making the best use of data at all levels will mean many countries train staff in the analysis and interpretation of data, as well as in the use of the computer software that can greatly facilitate this work. As electronic recording systems become more widely available, consideration should be given to storing individual patient data, which will make more detailed analysis of aggregated data possible (7-10). This strategy is an effective case management system to help ensure patients take quality anti-tuberculosis drugs, at the right dosage, for the appropriate length of time, and to minimize the development of resistance by preventing treatment failure. The strategy can be integrated successfully within general health services to achieve widespread coverage. DOTS does not require hospitalization or isolation; patients can remain in their homes and return to work in a few weeks (7-10).

Since the introduction of the DOTS strategy in the early 1990s, considerable progress has been made in global TB control. As of 2000, 148 countries had adopted the WHO DOTS strategy for TB control and one fourth of the global TB cases were treated under DOTS. The report of the Ad-hoc Committee on Tuberculosis Epidemic, convened by WHO in London in 1998, commended the achievements of a few countries but expressed concerns about the slow progress of DOTS implementation in most countries

with a high burden of TB. Identifying the major constraints to DOTS implementation, the committee recommended a comprehensive and multi-sectored approach to TB control. Subsequently, in late 1998, a global partnership was launched linking health, social and economic sectors in the fight against TB. The partnership, called "Stop TB Initiative", was hosted by WHO. In the year 2000, a high level Ministerial Conference of Ministers of health and finance of the top 20 high burden countries endorsed the "Stop TB Partnership" in what is called the "Amsterdam Declaration". Global targets for TB control were also set in 1991 and reaffirmed subsequently (8).

Most government health services now recognize TB control must go beyond DOTS, but the broader Stop TB Strategy is not yet fully operational in most countries. According to WHO TB report of 2007, DOTS which underpins the Stop TB Strategy, was being applied in 187 countries in 2005, or about 90% of the world's population. More than 90 million TB patients were reported to WHO between 1980 and 2005; 26.5 million patients were notified by DOTS programs between 1995 and 2005, and 10.8 million new smear-positive cases were registered for treatment by DOTS programs between 1994 and 2004. A total of 199 countries/areas reported about five million episodes of TB in 2005 (new patients and relapses); about 2.3 million new pulmonary smear-positive patients were reported by DOTS programs in 2005; and about 2.1 million were registered for treatment in 2004. The plans for human resources which are central to any public health programs made by national TB control programs (NTPs) in 2005-2006 were highly variable in quality. Seven of the 22 HBCs, including five African countries, had limited plans. NTPs in all WHO regions reported drug stock-outs, few laboratories, weak quality control, and limited facilities to carry out culture and drug susceptibility

testing; and many NTPs asked for further technical and financial assistance (80). Although the number of HIV-positive and multidrug-resistant TB patients diagnosed and treated was increasing in 2005, numbers were still lower than proposed in the Global Plan for 2006. The treatment success rate for MDR-TB patients in projects approved by the Green Light Committee (GLC) was close to 60%, and higher than in non-GLC projects (21).

Few NTPs have done an overview of TB research in their countries. Although TB control funds have increased enormously compared to previous years, reaching $ 2.0 billion (US) in 2007, interventions required by the Global Plan to Stop TB would cost an extra $ 1.1 billion (US) in 2007 (21).

In sum, the WHO TB report of 2007 draws four main conclusions about progress in TB control, based on routine monitoring and surveillance data from DOTS. First National TB Programs (NTPs) worldwide narrowly missed the 2005 targets for case detection (60%/70%) and treatment success (84%/85%). However, both targets were met in the Western Pacific Region, and in 26 countries including China, the Philippines and Viet Nam. Second, while the total number of patients diagnosed and treated under DOTS approached target levels in 2005, the numbers known to be HIV-positive or carrying drug-resistant bacteria (MDR-TB) were far fewer than anticipated by the Global Plan in 2006. Therefore, a major effort is needed to step up collaborative TB/HIV activities and the management of MDR-TB. Third, the global TB epidemic appears to be on the threshold of decline. The incidence rate (per capita) worldwide has evidently stabilized or begun to fall, following the earlier downturns in prevalence and mortality. The incidence rate is now stable or falling in all WHO regions, including Africa and Europe. These

findings, if robust, mean that MDG target 8 was met before 2005, and more than 10 years before the target date of 2015. However, the total number of new TB cases was still rising slowly in 2005 in the African, Eastern Mediterranean and South-East Asia regions. Moreover, in some Asian countries that reporting high rates of case detection and treatment success, incidence has not apparently been reduced as quickly as expected, for reasons that are not fully understood. This is linked to the fourth conclusion: the global TB burden is not yet falling fast enough to satisfy the more demanding targets set by the Stop TB Partnership within the MDG framework. At the current rate of progress, the 1990 prevalence and mortality rates will not be halved worldwide by 2015 (21). Further information can be found in Figures 16, and 17 in the appendixes.

DOTS-Plus

High levels of MDR-TB in some areas threaten TB control efforts. DOTS-Plus for MDR-TB is a comprehensive management initiative, built upon the five elements of the DOTS strategy. However, DOTS-Plus also takes into account specific issues, such as the use of second-line anti-TB drugs. The goal of DOTS-Plus is to prevent further development and spread of MDR-TB. DOTS-Plus is not intended for universal application. The underlying principle is that the first step in controlling MDR-TB is prevention by full implementation of DOTS. An effective DOTS-based TB control program is a prerequisite for implementation of DOTS-Plus (31). In 1999, WHO established the Working Group on DOTS-Plus for MDR-TB. The Working Group was renamed in May 2006 to the Stop TB Working Group on MDR-TB. Main achievements over the last few years in MDR-TB surveillance and control include: coordinating a network that has surveyed drug resistant TB in almost 100 countries worldwide;

establishment of an international TB reference laboratory network, consisting of 25 laboratories worldwide for global surveillance and MDR-TB control; establishment of the Green Light Committee (GLC) mechanism , a multi-institutional partnership to promote access to life-saving high-quality second-line drugs at reduced prices for the treatment of MDR-TB and under rigorous monitoring to prevent the creation of resistance to second-line drugs, the last line of defense against TB. By November 2006, 51 projects in 40 countries had been approved by the GLC for the treatment of about 25,000 MDR-TB patients. The activities of these projects are publishing evidence on feasibility, effectiveness and cost-effectiveness of MDR-TB management; developing guidelines on MDR-TB surveillance and management; conducting regional and country level workshops on MDR-TB, and technical assistance about MDR-TB especially to HBCs; conducting a project to pre-qualify second-line drug manufacturers and their products and to develop a list of quality-assured drugs; developing a 10-year strategic plan of the Working Group which forms part of the Global Plan to Stop TB, 2006-2015; and, management of MDR-TB as part of the new Strategy to Stop TB and the International Standards of TB Care (91). Further information is included in Figures 23, and 24 in the appendixes.

TB/HIV Control

As mentioned previously, TB and HIV are closely interlinked. TB is a leading cause of HIV-related morbidity and mortality. HIV is the most important factor fuelling the TB epidemic in populations with a high HIV prevalence. The WHO global strategic framework to control TB/HIV represents a coordinated response to the joint epidemics of TB and HIV. Collaboration between TB and HIV/AIDS programs is crucial in supporting

general health service providers. These providers need support in delivering the full range of HIV and TB prevention and care interventions. The TB/HIV Working Group of the Stop TB Partnership was established in 2001 with the aim of coordinating the global response to the HIV associated TB epidemic. The HIV pandemic presents a massive challenge to the global control of TB at all levels. However, to counteract the impact of HIV on TB, other interventions are required apart from effective TB case-finding and cure. These interventions include measures to decrease HIV transmission (e.g. promotion of condoms; treatment of sexually transmitted infections; voluntary counseling and HIV testing; safe and reduced intravenous drug use; reduction in the number of sexual partners; prevention of mother-to-child HIV transmission; HIV screening of blood for transfusion; application of universal HIV precautions by health care workers; antiretroviral therapy (ART) to improve or maintain immune function in people living with HIV infection; care for people living with HIV infection (e.g. treatment of HIV-related diseases, prevention of HIV-related infections, TB prevention, palliative care and nutritional support) (31).

According to WHO recent report on TB, the overall progress of implementation of collaborative TB/HIV activities, particularly in those countries with greater burden has been low. The TB/HIV Working Group will review its current strategy and operational framework to address these gaps, and ensure the delivery of collaborative TB/HIV activities for patients in need of the services. (92). Additional information is included in Figure 21 in the appendix.

Practical Approach to Lung Health (PAL)

PAL is an integrated strategy to manage respiratory patients in primary health care (PHC) settings with a focus on priority respiratory diseases, particularly TB, acute respiratory infections, including pneumonia, and chronic respiratory diseases, namely asthma and chronic obstructive pulmonary disease (COPD). Its objectives are to improve the quality of respiratory case management and the efficiency of the health system to deal with respiratory conditions. PAL relies on two pillars to be adapted into the health environment of a country: a) standardization of the respiratory condition management, and b) coordination among the relevant bodies to deal with respiratory care services within each district health system. Some other issues to fully promote PAL include: a) Price reduction schemes to increase access to medication for chronic respiratory diseases, especially in developing countries; b) Clear definition and development of the standards for reliable, affordable, and simple diagnostic equipment; c) Extension of clinical interventions beyond health facilities to the community level by conducting public health campaigns to promote respiratory health (93, 94).

Millennium Development Goals

World leaders agreed to a set of time bound and measurable goals and targets combating poverty, hunger, disease, illiteracy, environmental degradation and discrimination against women at the United Nations Millennium Summit in September 2000. They are placed at the heart of the global agenda, now called the Millennium Development Goals (MDGs). The Summit's Millennium Declaration also outlined a wide range of commitments in human rights, good governance and democracy. At the International Conference on Financing for Development in Monterrey, Mexico (2002)

leaders from both developed and developing countries started to match these commitments with resources and action, signaling a global deal in which sustained political and economic reform by developing countries will be matched by direct support from the developed world in the form of aid, trade, debt relief and investment. The MDGs thus provided a framework for the entire UN system to work coherently together towards a common end. The UN Development Group (UNDG) will help ensure that the MDGs remain at the centre of those efforts. On the ground in virtually every developing country, the UN is uniquely positioned to advocate for change, connect countries to knowledge and resources, and help coordinate broader efforts at the country level. The world is making progress toward the MDGs, but the majority of nations will reach the MDGs only if they get substantial support—advocacy, expertise and resources—from outside. The challenges for the global community, in both the developed and developing world, are to mobilize financial support and political will, re-engage governments, re-orient development priorities and policies, build capacity and reach out to partners in civil society and the private sector. To achieve MDGs, working on key dimensions such as practical assistance in support of country priorities, country-level monitoring, global monitoring, research leadership, and advocacy are essential. MDGs consist of eight specific aims, which have been expressed in general terms and accompanied by between one and six specific targets and by several indicators for measurement of progress towards each of the targets (95). These aims are:

1. Halve extreme poverty and hunger.
2. Achieve universal primary education.
3. Empower women and promote equality between women and men.

4. Reduce Child mortality: The accompanying target was to reduce the under-five mortality rate by two-thirds between 1990 and 2015.
5. Improve maternal health. The specific target was to reduce maternal mortality by three quarters between 1990 and 2015
6. To combat HIV/AIDS, malaria, TB, and other diseases. The two accompanying targets called for a halt and reversal by 2015 in the spread of diseases or incidence, especially HIV/AIDS, TB and Malaria. These diseases have erased a generation of development gains.
7. Ensure environmental sustainability. More than one billion people still lack access to safe drinking water
8. Create a global partnership for development, with targets for aid, trade and debt relief.

Although the MDGs are highly relevant for health—in the sense that faster progress towards any one of them could be expected to produce health gains— three of them (four, five and six) refer to health explicitly and the sixth to TB (95). Additional information on MDGs can be found in Figure 17 in the appendix.

The Global Plan to Stop TB 2006-2015 (Stop TB Strategy)

This plan was launched at the World Economic Forum in Davos, Switzerland, in January 2006, following 18 months of consultation and research by WHO TB experts. The global plan is for both developing and developed countries so everyone recognizes their role in fighting the TB epidemic through actions. TB can be overcome if richer countries step forward and adequately contribute technical and financial assistance, and at the same time, high burden countries make TB a priority. As preliminary steps in TB

control have been achieved in recent years, this Plan can further reduce TB burdens (96, 97). Full funding of this new global plan would promote achievement of MDGs; increase access to quality TB diagnosis and treatment for all; save 14 million lives; treat 50 million TB people; put 3 million TB-HIV co-infected patients on to ARVs; treat nearly one million people for MDR-TB; help introduce the first new TB drug in four years by 2010; help introduce a new vaccine by 2015; and provide rapid and inexpensive diagnostic tests at the point of care (96, 97).

The vision of the Stop TB Strategy is a world free of TB. Its goal is to dramatically reduce the global burden of TB by 2015 in line with MDG 6 and the Stop TB Partnership targets The objectives are: a) Achieve universal access to high-quality diagnosis and patient-centered treatment; b) Reduce the human suffering and socioeconomic burden associated with TB; c) Protect poor and vulnerable populations from TB, TB/HIV and multidrug-resistant TB; d) Support development of new tools and enable their timely and effective use. The Stop TB Strategy targets are based on MDG 6, target 8, "halted TB burden to half by 2015 and begun to reverse the incidence" which is endorsed by Stop TB Partnership. They are: a) detect at least 70% of new sputum smear-positive TB cases and cure at least 85% of these cases by 2005; b) Reduce prevalence of and deaths due to TB by 50% relative to 1990 by 2015; c) Eliminate TB as a public health problem (<1 case per million population) by 2050 (11).

Components of the Stop TB Strategy:

1. Pursue high-quality DOTS expansion and enhancement through: a) political commitment with increased and sustained financing; b) case detection through quality-assured bacteriology; c) standardized treatment with supervision and patient support; d)

an effective drug supply and management system; e) monitoring and evaluation system, and impact measurements.

2. Address TB/HIV, MDR-TB and other challenges by: a) implementing collaborative TB/HIV activities; b) Prevent and control multidrug-resistant TB; c) and Addressing prisoners, refugees and other high-risk groups and special situations (11)

3. Contribute to health system fortification by: A) Active participation in efforts to improve system-wide policy, human resources, financing, management, service delivery, and information systems; b) Share innovations that strengthen systems, including the practical approach to lung health (PAL);c) and adapt innovations from other fields (11).

4. Engage care providers with public-public, and public-private mix (PPM) approaches, and promoting International standards for TB care (ISTC) (11)

5. Empower people with TB, and communities via: a) advocacy, communication and social mobilization; b) allow community participation in TB care. c) And forming patients' charter for tuberculosis care (11).

6. Enable and promote research which is program-based and focus on developing new diagnostics, drugs and vaccines (11).

TB in WHO Eastern Mediterranean Region (EMR)

There are 22 countries[6] in WHO Eastern Mediterranean region, located in North Africa, Middle East, and Pakistan in Indian sub-continent. These countries differ in terms of political stability, income, population, climatological and geographical variables. TB is

[6] 22 countries in WHO East Mediterranean region are; Afghanistan, Bahrain, Djibouti, Egypt, Iran, Iraq, Jordan, Kuwait, Lebanon, Libyan Arab Jamahiriya, Morocco, Oman, Pakistan, Qatar, Saudi Arabia, Somalia, Sudan, Syrian Arab Republic, Tunisia, United Arab Emirates, West Bank and Gaza Strip, and Yemen (3).

an important public health problem in this region. Every year the disease kills about 136,000 people and affects over 630,000 more, fueled by political and economic instability, migration and displacement, poverty, malnutrition, low coverage of health services, smoking, HIV/AIDS and drug-resistant strains (12-17). HIV is the most significant risk factor for progression from LTBI to active TB. Although the HIV/AIDS threat in the region appears to be relatively modest and so far there has been no evidence of an impact of HIV on TB epidemiology in the region, there is a need to jointly address HIV infection and TB more effectively (17).

Figure 2. WHO Eastern Mediterranean Region (EMR) (98)

Since the introduction of the DOTS strategy in mid-1990, most countries have DOTS program in the Eastern Mediterranean region and strive to expand DOTS services throughout the network of health facilities of ministries of health to achieve 100% population coverage as well as high treatment success rates. In 2005, the regional DOTS coverage was close to 90% and the regional average treatment success rate was about

84%. There are many middle income countries in the region with a well developed public health care infrastructure. Political commitment to TB control is generally good. Most countries have thus laid the foundation for effective TB control. In other words, they have completed the first stage in the development of TB control, which is to achieve basic DOTS coverage and good treatment outcomes within the existing programs. A few countries, such as Morocco and Tunisia, have already achieved the 2005 global targets of detecting at least 70% of new smear-positive cases and treating successfully at least 85% of these cases. TB incidence has started to decline in these countries. There is increasing awareness in the region of the impact of HIV on TB. Initial steps have been taken to establish HIV surveillance among TB patients and to implement collaborative TB/HIV activities where appropriate. DOTS-Plus pilot projects have been implemented in Egypt, Jordan, Lebanon, Syrian Arab Republic and Tunisia, and the Practical Approach to Lung Health (PAL) strategy has been initiated in Jordan, Morocco, Syrian Arab Republic and Tunisia (12, 15, 17-19).

There are still many challenges to address in this region. Geographical expansion of DOTS is incomplete in countries with complex emergencies because of poor health infrastructure or an unsafe environment, namely Afghanistan, Iraq, Somalia and Sudan (South and Darfur). The other countries in the region are now in the second stage in the development of TB control– the stage of further improving quality and access. They are struggling with low case detection: the regional case detection rate was expected to be only 45% by the end of 2005. Case detection in the two high-burden countries of the region – Pakistan and Afghanistan – is still low, at about17% and 18%, respectively, due to many factors. Key components of DOTS, particularly case-finding and surveillance,

are not always of high quality. In many countries of the region, the private health care sector is booming but is not yet involved in DOTS. In addition, important segments of the public health care sector, such as social security health services or army health services, are not yet involved. Coverage of drug resistance surveillance is low but is being expanded. The impact of HIV on TB is becoming increasingly important in countries with a generalized HIV epidemic (e.g. Djibouti, Somalia, Sudan) and in those where injecting drug use is an important cause of HIV infection (e.g. the Islamic Republic of Iran). The challenge will be to implement collaborative TB/HIV activities to address HIV-related TB in settings where health systems are weak and health service delivery is complicated by civil conflict. The first priority is to improve further the quality of key basic components of DOTS, such as laboratory diagnosis, surveillance and drug management, and to develop and sustain adequate human resources to deliver quality DOTS. Public-private partnership to provide DOTS should be scaled up widely. The involvement of the NGO sector will continue to be essential in areas with complex emergencies. To facilitate implementation of DOTS-Plus, culture and drug susceptibility testing services should be scaled up (17-20).

DOTS-Plus will be expanded in a stepwise approach to reach 100% coverage by 2015. Scaling up culture services will also improve the diagnosis of smear-negative TB cases, which is particularly important for areas with high HIV prevalence. To further improve quality across different health sectors, and help boost case detection, PAL should also be implemented widely in the region, community DOTS should be scaled up in selected rural areas. Collaborative TB/HIV activities need to be implemented and strengthened in settings with a high HIV burden. Operational research activities should

be continued to solve problems identified through the TB surveillance and TB control information system (17-20).

Countries in the Eastern Mediterranean region should be supported in adapting, developing and implementing special strategies to control TB, especially in poor settings and in big cities. To realize sustainable political, technical and financial support to TB control, Stop TB Partnerships should be developed at regional and national levels, and strategic approaches for communication, advocacy and social mobilization should be adapted and implemented. Successful implementation of the activities described above is expected to increase case detection rapidly to 73% by 2010 and 80% by 2015; treatment success rate is expected to increase from 84% to 87% in 2010 and then it be sustained at this level. TB incidence, prevalence and death rate are already falling in the region; moreover, planned activities are predicted to boost the decline further, so the 2015 Partnership targets, linked to the MDG target, will be met in the Eastern Mediterranean region. During the period of the plan (2006–2015), it is estimated that 3.6 million people will be treated under DOTS programs and 48 000 under DOTS-Plus. In addition, 36 000 TB patients will be enrolled on antiretroviral therapy. The combined effect of all interventions will be to prevent about 798 000 deaths, about four times as many as where no DOTS programs are implemented, or about 196 000 deaths in comparison with a situation in which TB control efforts are sustained at 2005 levels. The total estimated cost of DOTS expansion, DOTS-Plus and TB/HIV control activities in the Eastern Mediterranean region from 2006 to 2015 is about $2.6 billion (US) (12, 13, 15, 17-20, 99). Additional information is included in Table 9 in the appendix.

CHAPTER III
METHODS AND PROCEDURES

The primary objective of this study was to identify and describe the progress and barriers of TB control programs in 22 EMR countries of WHO toward MDGs and 1991 National Health Assembly targets for DOTS. Also, the study explored the relationship between TB burden (morbidity and mortality) and DOTS in EMR countries and following variables: political stability, population density, GDP, income, healthcare force, health expenditure, HIV prevalence, immunization coverage, sanitation, adult literacy rate, adult smoking rate, national poverty level and malnutrition. The research specific questions were:

- Has the Eastern Mediterranean region made any progress towards achieving MDGs and DOTS?
- How is TB/HIV co-morbidity in the region?
- Are there relationships between TB burden and DOTS in EMR countries and sociopolitical variables?
- What are some of the data gaps, challenges and accomplishments to be used as lessons for future interventions?

Data Sources

TB data (incidence, prevalence, death, DOTS coverage, treatment, TB-HIV co-infection), world health statistics, and health human resources data were publicly available from WHO Global Health Atlas from 1980 to 2005 and were retrieved for use

in this study. Other demographic, political, and socioeconomic variables were retrieved from World Bank and World Resource Institute (100) online databases as well as the American Cancer Society (101) webpage.

WHO's Communicable Disease Global Atlas is a single platform that brings together for analysis and comparison standardized data and statistics for infectious diseases at country, regional, and global levels. The analysis and interpretation of data are further supported through information on demography, socioeconomic conditions, and environmental factors. In so doing, the Atlas specifically acknowledges the broad range of determinants that influence patterns of infectious disease transmission. The system aims to provide a single point of access to data, reports and documents on the major diseases of poverty including malaria, HIV/AIDS, and tuberculosis, as well as the diseases on their way towards eradication and elimination, but yet prone to epidemics such as meningitis, cholera, and yellow fever. Anti-infective drug resistance and emerging infections are covered as well. The database is updated on an ongoing basis and in addition to epidemiological information, the system aims to provide information on essential support services such as the network of communicable diseases collaborating centers, the activities of the Global Outbreak Alert and Response Network, etc.

WHO collects TB data annually from NTPs or relevant public health authorities in 212 countries via a standard data collection forms which are used to compile aggregated national data. The process of national and international reporting is distinct from WHO's recommendation about procedures for recording and reporting data by NTPs within countries, from district level upwards. Completed forms are collected and reviewed at all levels of WHO: country offices, regional offices and at headquarters. An

acknowledgement form that tabulates all submitted data is sent back to the NTP correspondent to complete any missing responses and to resolve any inconsistencies. Then using the complete set of data for each country, a constructed profile tabulating all key indicators, including epidemiological data, and financial data, is estimated and returned to each NTP for review (21, 102).

Earth Trends, an online database, was launched in 2001 by the World Resource Institute (100) based in Washington DC. Earth Trends gathers data from the world's leading statistical agencies, along with WRI-generated maps and analysis into a single database. These resources are made available to the public at no charge. Inside this researchable database, there is time –series information for over 600 variables, more than 200 country profiles, as well as data tables, maps, and feature stories on a variety of environmental, social, and economic topics (100).

World Bank Governance Indicators (WGI) reports aggregate and individual governance indicators for 212 countries and territories over the period 1996–2006. The aggregate indicators combine the views of a large number of enterprise, citizen and expert survey respondents in industrialized and developing countries. The individual data sources underlying the aggregate indicators are drawn from a diverse variety of survey institutes, think tanks, non-governmental organizations, and international organizations (103). World Development Indicators Online (104) provides direct access to more than 700 development indicators, with time series for 208 countries and 18 country groups from 1960 to 2006. Most social data are collected annually. Some economic and financial data are available on monthly or quarterly basis. The World Bank also publishes annual socio-economic data in its data publications and on its web site (103-105).

The Tobacco Atlas, second edition published by American Cancer Society (101) and the International Union Against Cancer (IUAC) in 2006, maps distinct features of the tobacco pandemic, including prevalence, mortality, trade, smuggling, and research (101).

Ethical Considerations

The data were retrieved from publicly available on line databases, and no contact was made with any entities. However, the Institutional Review Board (IRB) at Georgia State University (GSU) approved the research methods, and granted exempted status. The approved protocol number was 00000129 (see Appendix A).

Quality of data

As mentioned, the data were retrieved from WHO, WB, WRI and ACS. TB detected under DOTS/2003 and TB successful treatment rate under DOTS 2002 of WHO TB database and WHO World Health Statistics database were compared to investigate data quality. For a few countries, the first variable was quite different. The second variable was similar in both databases except for Yemen. West Bank and Gaza data were missing in the World Health Statistics. Based on a comparison of particular values in these databases, the quality of data is under question because the same variable value was not only different in different organization databases, but it may also have been different in the same organization's databases. In addition, there were a number of missing values for some variables. Variables used in this study and their respective sources are noted in

Table 1. List of variables with their respective sources

No	Variable	years	Source
1	Eastern Mediterranean Region Countries		
2	Whole country new smear-positive case detection rate (%)	1995-2005	WHO[1]
3	DOTS new smear-positive case detection rate (%)	1995-2005	WHO
4	DOTS population coverage (%)	1995-2005	WHO
5	New and relapse cases (per 100 000 population)	1980-2005	WHO
6	DOTS treatment success (%) -> Total	1994-2004	WHO
7	Non-DOTS treatment success (%) -> Total	1994-2004	WHO
8	TB incidence, all forms (per 100 000 population per year) -> Total	1990-2005	WHO
9	TB incidence, all forms in HIV+ adults (per 100 000 population per year) -> Total	1990-2005	WHO
10	TB prevalence, all forms in HIV+ adults (per 100 000 population per year) -> Total	1990-2005	WHO
11	TB prevalence, all forms (per 100 000 population per year) -> Total	1990-2005	WHO
12	TB mortality, all forms in HIV+ adults (per 100 000 population per year) -> Total	1990-2005	WHO
13	TB mortality, all forms (per 100 000 population per year) -> Total	1990-2005	WHO
14	Sanitation access coverage -> Rural	2002	WHO
15	Sanitation access coverage -> Urban	2002	WHO
16	General government expenditure on health -> Total	1998-2002	WHO
17	Total number of health workers per 10000 population -> Total	1997, 2001-2003	WHO
18	Adult literacy rate -> Total	2005	WHO
19	Income per capita	2006	WDI[2]
20	Political Stability and Absence of Violence Index	1996-2006	WGI[3]
21	GDP, current US dollars	1990-2005	WRI[4]
22	Immunization rate for tuberculosis in one-year-olds	2005	WRI
23	Population	1980-2008	WRI
24	Access to improved sanitation	1990, 2004	WRI
25	Adults and children living with HIV	2003, 2005	WRI
26	Physicians per 100,000 people	1990-2004 (one)	WRI
27	National poverty rates	1987-2004 (one)	WRI
28	Underweight children under 5--moderate and severe %	1996-2005 (one)	WRI
29	Literacy rate, all adults %	2000-2004 (one)	WRI
30	Population density per square kilometer	1980-2008	WRI
31	Adult smoking prevalence %	2006	ACS[5]
32	Malnutrition	2001-2006	WDI
33	Per capita total expenditure on health (int'l dollar rate) -> Total	1998-2002	WHO

[1]World health organization (WHO), [2]World Development Indicators (WDI), [3]World Bank Governance Indicators (WGI), [4]World Resource Institute (WRI), [5]American Cancer Society (ACS)

Statistical Analyses

Data were retrieved from WHO, WB, WRI and ACS Tobacco Atlas. After cleaning, entering, and merging data from aforementioned sources, SPSS (version 15) and Microsoft Excel were used for data analysis. Data analyses were conducted in three categories;

a) TB data trends over period of time. Microsoft Excel was used to create graphs. Paired Samples t-tests were used to test for significant change over time. In the data tables, zero (0) means no report where not applicable (N/A) or dot (.) means missing value.

b) TB data comparison; Microsoft Excel was used to draw comparison graphs and Paired Samples t-tests were used to show test of significance for two variables at the entire period as well as at the beginning and at the end of the period. As there were lots of missing values, the mean of data were computed in two periods of time for a variable to show comparison at the beginning (before 2000) and at the end (2000-2005).

c) Comparison of TB burden and DOTS data with different demographic, socioeconomic, health and political variables. The data were not available for all variables during the entire period; one variable data was available for more than 20 years whereas other one existed for only one year. To solve this problem, the mean of data for 2000-2006 was computed for each variable. Also data were available in different databases with differences in values and time (2000-2006), so the mean of them were computed to fill the gap of missing value and time differences. Data with more than two categories and data with minus and plus values were computed to dichotomous variables.

Bivariate correlation was used to explore the association of dependent variable (TB burden and DOTS) with independent variables (different continuous variables).

CHAPTER IV

RESULTS

The primary objective of this study was to identify and describe the progress and barriers of TB control programs in 22 EMR countries of WHO toward MDGs and 1991 National Health Assembly targets for DOTS. Also, the study sought to describe the TB/HIV co-morbidity situation and the relationships of TB burden (incidence, prevalence and mortality) and DOTS with sociopolitical variables.

Comparison of TB burden and DOTS data trend (1990-2005)

The first research question focused on whether the EMR has made progress toward MDGs to reduce TB burden and to reverse TB incidence. The progress in this region was assessed by comparing values from 1990 or 1994/95 to values from 2005 or 2004, using a paired-t test. The results for variables related to TB burden and DOTS are summarized in Table 2.

Table 2. Comparison of TB burden (incidence, prevalence, and mortality) and DOTS between 1990 and 2005.

Variable	Beginning Mean	Ending Mean	Mean difference	95% CI		SD	df	Sig. (2-tailed)
				Lower	Upper			
TB incidence, all forms (per 100 000 population per year) -> Total/ 1990 & 2005	**107**	**97.3**	**9.7**	**-12.2**	**31.6**	**49.4**	**21**	**0.37**
TB incidence, all forms in HIV+ adults (per 100 000 population per year) -> Total/1990 &2005	**0.6**	**6.8**	**-6.2**	**-16.8**	**4.3**	**19.1**	**14**	**0.23**
TB prevalence, all forms (per 100 000 population per year) -> Total/ 1990 &2005	**227.8**	**143.3**	**84.5**	**24.5**	**144.6**	**135.5**	**21**	**0.01**
TB prevalence, all forms in HIV+ adults (per 100 000 population per year) -> Total/1990 &2005	**0.3**	**3.4**	**-3.1**	**-8.4**	**2.2**	**9.5**	**14**	**0.23**
TB mortality, all forms (per 100 000 population per year) -> Total/ 1990 &2005	**23.6**	**16.9**	**6.7**	**-0.9**	**14.2**	**17**	**21**	**0.08**
TB mortality, all forms in HIV+ adults (per 100 000 population per year) -> Total/ 1990 & 2005	**0.3**	**2.1**	**-1.8**	**-4.7**	**1.05**	**5.2**	**14**	**0.2**
DOTS population coverage (%)/1995 &2005	**46.1**	**99.1**	**-53**	**-92.3**	**-13.7**	**47**	**7**	**0.02**
Whole country new smear-positive case detection rate (%)/1995 & 2005	**49.4**	**60.8**	**-11.4**	**-25.3**	**2.5**	**27.1**	**16**	**0.10**
DOTS new smear-positive case detection rate (%)/1995 &2005	**45.1**	**61.2**	**-16.1**	**-36.7**	**4.4**	**24.6**	**7**	**0.11**
DOTS treatment success (%) -> Total/1994 & 2005	**79**	**82**	**-3**	**-12.2**	**6.2**	**8.8**	**5**	**0.44**

TB incidence, all forms had been reduced 9% in EMR between 1990 and 2005. As noted in Table 2, the average decrease for a country was about 10 cases per 100 000. This decline was not statistically different from 0 (Table 2). For the entire region (countries reporting), TB incidence all forms in HIV+ adults increased from 8 to 102 per 100,000 populations during this period. Although not statistically significant, the average country increase was 6 cases per 100 000. The trends (Figure 3) show that except for DJI and SDN, all the countries had decreased TB incidence in this period. It is worth noting that LBN, JOR, and OMN had reduced TB incidence, all forms over 50% in this period. PAK and IRQ had had the same TB incidence rates during the entire period. Furthermore, TB incidence all forms in HIV+ adults was increased in DJI, SOM, and SDN. Further information is included in Table 10 and Figure 9 in the appendixes.

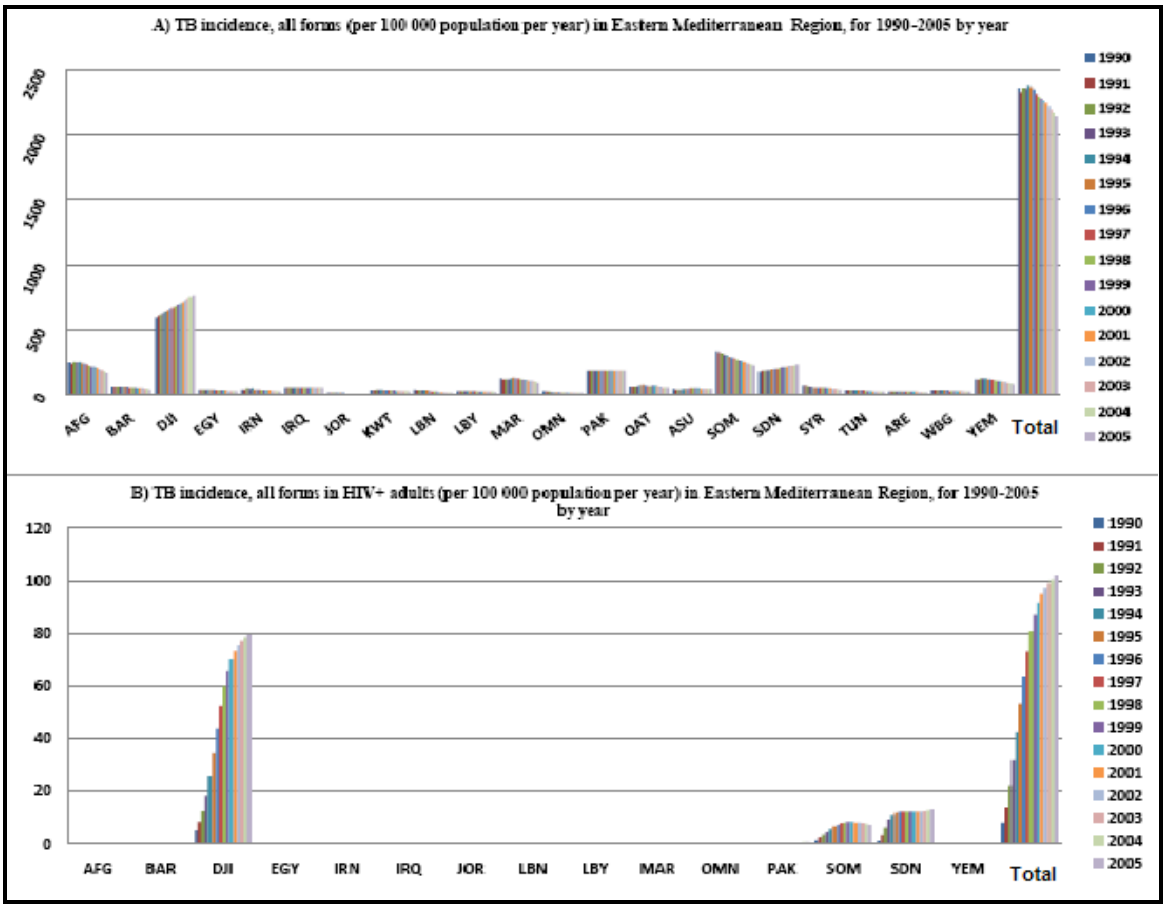

Figure 3. TB incidence in WHO Eastern Mediterranean Region, for 1990 to 2005 by year

MDGs target for TB prevalence was to reduce it by 50% in 2005. Between 1990 and 2005, TB prevalence had reduced 37% for the entire region. As noted in Table 3, the average decrease for countries in this region was approximately 84 cases per 100 000 representing a statistically significant drop in the average number of cases ($p<.05$). TB prevalence all forms in HIV+ adults increased from a total of 4.2 cases per 100 000 in the region in 1990 to 50.4 in 2005. The average increase at the country level was 3.1. As shown in Figure 4, all countries show a decrease in TB prevalence between 1990 and 2005. AFG, BAR, JOR, KWT, LBN, LBY, OMN, SOM, and SYR reduced TB

prevalence 50% or over 50% in this period. The reasons in AFG may be related to interventions such as DOTS, increased access to basic health services (9% of total population had access to basic health services in 2001 and according to AFG ministry of public health, it increased to 65% in 2007), and community participation. The data in SOM also shows an increase in health expenditure and increase in DOTS population coverage. Though DJI showed a decrease in the TB prevalence rate, but it was still the country with the highest rate in 2005. In terms of co-morbidity with HIV, TB prevalence, all forms in HIV+ adults has increased in DJI, SDN and SOM during this period. Table 11 and Figure 10 in the appendixes provide more information about TB prevalence trends in EMR between 1990 and 2005.

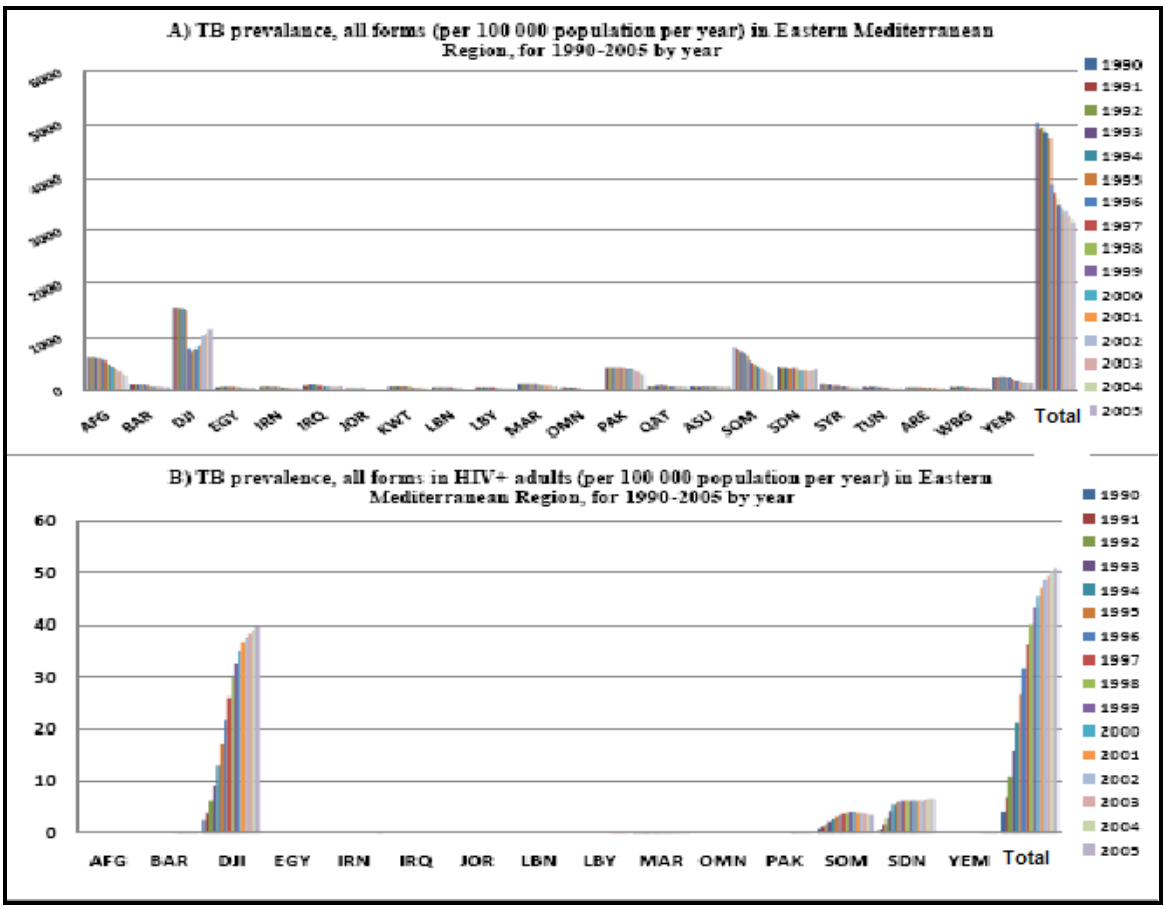

Figure 4. TB prevalence in WHO Eastern Mediterranean Region, for 1990-2005 by year

MDGs target for TB mortality was to show a decrease of 50% in 2005. The results show that TB mortality, all forms per 100,000 populations in the WHO Eastern Mediterranean Region, had decreased 28% between 1990 and 2005. This decrease in country level is 9 deaths, which is not statistically significant (Table3). In EMR, TB mortality all forms in HIV+ adults had increased from 4.5 in 1990 to 31.5 in 2005 which is 2 deaths at the country level. Most countries showed a decreasing trend in TB mortality between 1990 and 2005 (Figure 5), KWT, LBN, LBY, OMN, SOM, and SYR reduced

TB mortality all forms 50% or over 50%. TB mortality all forms in DJI and SDN increased. TB mortality all forms in HIV+ adults had increased in DJI, SDN and SOM during this period. Table 12 and Figure 11 in the appendixes provide more information about TB mortality trend in EMR for 1990 and 2005 by year.

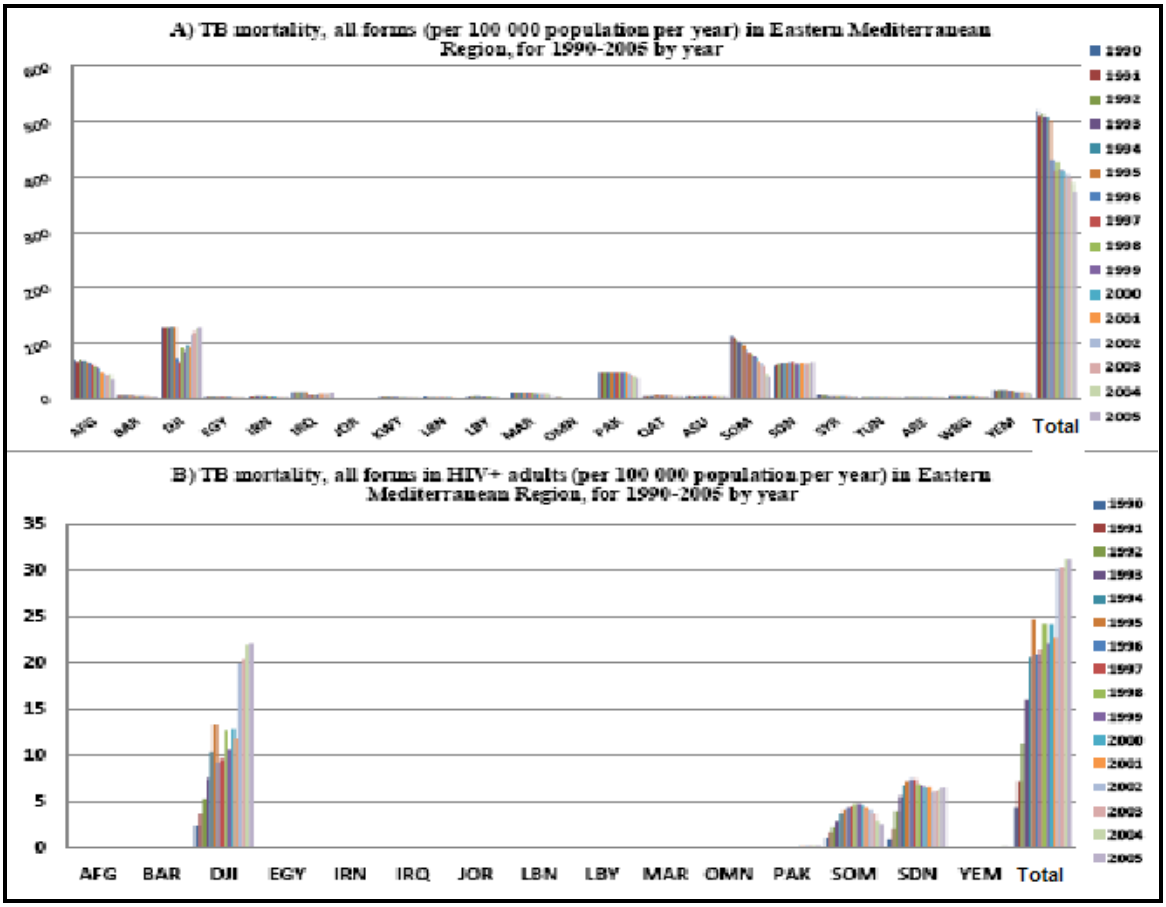

Figure 5. TB mortality in WHO Eastern Mediterranean Region, for 1990-2005 by year

DOTS population coverage had increased 77 times in the whole region. As noted in Table 3, DOTS population coverage for specific countries (n=7) in the EMR region increased from 46% in 1995 to 99% in 2005. This represents a statistically significant increase (p=.02). In 2005, all the EMR countries except ARE, AFG and IRQ had DOTS

population coverage over 90%. Figure 6 and Table 13 in the appendices provide more information about DOTS population coverage in EMR during 1995 and 2005.

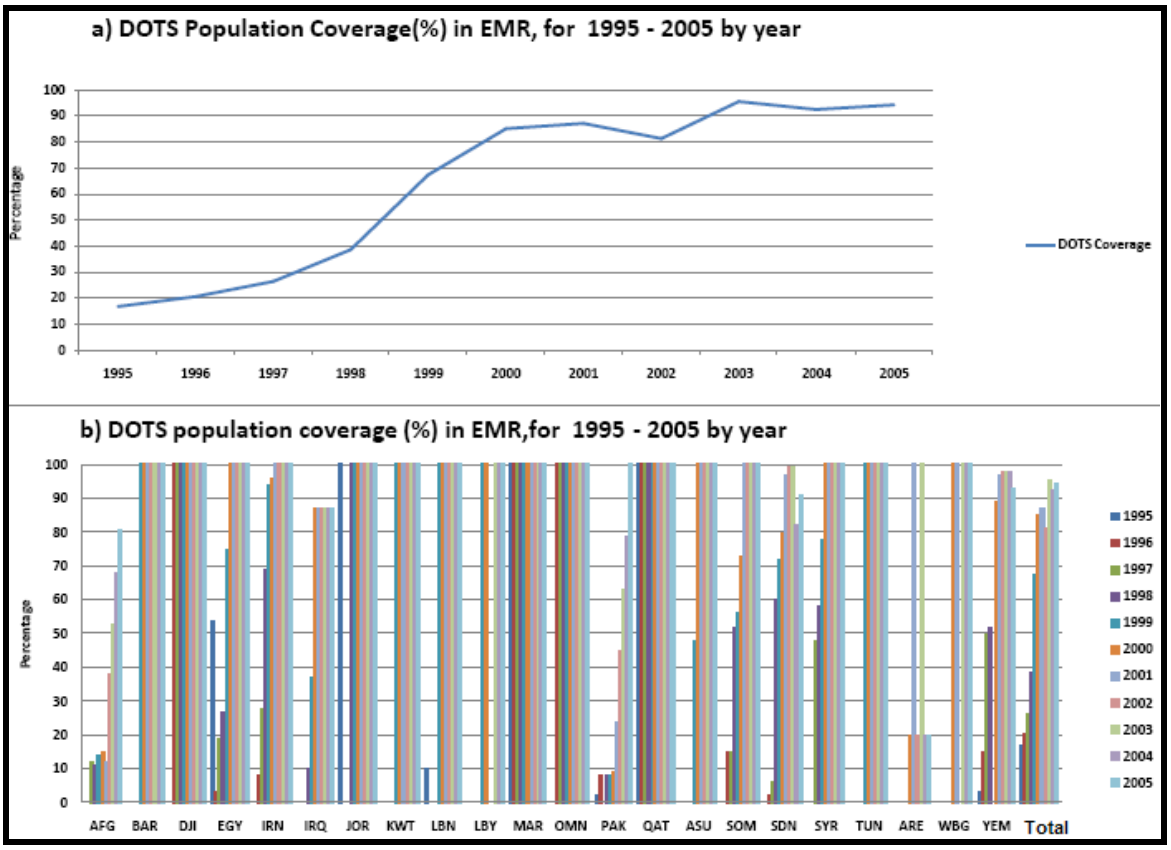

Figure 6. DOTS population coverage in WHO Eastern Mediterranean Region, for 1995-2005 by year

The 1991 National Health Assembly target for DOTS new smear-positive case detection rate was 70% by 2005. The result shows that DOTS new smear-positive case detection rate increased 45 times in the region between 1995 and 2005, which is 16% at the country level; however, this increase was not statistically significant (Table 2). In 2005, LBY, MAR and OMN had over 100% DOTS new smear-positive case-detection rates whereas DOTS new smear- positive case detection rates were lower in WBG (2%), ARE (19%) and SDN (35%). Figures 7, 12 and Table 14 in the appendices provide

further information about TB new smear-case detection rates in EMR during 1995 and 2005.

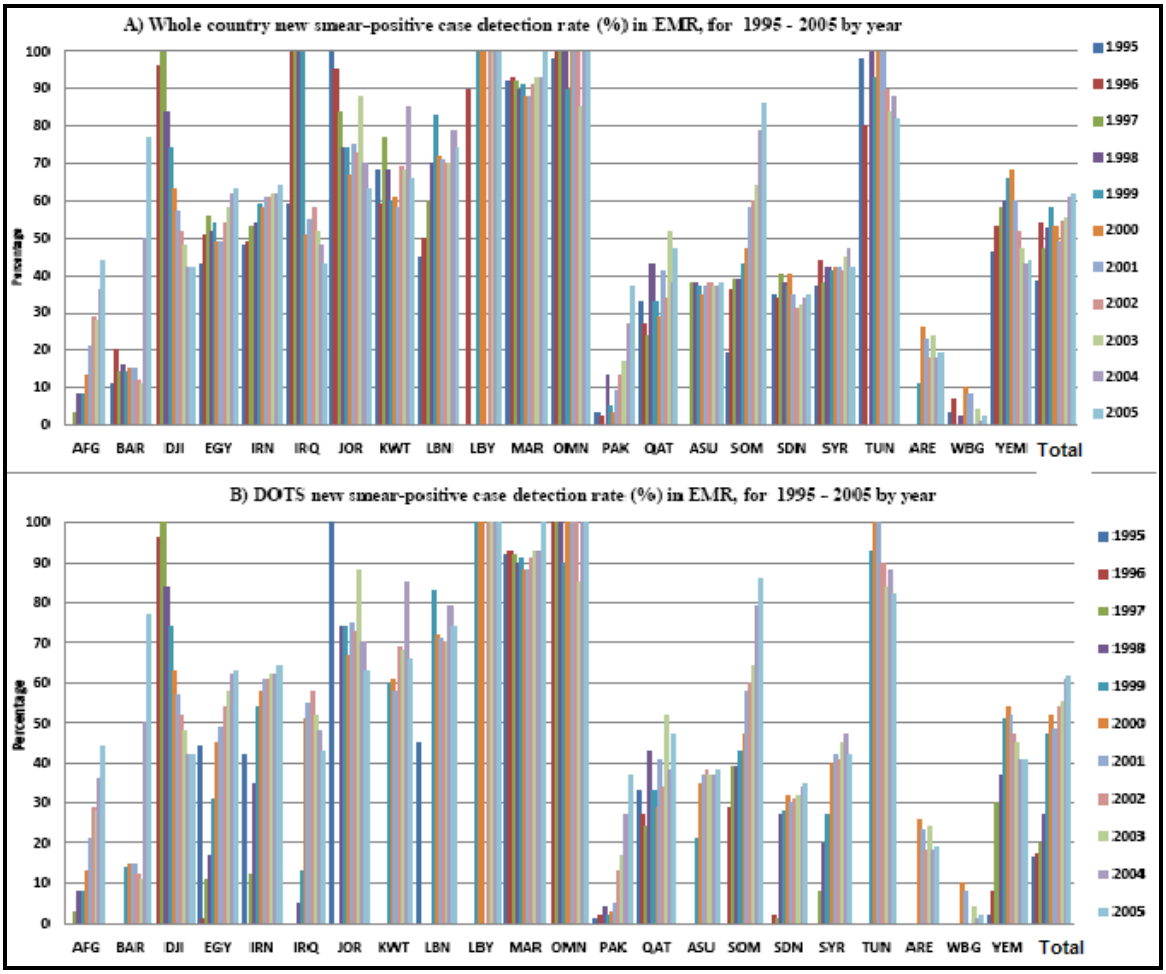

Figure 7. TB new smear-positive case detection rates in WHO Eastern Mediterranean Region, for 1995-2005 by year

The 1991 National Health Assembly target for DOTS treatment success rate was 85% by 2005. The result shows that DOTS treatment success in the EMR region had increased 58 times in 2004. On average, there was a 3% increase per country which was not statistically significant (Table 2). All countries in the region show an increase in

DOTS treatment success. Figures 8, 13 and Table 15 in the appendices provide more information about DOTS treatment success in EMR.

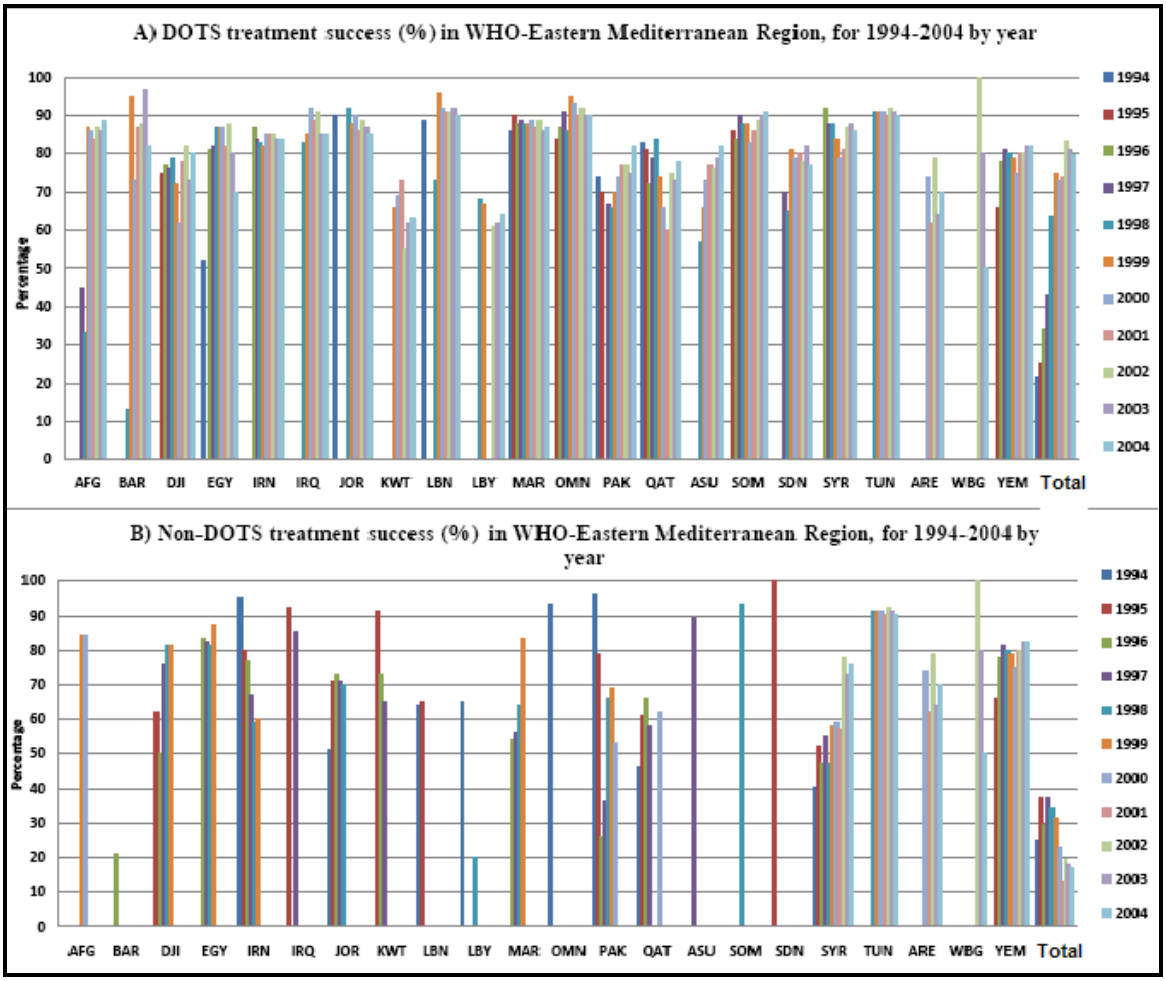

Figure 8. DOTS and Non-DOTS treatment success in WHO Eastern Mediterranean Region, for 1994-2004 by year

<u>TB burden comparison with TB/HIV co-morbidity rates (1990-2005)</u>

The second research question focused on the TB/HIV co-morbidity situation in the EMR region. TB burden all forms was compared with TB burden all forms in HIV+ adults per 100,000 populations. Graphical methods and paired samples t-tests were used to compare the two variables over the entire period as well as at the beginning and at the

end of the period, respectively. Because of the number of missing values over the time period, the mean of data were computed in two periodic times for a variable to show comparison at the beginning (1990- 2000) and at the end (2000-2005). Table 3 summarizes the results of paired samples t-tests used to compare TB burden all forms with TB burden all forms in HIV+ adults per 100,000 populations.

Table 3. Comparison of TB Burden (incidence, prevalence and mortality), all forms with TB burden, all forms in HIV+ adults per 100,000 populations between 1990 and 2005.

Variable	First Variable Mean	Sec. Variable Mean	Mean difference	95% CI		s.d.	df	Sig. (2-tailed)
				Lower	Upper			
TB incidence, all forms with TB incidence, all forms in HIV+ adults (per 100 000 population per year) -> Total/1990-2005	**134.6**	**4.4**	**130.2**	**41.1**	**219.2**	**160.8**	**14**	**0.007**
TB incidence, all forms with TB incidence, all forms in HIV+ adults (per 100 000 population per year) -> Total/1990-1999	**136.8**	**3.2**	**133.6**	**46.2**	**220.9**	**157.8**	**14**	**0.005**
TB incidence, all forms with TB incidence, all forms in HIV+ adults (per 100 000 population per year) -> Total/2000-2005	**130.9**	**6.5**	**124.4**	**32.1**	**216.9**	**166.8**	**14**	**0.012**
TB prevalence, all forms with TB prevalence, all forms in HIV+ adults (per 100 000 population per year) -> Total/1990-2005	**239.5**	**2.2**	**237.3**	**66.6**	**406.0**	**304.6**	**14**	**0.009**
TB prevalence, all forms with TB prevalence, all forms in HIV+ adults (per 100 000 population per year) -> Total/1990-1999	**263.9**	**1.5**	**262.4**	**78.7**	**446.0**	**331.6**	**14**	**0.008**
TB prevalence, all forms with TB prevalence, all forms in HIV+ adults (per 100 000 population per year) -> Total/2000-2005	**198.8**	**3.3**	**195.5**	**50.3**	**340.8**	**262.2**	**14**	**0.012**
TB mortality, all forms with TB mortality, all forms in HIV+ adults (per 100 000 population per year) -> Total/1990-2005	**27.6**	**1.4**	**26.2**	**8.3**	**44.1**	**32.4**	**14**	**0.007**
TB mortality, all forms with TB mortality, all forms in HIV+ adults (per 100 000 population per year) -> Total/1990-1999	**29.4**	**1.1**	**28.3**	**8.9**	**47.6**	**34.9**	**14**	**0.007**

TB mortality, all forms with mortality, all forms in HIV+ adults (per 100 000 population per year) -> Total/2000-2005	**24.5**	**1.8**	**22.7**	**6.6**	**38.7**	**28.9**	**14**	**0.009**

The difference between TB burden (incidence, prevalence and mortality), all forms with TB burden, all forms in HIV+ adults per 100,000 population was much at the beginning and it lessened in 2005 which suggests that TB/HIV co-morbidity had gradually increased in the region. It should be mentioned that this difference was statistically significant during the entire period (Table 3). Figures 3-5, Figures 9-11, and Tables 10-12 provide further information about this comparison in EMR.

DOTS comparison with Whole country new-smear positive case detection rate and Non-DOTS treatment success rates (1995-2005)

DOTS data were compared with Whole country new-smear positive case detection rates and Non-DOTS treatment success rates. Graphs and paired samples t-tests were used to compare the two variables for the entire period as well as at the beginning and at the end of the period. Because of the number of missing values over the time period, the mean was computed for two periodic times for the purpose of comparison of the beginning (1994- 2000) and end (2000-2005) of the period. Table 4 summarizes the results of paired samples t-tests to compare DOTS data with Whole country new-smear positive case detection rates and Non-DOTS treatment success rates.

Table 4. Comparison of DOTS new-smear positive case detection and treatment success rates with Whole country new-smear positive case detection rate and Non-DOTS treatment success rate, 1995-2005

Variable	First variable Mean	Sec. variable Mean	Mean difference	95 CI		s.d.	df	Sig. (2-tailed)
				Lower	Upper			
Whole country new smear-positive case detection rate (%)/1995-2005 - DOTS new smear-positive case detection rate (%)/1995-2005	**57.1**	**52.9**	**4.2**	**-1.1**	**9.5**	**11.9**	**21**	**0.12**
Whole country new smear-positive case detection rate (%)/1995-1999 - DOTS new smear-positive case detection rate (%)/1995-1999	**61.2**	**48.8**	**12.4**	**-2.1**	**26.8**	**30.9**	**19**	**0.09**
Whole country new smear-positive case detection rate (%)/2000-2005 - DOTS new smear-positive case detection rate (%)/2000-2005	**56.9**	**56.5**	**0.4**	**-0.1**	**0.9**	**1.3**	**21**	**0.13**
DOTS treatment success (%) -> Total/1994-2004 - Non-DOTS treatment success (%) -> Total/1994-2004	**78.9**	**71.5**	**7.4**	**-2.1**	**16.9**	**19.1**	**17**	**0.12**
DOTS treatment success (%) -> Total/1994-1999 - Non-DOTS treatment success (%) -> Total/1994-1999	**75.6**	**67.8**	**7.8**	**-0.7**	**16.2**	**15.9**	**15**	**0.07**
DOTS treatment success (%) -> Total/2000-2004 - Non-DOTS treatment success (%) -> Total/2000-2004	**82.4**	**66.9**	**15.5**	**-1.7**	**32.7**	**10.8**	**3**	**0.07**

In 1995, there was a 22% difference between Whole country (38%) and DOTS (16%) new smear-positive case detection rates in the region. DOTS new smear-positive case detection rate increased tremendously to 61% and there was only a 1% difference with Whole country new smear-positive case detection rate (62%) in 2005. The result of paired sample t-tests shows the average country difference was 4.2 which was not statistically significant during the entire period (Table 4). Tables 14, Figures 7, and 12 also provide information about mentioned difference.

As a whole in the region, DOTS treatment success rate was 3 times lower than Non-DOTS in 1994, but it increased remarkably and it was 63 times higher than Non-DOTS in the region by 2004. As noted in Table 4, the average difference between DOTs and Non-DOTS treatment success rate was 7.4 for the entire period which was not statistically significant. Figures 8, 13 and Table 15 also provide information about DOTS and Non-DOTS treatment success comparison.

TB burden and DOTS comparison with some sociopolitical variables (2000-2006)

The final research question focused on the exploration of associations between TB burden and DOTS and specific sociopolitical variables in EMR countries. Data was not available for all variables during the entire period. For example, one variable had data available for more than 20 years whereas another variable had data for only one year. To solve this problem, the mean of all data for 2000-2006 was computed. Also, the same data was available in different databases with some differences in values and time (2000-2006), so the mean of them was computed to fill the gap of missing values and time differences. Income per capita variable with more than two values and political stability with minus and plus values were

recoded to dichotomous variables. Bivariate correlations were used to explore the association of the dependent variable (TB burden and DOTS) with independent variables.

Table 5. Association of TB incidence with some demographic, health, socio-economic and political variables

Variable	Spearman's rho	Sample size	Sig. (2-tailed)
DOTS population coverage (%)/2000-2005	-.090	22	.690
Adult smoking prevalence %/ 2006	.195	21	.397
Adult Literacy Rate total (%)/ 2000-2005	-.620**	19	.005
National poverty rates/1987-2004	.771	6	.072
Physicians per 100,000 people/ 1990-2004	-.747**	21	.000
Immunization rate for tuberculosis in one-year-olds/2005	-.699**	18	.001
Malnutrition/ 2001-2006	.669**	22	.001
Population density per square kilometer/2000-2006	-.119	22	.597
Income per capita/2006	-.094	22	.677
Political Stability and Absence of Violence Index/2000-2006	-.385	22	.077
Total number of health workers per 100 000 population -> Total/2001-2003	-.623**	20	.003
General government expenditure on health -> Total/2000-2002	-.287	21	.207
GDP, current US dollars/2000-2005	-.132	21	.567
Access to improve sanitation (%)/2002-2004	-.635**	21	.002
Adults and children living with HIV/ 2003-2005	.154	13	.615

The dependent variable is TB incidence all forms per 100,000 populations
**p<.01

The results of bivariate correlation analysis (Table 5) shows that TB incidence has a positive relationship with malnutrition, national poverty level (NPL), HIV and adult smoking rate (ASR). The associations between TB incidence and malnutrition (r_s=.67,

p<.01) and TB incidence and national poverty level (r_s=.77, p=.07) were relatively strong. As the malnutrition rate increases and as NPL increases, TB incidence per 100,000 population increases.

Adult literacy rate (ALR), total number of health workers and physicians, access to improved sanitation, gross domestic product (GDP), general government expenditure on health, TB immunization, income per capita, political stability, DOTS population coverage and population density have an inverse association with TB incidence within a county. As ALR increases, TB incidence decreases (r_s =-.62, p=.005). An increase in total number of physicians (r_s =-.75, p<.001) is associated with decreases in TB incidence and an increase in total number of health workers is associated with a decrease in TB incidence (r_s =-.62, p<.01). Access to improved sanitation is associated with decreased TB incidence (r_s =-.64, p<.01). Although not statistically significant, GDP and general government expenditure on health seems to be associated with lower TB incidence within a country. Higher BCG immunization rates are associated with lower TB incidence (r_s =-.70, p<.01). In addition, there appears to be a moderate negative association between TB incidence and political stability (r_s =-.39, p=.077).

Table 6. Associations between TB prevalence and some demographic, health, socio-economic and political variables.

Variable	Spearman's rho	Sample size	Sig. (2-tailed)
DOTS population coverage (%)/2000-2005	-.200	22	.373
Adult smoking prevalence %/ 2006	.216	21	.348
Adult Literacy Rate total (%)/ 2000-2005	-.594**	19	.007
National poverty rates/1987-2004	.886*	6	.019
Physicians per 100,000 people/ 1990-2004	-.718**	21	.000
Immunization rate for tuberculosis in one-year-olds/2005	-.687**	18	.002
Malnutrition/ 2001-2006	.685**	22	.000
Population density per square kilometer/2000-2006	-.092	22	.684
Income per capita/2006	-.094	22	.677
Political Stability and Absence of Violence Index/2000-2006	-.385	22	.077
Total number of health workers per 100 000 population -> Total/2001-2003	-.642**	20	.002
General government expenditure on health -> Total/2000-2002	-.251	21	.272
GDP, current US dollars/2000-2005	-.160	21	.489
Access to improve sanitation (%)/2002-2004	-.637**	21	.002
Adults and children living with HIV/ 2003-2005	.225	13	.460

The dependant variable is TB prevalence per 100,000 populations
** p<.01
* p<.05.

Table 6 contains the results of the bivariate correlation analysis of TB prevalence with sociopolitical variables. As might be expected, the results are very similar to those for incidence. TB prevalence was positively associated with malnutrition, national

poverty level (NPL), HIV and adult smoking rate (ASR). Higher malnutrition rates, were associated with higher TB prevalence (r_s =.69, p<.001). Increases in NPL were associated with increases in TB prevalence (r_s =.89, p<.05).

Adult literacy rate (ALR), total number of health workers and physicians, access to improved sanitation, gross domestic product (GDP), general government expenditure on health, BCG immunization, income per capita, political stability, DOTS population coverage and population density have an inverse relationship with TB prevalence. As ALR increases, TB prevalence decreases (r_s =-.59, p<.01). A higher number of physicians per 100,000 population is associated with lower TB prevalence (r_s =-.72, p<.001) and a higher total number of health workers is associated with lower TB prevalence (r_s =-.64, p<.01). Access to improved sanitation is associated with decreased TB prevalence (r_s =-.64, p<.01). A higher BCG immunization rate is associated with decreased TB prevalence (r_s =-.69, p<.01). TB prevalence shows evidence of an association with political stability (r_s =-.39, p=.077) with more stable countries having lower TB prevalence.

Table 7 shows the results of bivariate correlation analyses for TB mortality and sociopolitical variables. These results suggest that TB mortality has a positive relationship with malnutrition, national poverty level (NPL), HIV and adult smoking rate (ASR). Similar to previous results, as malnutrition rate increases TB mortality increases (r_s =-.69, p<.001). Increases in NPL are also associated with increases in TB mortality (r_s =-.89, p<.05).

Table 7. Association between TB mortality and some demographic, health, socio-economic and political variables.

Variable	Spearman's rho	Sample size	Sig. (2-tailed)
DOTS population coverage (%)/2000-2005	-.469*	22	.028
Adult smoking prevalence %/ 2006	.244	21	.287
Adult Literacy Rate total (%)/ 2000-2005	-.594**	19	.007
National poverty rates/1987-2004	.886*	6	.019
Physicians per 100,000 people/ 1990-2004	-.739**	21	.000
Immunization rate for tuberculosis in one-year-olds/2005	-.726**	18	.001
Malnutrition/ 2001-2006	.686**	22	.000
Population density per square kilometer/2000-2006	-.123	22	.587
Income per capita/2006	-.120	22	.595
Political Stability and Absence of Violence Index/2000-2006	-.411	22	.058
Total number of health workers per 100,000 population -> Total/2001-2003	-.670**	20	.001
General government expenditure on health -> Total/2000-2002	-.285	21	.210
GDP, current US dollars/2000-2005	-.133	21	.567
Access to improve sanitation (%)/2002-2004	-.649**	21	.001
Adults and children living with HIV/ 2003-2005	.462	13	.112

The dependant variable is TB mortality per 100,000 populations
** p<.01
* p<.05.

Adult literacy rate (ALR), total number of health workers and physicians, access to improved sanitation, general domestic product (GDP), general government expenditure on health, BCG immunization, income per capita, political stability, DOTS population coverage and population density per 100,000 have inverse relationships with TB

mortality. As ALR increases TB mortality decreases (r_s =-.59, p<.01). Increases in total number of physicians per 100,000 population is associated with decreases in TB mortality (r_s =-.74, p<.001) and a higher total number of health workers is associated with lower TB mortality (r_s =-.67, p=.001). Again, greater access to improved sanitation is associated with lower TB mortality (r_s =-.65, p=.001). A higher BCG immunization rate is also associated with lower TB mortality (r_s =-.73, p=.001). TB mortality appears to be lower in stable countries compared with unstable countries (r_s =-.41, p=.058). Higher DOTS population coverage is associated with lower TB mortality (r_s =-.47, p=.028). Population density has a weak and no significant negative association with TB mortality in this region.

Table 8 shows the results of the bivariate correlation analysis for DOTS population coverage and sociopolitical variables. DOTS population coverage has an inverse relationship with malnutrition, HIV, national poverty level (NPL) and adult smoking rate (ASR). Higher malnutrition rates are associated with lower DOTS population coverage (r_s =-.70, p<.001). Higher NPL is also associated with lower DOTS coverage (r_s =-.78, p=.069).

Adult literacy rate (ALR), total number of health workers, number of physicians, access to improved sanitation, general government expenditure on health, BCG immunization have a positive relationship with DOTS. Higher ALR is associated with higher DOTS coverage (r_s =.65, p<.01). A higher total number of physicians per 100,000 population is associated with higher levels of DOTS coverage (r_s =.44, p<.05) and a higher total number of health workers is associated with greater DOTS coverage (r_s =.54, p<.05). Greater access to improved sanitation is associated with higher levels of

Table 8. Association between DOTS population coverage and some demographic, health, socio-economic and political variables.

Variable	Spearman's rho	Sample size	Sig. (2-tailed)
Adults and children living with HIV/ 2003-2005	-.378	13	.203
Adult smoking prevalence %/ 2006	-.118	21	.610
Adult Literacy Rate total (%)/ 2000-2005	.648**	19	.003
National poverty rates/1987-2004	-.778	6	.069
Physicians per 100,000 people/ 1990-2004	.440*	21	.046
Immunization rate for tuberculosis in one-year-olds/2005	.450	18	.061
Malnutrition/ 2001-2006	-.696**	22	.000
Population density per square kilometer/2000-2006	.209	22	.351
Income per capita/2006	.129	22	.567
Political Stability and Absence of Violence Index/2000-2006	.129	22	.567
Total number of health workers per 100,000 population -> Total/2001-2003	.543*	20	.013
General government expenditure on health -> Total/2000-2002	.293	21	.197
GDP, current US dollars/2000-2005	-.084	21	.716
Access to improve sanitation (%)/2002-2004	.469*	21	.032

The dependant variable is DOTS population coverage
** p<.01
* p<.05.

DOTS coverage (r_s =.47, p<.05). Although not statistically significant, higher general government expenditure on health is associated with greater DOTS coverage (r_s =.29, p=.197). Higher BCG immunization rates are associated with higher DOTS

coverage (r_s =.45, p=.061) . DOTS population coverage has a positive and weak association with population density per 100,000 and political stability.

CHAPTER V

DISCUSSION

The objective of this study was to determine TB progress in the WHO Eastern Mediterranean Region (EMR) toward MDGs of halting global TB burden (prevalence and death rate) by 50% in 2015 and to eliminate TB by 2050 compared with 1990. Also, the study explored the progress toward the 1991 44th World Health Assembly targets for DOTS to detect at least 70% of new sputum smear-positive TB cases, and to cure 85% of reported TB cases by 2005 (11). Finally, the study was designed to explore the potential associations of TB burden and DOTS population coverage with some demographic, health, socio-economic and political factors.

TB incidence, all forms has decreased about 9 % in the WHO EMR during the time from 1990 to 2005 which is about a 10 case decrease for individual countries. However, TB incidence, all forms in HIV+ adults has increased during this same time period. TB prevalence, all forms has decreased 37% per 100,000 populations in the region which is an 84 case decrease in each country of the region. However, TB prevalence, all forms in HIV+ adults has increased during the time period from 1990 to 2005. While TB mortality has decreased by 28% between 1990 and 2005, TB morality all forms in HIV+ adults has dramatically increased in the region. TB incidence, all forms, and TB mortality, all forms in DJI and SDN had increased during this period. PAK and IRQ had constant TB incidence, all forms rates between 1990 and 2005. It is worth noting that LBN, and OMN reduced TB burden all forms, and JOR reduced TB incidence and prevalence more than 50% in the region in this period. KWT, LBY, SOM, and SYR reduced TB prevalence and mortality all forms more than 50% between 1990 and 2005.

AFG and BAR reduced TB prevalence over 50% in this period. TB/HIV co-morbidly and mortality has increased between 1990 and 2005 especially in three countries (DJI, SOM and SDN).

In sum, the WHO EMR as a region had declined TB burden, all forms across the region, but still did not meet MDG 6 target 8 of reducing to 50%. LBN, and OMN are the only two countries that met MDGs 6 target 8 for TB in 2005 . However, TB/HIV co-morbidity is growing fast in the region especially in higher HIV epidemic countries such as DJI, SDN, and SOM.

DOTS population coverage had increased 77 fold between 1995 and 2005, which is about a 53% increase at the individual country level. This represented a significant increase in DOTS coverage. In 2005, ARE with 20%, AFG with 81% and IRQ with 87% coverage had lower DOTS population coverage compared with other countries in the region.

DOTS new smear-positive case detection rate had increased 45 fold between 1995 and 2005 which is about a 16% increase in each country of the region. In 2005, LBY, MAR and OMN had over 100% DOTS smear-positive case detection rates whereas WBG with 2%, ARE 19% and SDN with 35% had lower DOTS smear-positive case detection rates. Though the EMR had increased DOTS new-smear positive case detection rate, 61% in 2005, it still did not achieve 1991 NHA target of 70% DOTS new-smear positive case detection rate.

DOTS treatment success rate had increased 58% in the EMR which is about a 3% increase in each country of the region. This indicated progress and the replacement of Non-DOTS treatment programs. Three countries, however, WBG with 50%, KWT with 63%, and LBY with 64% had lower DOTS treatment success rates in 2005. In spite of increasing DOTS treatment success rate to 80% in 2005, the EMR as a region did not meet the 1991 NHA target of 85% DOTS treatment success rate.

In sum, the WHO EMR increased its DOTS population coverage, as demonstrated by the DOTS new smear-positive case detection rate and DOTS treatment success rate between 1994 or 1995 and 2004 or 2005, but still did not meet 1991 Forty-fourth World Health Assembly targets of 70 % DOTS new smear-positive case detect rate and an 85% DOTS treatment success rate.

It is worth mentioning that LBM and OMN are the only two countries who achieved both MDGs and DOTS targets between 1990 and 2005.

Pertaining to other demographic, health, socio-economic and political factors in this study, health workforce, improved sanitation, BCG immunization, adult literacy rate, political stability, government total health expenditure on health and income had inverse relationships with TB burden and positive relationships with DOTS population coverage. However, malnutrition, national poverty level (NPL), HIV and adult smoking rate (ASR) had positive relationships with TB burden and inverse relationships with DOTS population coverage.

Total numbers of health workers and physicians had inverse relationships with TB burden and positive relationships with DOTS population coverage. The results suggested increasing the number of health care workers and physicians per 100,000 had the effect of decreasing TB incidence, prevalence and mortality rates and increasing DOTS population coverage.

BCG immunization had an inverse relationship with TB burden and a positive relationship with DOTS within a country. Increasing BCG immunization coverage seems to have the effect of decreasing TB incidence, prevalence and mortality.

Adult literacy rate had an inverse relationship with TB burden and a positive relationship with DOTS. In countries where the adult literacy rate was high, TB incidence, prevalence and mortality rates were low. Also, higher adult literacy rate was associated with greater DOTS population coverage.

Access to improved sanitation within a country was associated with decreased TB incidence, prevalence and mortality as well as increased DOTS population coverage.

Developed and stable countries seemed to have somewhat lower rates of TB incidence, prevalence and mortality. However, developed and stable countries seemed to have only slightly higher DOTS population coverage. While the relationship between political stability and the TB burden variables was moderate, the relationship with DOTS coverage was relatively weak.

GDP and government general health expenditure had weak to moderate relationships with TB burden and DOTS. In this region, higher GDP and general health expenditure within a country was associated with lower TB incidence, prevalence and mortality rates. In additions, higher government general health expenditures were

associated with greater DOTS coverage. Interestingly, higher GDP seemed to be associated with lower DOTS population coverage. However, it should be noted that the correlation coefficient was small and not statistically significant (r_s =-.08, p=.716).

National poverty level (NPL), HIV and malnutrition had direct relationships with TB burden and inverse relationships with DOTS population coverage. When NPL increased within a country, TB incidence, prevalence and mortality rates increased. Although these relationships were strong (coefficients >.70) and statistically significant, it should be noted the sample size was restricted to only seven of the countries in the region. Again, NPL and malnutrition seemed to have strong negative relationships with DOTS population coverage. HIV and Adult smoking rates appeared to have weak positive relationships with TB incidence, prevalence and mortality rates as well as weak negative relationships with DOTS population coverage. While none of these relationships were statistically significant, the relationship between HIV and TB mortality remained noteworthy as it suggested a moderate relationship between HIV and TB mortality (r_s = .46, p=.112).

The other interesting point was an increase in population density decreased TB incidence, prevalence and mortality rates whereas it increased DOTS population coverage.

Study Limitations

This was an ecological study--using secondary data-- from WHO World Atlas, WB, WRI and ACS. The findings of this study describing the current overall situation regarding TB for the WHO Eastern Mediterranean region may not be generalized to other

regions in the world or to individual countries in the region. To get more in depth data on the TB situation, it would be more ideal to have research being performed at the individual country level which would only be possible given more available resources and time.

The unit of analysis was at the country level for one specific region, so the sample size was small (n=22), which has implications (sampling bias, reduced power, less precision) for any statistical analysis focused specifically on hypothesis testing. However, the main purpose of this study was to describe the TB situation in this region, not to test hypotheses with the purpose of generalizing beyond the countries included in the study. In this case, it is more useful to consider the analyses presented in terms of describing the characteristics of the TB situation in the EMR.

For some variables, data were not available on an annual basis for all countries which lead to a considerable amount of missing data. Many variables were not always available for the entire period. For instance, one variable was available for 20 years, whereas another was only available for one year. Analysis of data by gender and age was also not possible due to limitations of reporting methods. The quality of data available through the sources used in this study was not clear. For example, differences were noted for the same variable included in different databases as well as differences for some variables included in the same database in more than one location. And finally, TB/HIV all ages, MDR-TB and XDR-TB data were not accessible in WHO World Atlas.

Conclusions and Recommendations

Policy makers and Stop TB stakeholders, in collaboration with scientists and research institutes, may wish to consider the following recommendations regarding the improvement of the ongoing TB surveillance and intervention programs in the Eastern Mediterranean Region of WHO.

We need to allocate more resources to achieve MDG6 (halve TB prevalence and mortality by 2015 and reverse the incidence of TB) by implementation and extending Stop TB Strategy in the region, which will also help to achieve targets of 70% of DOTS detection rate and 85% DOTS treatment success rate in the region.

We should prioritize countries with high TB burden such as AFG and PAK as well as countries with high TB/ HIV burden such as DJI, SDN and SOM. Strong commitments and further involvement of economic developed countries such as ARE, KWT and ASU toward implementation of Stop TB strategy in the region are required.

Enhance coordination and share experiences via conducting annual meetings and conferences. This will help the members to see their progress, become aware of the interventions and replicate some feasible interventions to their settings.

Conduct detailed country situation analysis and assessments of TB control programs, setting targets for each country and tracking the progress. This will help each country to achieve MDGs via DOTS and Stop TB Strategy.

Perform advocacy, increasing TB information education and communication (IEC), and social mobilization, especially in countries with a high burden of TB, MDR-TB, XDR-TB and TB/HIV co-morbidity.

Improve TB surveillance system by collecting annual data from all the countries, and using unified reporting formats to decrease missing values. Also, improve quality of data and coordination among data producing organizations.

Finally, conduct research and surveillance about some other TB relevant variables such as TB/HIV all ages, MDR-TB, XDR-TB, age categories and gender. Also, conducting further research to explore the associations between TB variables and other sociopolitical variables used in this study.

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APPENDIXES

Appendix A: IRB Protocol Approval

INSTITUTIONAL REVIEW BOARD

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February 22, 2008

Principal Investigator: Eriksen, Michael P

Co-PIs: Derek Shendell, Frances Mccarty, Solomon I Okosun

Student PI: Khoaja M Khaled

Protocol Department: Institute of Public Health

Protocol Title: An overview of the progress of TB programs toward Millennium Development Goals (MDG) in East Mediterranean Region (EMRO) of World Health Organization (WHO)

Submission Type: Protocol H08337

Review Type: Exempt Review

Approval Date: February 22, 2008

The Georgia State University Institutional Review Board (IRB) reviewed and approved your IRB protocol entitled An overview of the progress of TB programs toward Millennium Development Goals (MDG) in East Mediterranean Region (EMRO) of World Health Organization (WHO). The approval date is listed above.

Exempt protocols do not require yearly renewal. However, if any changes occur in the protocol that would change the category of review, you must re-submit the protocol for IRB review. When the protocol is complete, a Study Closure Form must be submitted to the IRB.

Any adverse reactions or problems resulting from this investigation must be reported immediately to the University Institutional Review Board. For more information, please visit our website at www.gsu.edu/irb.

Sincerely,

Susan Laury, IRB Vice Chair

Federal Wide Assurance Number: 00000129

Appendix B: Tables

Table 9. Countries in WHO Eastern Mediterranean Region (100-105, 108)

Countries in WHO Eastern Mediterranean Region

S/N	Country	Ab (WHO)	Government (CIA)	Capital (CIA)	Location (CIA)	Population in X1000/ 2006 (WRI)	Population density per square kilometer/2006 (WRI)	Income per capita/2006 (WB)	Political Stability and Absence of Violence Index/2006 (WB)	General government expenditure on health (2000-2002) (WHO)	GDP, current US dollars/2005 (WRI)	Access to improved sanitation/ 2002-2004, (WHO, WRI)	Malnutrition (2001-2006) (WD)	Adult literacy rate (2000-2005) (WHO, WRI)	Total number of health workers per 10000 population -> Total/2001-2003 (WHO)	Physicians per 100,000 people/ 1990-2004 (WRI)	National poverty rates/1987-2004 (WRI)	Adult smoking prevalence %/ 2006 (ACS)	Immunization rate for DPT in one-year-olds %/2005 (WRI)	Immunization rate for tuberculosis in one-year-olds/2005 (WRI)	Per capita total expenditure on health (Int.Dollar per person)/1998-2002 (WHO)
1	Afghanistan	AFG	Islamic republic	Kabul	Southern Asia	31082	47.7	1	-2.29	16	7308	18.33	39.15	28.1	4	18.6	.	49.5	76	73	26
2	Bahrain	BAR	consittional monarchy	Manama	Middle East	739	1040.8	4	-0.42	10.67	12914	100	9	86.75	64	108.7	.	10.2	98	.	813
3	Djibouti	DJI	Republic	Djibouti	Eastern Africa	807	34.8	2	-0.2	10.33	709	54.67	26.9	.	10	18.1	.	42.5	71	52	72
4	Egypt	EGY	Republic	Cairo	Northern Africa	75437	75.8	2	-0.87	6	89369	70	7.3	63.7	49	53.5	16.7	28.8	98	98	235
5	Iran	IRN	Islamic Republic	Tehran	Middle East	70324	43	2	-1.25	10.33	189784	82	11	77	28	45	.	10.6	95	99	498
6	Iraq	IRQ	Parlimentary democracy	Baghdad	Middle East	29551	67.6	2	-2.91	1	.	74	12	74.1	18	65.8	.	22.5	81	93	64
7	Jordan	JOR	Consittional monarchy	Amman	Middle East	5837	66.1	2	-0.53	12.67	12712	90.67	4.2	90.45	52	203	14.2	29.8	95	89	440
8	Kuwait	KWT	Consittional emirate	Kuwait	Middle East	2765	155.2	4	0.28	6	80781	.	10	88.15	58	152.5	.	17	99	.	567
9	Lebanon	LBN	Republic	Beirut	Middle East	3614	353.3	3	-1.76	9.67	21944	95	3.95	.	40	325.3	.	35.7	92	.	730
10	Libyan Arab Jamahiriya	LBY	Jamahiriya	Tripoli	Northern Africa	5968	3.4	3	0.24	5	38756	96.67	5	82	62	129	.	4	98	99	327
11	Morocco	MAR	Consittional monarchy	Rabat	Northern Africa	31943	71.6	2	-0.31	4.67	51621	62.33	10.1	51.65	14	51.5	19	14.3	98	95	218
12	Oman	OMN	Monarchy	Muscat	Middle East	2612	8.4	3	0.66	7	.	79	18	77.7	46	131.9	.	8.6	99	98	419
13	Pakistan	PAK	Federal republic	Islam Abad	Southern Asia	161209	209.1	1	-1.92	3.33	110732	62	37.2	45.95	12	73.9	32.6	16	72	82	48
14	Qatar	QAT	Emirate	Doha	Middle East	839	76.3	4	0.86	7	4014	100	6	86.5	78	221.7	.	4.6	97	99	685
15	Saudi Arabia	ASU	Monarchy	Riyadh	Middle East	25193	11.7	4	-0.65	11.33	42463	100	14	78.7	48	137.5	.	9.3	96	96	578
16	Somalia	SOM	Parlimentary Federal	Mogadishu	Eastern Africa	8496	13.5	1	-2.75	4	309778	29	29.5	.	.	4	.	.	35	50	.
17	Sudan	SDN	Government of National Unity	Khartoum	Northern Africa	36992	15.6	1	-2.18	5.33	.	36	41	59.95	10	22	.	12.5	59	57	54
18	Syrian Arab Republic	SYR	Republic	Damascus	Middle East	19512	106.2	2	-0.88	7	27542	81	7	81.3	33	139.9	.	25	99	99	116
19	Tunicia	TUN	Republic	Tunic	Northern Africa	10210	65.7	2	0.21	7.67	26320	79	4	73.65	38	134.1	7.6	26	98	.	409
20	United Arab Emirates	ARE	Federation	Abu Dhabi	Middle East	4657	55.7	4	0.68	7	28683	99.33	14	77	52	202.3	.	9.3	94	98	623
21	West Bank and Gaza Strip	WBG	Republic	Jerusalem	Middle East	3822	634.9	2	-2	.	129702	73	4.95	92.4	.	.	.	22	99	99	.
22	Yemen	YEM	Republic	Sanaa	Middle East	21639	41	1	-1.4	4.67	15066	44.33	45.8	49	7	32.5	41.8	53.3	86	66	89
Total						553248.0	145.3	2.4	-0.9	7.1	1200198.0	69.4	16.4	62.0	32.9	103.2	6.0	20.5	88.0	70.1	318.7

World health organization (WHO), World bank (WB) , World Resource Institute (WRI), American Cancer Society (ACS), and Cenral Intelligence Agency (CIA)

Table 10. TB incidence, all forms (A), and TB incidence, all forms in HIV+ adults (B) per 100,000 populations per year, for 1990-2005

A) TB incidence, all forms (per 100 000 population per year) -> Total

Applied Time Period: from 1990 to 2005

S/N	Country	Ab	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
1	Afghanistan	AFG	244	237	252	248	252	242	238	228	220	214	209	203	195	187	178	168
2	Bahrain	BAR	58	57	60	59	60	58	57	55	53	51	50	49	47	45	43	40
3	Djibouti	DJI	595	605	615	625	636	646	657	668	679	690	702	714	725	738	750	762
4	Egypt	EGY	36	35	37	37	37	36	35	34	33	32	31	30	29	28	26	25
5	Iran (Islamic Republic of)	IRN	36	37	47	45	46	40	39	35	32	31	31	30	29	27	25	23
6	Iraq	IRQ	56	56	56	56	56	56	56	56	56	56	56	56	56	56	56	56
7	Jordan	JOR	12	11	10	10	10	10	9	8	7	6	6	5	5	5	5	5
8	Kuwait	KWT	34	33	35	35	35	34	33	32	31	30	29	28	27	26	25	24
9	Lebanon	LBN	37	34	33	32	32	31	27	23	21	20	18	16	14	12	12	11
10	Libyan Arab Jamahiriya	LBY	27	26	28	27	28	26	26	25	24	23	23	22	21	20	19	18
11	Morocco	MAR	124	120	117	119	123	127	125	122	117	114	111	109	105	101	95	89
12	Oman	OMN	26	23	19	16	14	14	14	13	12	12	12	13	12	12	11	11
13	Pakistan	PAK	181	181	181	181	181	181	181	181	181	181	181	181	181	181	181	181
14	Qatar	QAT	60	59	59	63	72	76	71	65	63	67	67	65	60	56	56	55
15	Saudi Arabia	ASU	44	39	38	38	41	43	45	46	48	48	47	45	44	42	42	41
16	Somalia	SOM	331	323	314	306	298	291	283	276	269	262	255	249	242	236	230	224
17	Sudan	SDN	178	181	184	187	190	194	197	200	203	207	210	214	217	221	224	228
18	Syrian Arab Republic	SYR	71	69	64	60	55	53	51	53	53	52	49	46	44	42	39	37
19	Tunisia	TUN	31	30	31	32	33	31	31	30	28	27	25	24	23	23	24	24
20	United Arab Emirates	ARE	23	22	24	23	24	23	22	21	21	20	20	19	18	17	17	16
21	West Bank and Gaza Strip	WBG	31	30	32	31	32	31	30	29	28	27	26	26	25	24	22	21
22	Yemen	YEM	119	115	122	121	123	118	116	111	107	104	102	99	95	91	86	82
Total			2354	2323	2358	2351	2378	2361	2343	2311	2286	2274	2260	2243	2214	2190	2166	2141

B) TB incidence, all forms in HIV+ adults (per 100 000 population per year) -> Total

Applied Time Period: from 1990 to 2005

S/N	Country	Ab	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
1	Afghanistan	AFG	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2	Bahrain	BAR	0	0	0	0	0	0	0	0	0.1	0.1	0.1	0.2	0.2	0.3	0.3	0.4
3	Djibouti	DJI	5.2	8.1	12.4	18.2	25.7	34.4	43.6	52.3	59.7	65.7	70.1	73.3	75.5	77.1	78.2	79.4
4	Egypt	EGY	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5	Iran (Islamic Republic of)	IRN	0	0	0	0	0	0	0	0	0	0	0	0	0.1	0.1	0.1	0.1
6	Iraq	IRQ	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7	Jordan	JOR	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8	Lebanon	LBN	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.1
9	Libyan Arab Jamahiriya	LBY	0	0	0	0	0	0	0	0	0	0.1	0.1	0.1	0.1	0.2	0.2	0.2
10	Morocco	MAR	0.1	0.2	0.2	0.2	0.2	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3
11	Oman	OMN	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12	Pakistan	PAK	0	0	0	0	0	0	0.1	0.1	0.1	0.1	0.2	0.3	0.4	0.5	0.6	0.7
13	Somalia	SOM	1.6	2.4	3.3	4.4	5.5	6.5	7.3	7.9	8.2	8.3	8.3	8.2	8	7.7	7.5	7.2
14	Sudan	SDN	1.3	3.1	6	8.9	10.9	11.8	12.2	12.3	12.3	12.3	12.3	12.3	12.4	12.5	12.7	13
15	Yemen	YEM	0	0	0	0	0	0	0	0	0	0	0	0.1	0.1	0.2	0.3	0.4
Total			8.2	13.8	21.9	31.7	42.3	53	63.5	72.9	80.7	86.9	91.4	94.8	97.1	98.9	100.2	101.8

Table 11. TB prevalence, all forms (A), and TB prevalence, all forms in HIV+ adults (B) per 100,000 populations per year, for 1990-2005

A) TB prevalence, all forms (per 100 000 population per year) -> Total

Applied Time Period: from 1990 to 2005

S/N	Country	Ab	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
1	Afghanistan	AFG	607	584	612	595	595	571	562	530	489	485	449	418	382	368	317	288
2	Bahrain	BAR	92	90	95	94	95	91	90	86	83	70	61	62	58	55	48	43
3	Djibouti	DJI	1535	1533	1527	1518	1507	1493	768	711	755	760	832	846	1034	1065	1153	1161
4	Egypt	EGY	48	46	49	48	49	47	56	51	49	45	42	40	38	36	34	32
5	Iran (Islamic Republic of)	IRN	50	51	66	63	64	55	61	52	45	41	40	39	37	35	33	30
6	Iraq	IRQ	88	88	88	88	88	88	84	84	82	80	71	70	68	67	72	76
7	Jordan	JOR	12	11	10	10	10	10	13	12	8	7	7	6	6	5	6	6
8	Kuwait	KWT	68	66	70	69	71	68	67	64	62	36	36	36	31	30	28	28
9	Lebanon	LBN	42	39	37	37	37	35	42	35	32	21	20	17	15	13	12	12
10	Libyan Arab Jamahiriya	LBY	41	40	42	41	42	40	40	38	37	23	23	22	21	20	19	18
11	Morocco	MAR	108	104	102	104	108	111	103	105	102	96	95	95	86	88	82	75
12	Oman	OMN	41	36	30	25	22	22	15	15	13	14	12	14	12	13	12	11
13	Pakistan	PAK	429	428	427	425	424	424	423	423	417	423	416	410	379	358	329	297
14	Qatar	QAT	71	69	70	74	85	89	85	82	75	81	79	78	73	69	70	65
15	Saudi Arabia	ASU	69	61	59	60	65	68	71	73	76	72	67	64	61	60	59	58
16	Somalia	SOM	795	761	728	696	665	635	542	507	494	466	435	405	386	344	306	286
17	Sudan	SDN	434	431	427	422	419	417	421	429	388	392	383	397	389	376	380	400
18	Syrian Arab Republic	SYR	111	107	100	94	85	83	79	80	75	72	63	57	55	51	49	46
19	Tunisia	TUN	49	46	49	50	51	49	48	46	44	31	29	27	27	27	28	28
20	United Arab Emirates	ARE	36	35	37	37	37	36	34	33	31	32	29	29	28	26	25	24
21	West Bank and Gaza Strip	WBG	49	47	50	49	50	48	47	46	44	43	40	40	38	37	35	33
22	Yemen	YEM	236	230	244	240	244	234	227	206	195	178	167	157	152	148	139	136
Total			5011	4903	4919	4839	4813	4714	3878	3708	3606	3468	3396	3329	3354	3289	3236	3151

B) TB prevalence, all forms in HIV+ adults (per 100 000 population per year) -> Total

Applied Time Period: from 1990 to 2005

S/N	Country	Ab	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
1	Afghanistan	AFG	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2	Bahrain	BAR	0	0	0	0	0	0	0	0	0	0	0.1	0.1	0.1	0.1	0.2	0.2
3	Djibouti	DJI	2.6	4	6.2	9.1	12.9	17.2	21.8	26.1	29.9	32.8	35	36.6	37.7	38.5	39.1	39.7
4	Egypt	EGY	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5	Iran (Islamic Republic of)	IRN	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.1	0.1
6	Iraq	IRQ	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7	Jordan	JOR	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8	Lebanon	LBN	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
9	Libyan Arab Jamahiriya	LBY	0	0	0	0	0	0	0	0	0	0	0	0.1	0.1	0.1	0.1	0.1
10	Morocco	MAR	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.2	0.2	0.2	0.2	0.2	0.2	0.2
11	Oman	OMN	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12	Pakistan	PAK	0	0	0	0	0	0	0	0	0	0	0.1	0.1	0.2	0.2	0.3	0.3
13	Somalia	SOM	0.8	1.2	1.7	2.2	2.8	3.3	3.7	3.9	4.1	4.2	4.2	4.1	4	3.9	3.7	3.6
14	Sudan	SDN	0.7	1.6	3	4.4	5.4	5.9	6.1	6.2	6.2	6.2	6.1	6.2	6.2	6.3	6.4	6.5
15	Yemen	YEM	0	0	0	0	0	0	0	0	0	0	0	0	0.1	0.1	0.1	0.2
Total			4.2	6.9	11	15.8	21.2	26.5	31.7	36.3	40.3	43.4	45.7	47.4	48.6	49.4	50.2	50.9

Table 12. TB mortality, all forms (A), and TB mortality, all forms in HIV+ adults (B) per 100,000 populations per year, for 1990-2005

A) TB mortality, all forms (per 100 000 population per year) -> Total

Applied Time Period: from 1990 to 2005

S/N	Country	Ab	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
1	Afghanistan	AFG	69	67	70	68	68	65	64	61	57	56	52	49	45	43	44	35
2	Bahrain	BAR	7	7	7	7	7	7	7	6	6	6	5	5	5	4	4	4
3	Djibouti	DJI	127	127	128	128	129	129	73	65	92	86	95	93	117	120	126	128
4	Egypt	EGY	4	4	4	4	4	4	4	4	4	4	4	3	3	3	3	3
5	Iran (Islamic Republic of)	IRN	4	4	5	5	5	5	5	4	4	4	4	3	3	3	3	3
6	Iraq	IRQ	12	12	12	12	12	12	8	8	8	8	10	10	9	9	10	11
7	Jordan	JOR	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8	Kuwait	KWT	4	4	4	4	4	4	4	3	3	3	3	3	3	3	3	2
9	Lebanon	LBN	4	3	3	3	3	3	3	2	2	2	2	2	1	1	1	1
10	Libyan Arab Jamahiriya	LBY	4	4	5	5	5	4	4	4	4	2	2	2	2	1	1	1
11	Morocco	MAR	11	11	11	11	11	11	11	11	11	10	10	10	9	9	9	7
12	Oman	OMN	2	2	2	1	1	1	1	1	1	1	1	1	1	1	1	1
13	Pakistan	PAK	49	49	49	49	49	49	49	49	48	49	48	48	45	43	43	37
14	Qatar	QAT	6	6	6	6	7	8	7	7	7	7	7	7	6	6	6	6
15	Saudi Arabia	ASU	5	5	4	4	5	5	5	5	6	6	5	5	5	5	5	5
16	Somalia	SOM	115	111	107	103	100	96	97	93	91	78	75	67	64	58	46	40
17	Sudan	SDN	60	61	62	63	64	64	65	66	61	62	61	63	61	62	63	65
18	Syrian Arab Republic	SYR	8	7	7	7	6	6	6	6	6	6	5	5	5	4	4	4
19	Tunisia	TUN	3	3	3	3	3	3	3	3	3	3	2	2	3	3	3	3
20	United Arab Emirates	ARE	3	3	3	3	3	3	2	2	2	2	2	2	2	2	2	2
21	West Bank and Gaza Strip	WBG	6	5	6	6	6	5	5	5	5	5	5	4	4	4	4	4
22	Yemen	YEM	16	15	16	16	16	16	15	15	14	13	13	12	12	12	11	10
	Total		520	511	515	509	509	501	429	411	426	404	412	397	406	397	396	378

B) TB mortality, all forms in HIV+ adults (per 100 000 population per year) -> Total

Applied Time Period: from 1990 to 2005

S/N	Country	Ab	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
1	Afghanistan	AFG	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2	Bahrain	BAR	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
3	Djibouti	DJI	2.3	3.6	5.3	7.5	10.3	13.4	9.2	9.6	12.7	10.6	12.9	11.7	19.9	20.4	21.9	22
4	Egypt	EGY	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5	Iran (Islamic Republic of)	IRN	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
6	Iraq	IRQ	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7	Jordan	JOR	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8	Lebanon	LBN	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
9	Libyan Arab Jamahiriya	LBY	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10	Morocco	MAR	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
11	Oman	OMN	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12	Pakistan	PAK	0	0	0	0	0	0	0	0	0	0	0.1	0.1	0.2	0.2	0.2	0.2
13	Somalia	SOM	1.1	1.6	2.2	2.9	3.6	4.1	4.3	4.5	4.7	4.7	4.6	4.3	4.1	3.6	2.9	2.5
14	Sudan	SDN	0.9	2	3.8	5.6	6.7	7.2	7.4	7.4	6.8	6.7	6.5	6.6	6	6.1	6.2	6.5
15	Yemen	YEM	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.1	0.1
	Total		4.3	7.2	11.3	16	20.6	24.7	20.9	21.5	24.2	22	24.1	22.7	30.2	30.3	31.3	31.3

Table 13. DOTS population coverage (%), for 1995-2005 by year

DOTS population coverage (%) -> Total

For 1995 - 2005 by year

S/N	Country	Ab	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
1	Afghanistan	AFG	n/a	n/a	12	11	14	15	12	38	53	68	81
2	Bahrain	BAR	n/a	0	0	0	100	100	100	100	100	100	100
3	Djibouti	DJI	n/a	100	100	100	100	100	100	100	100	100	100
4	Egypt	EGY	54	3	19	27	75	100	100	100	100	100	100
5	Iran (Islamic Republic of)	IRN	0	8	28	69	94	96	100	100	100	100	100
6	Iraq	IRQ	n/a	0	0	10	37	87	87	87	87	87	87
7	Jordan	JOR	100	0	0	100	100	100	100	100	100	100	100
8	Kuwait	KWT	n/a	0	0	0	100	100	100	100	100	100	100
9	Lebanon	LBN	10	0	0	0	100	100	100	100	100	100	100
10	Libyan Arab Jamahiriya	LBY	n/a	0	n/a	0	100	100	n/a	n/a	100	100	100
11	Morocco	MAR	100	100	100	100	100	100	100	100	100	100	100
12	Oman	OMN	n/a	100	100	100	100	100	100	100	100	100	100
13	Pakistan	PAK	2	8	n/a	8	8	9	24	45	63	79	100
14	Qatar	QAT	100	100	100	100	100	100	100	100	100	100	100
15	Saudi Arabia	ASU	n/a	n/a	0	0	48	100	100	100	100	100	100
16	Somalia	SOM	n/a	15	15	52	56	73	100	100	100	100	100
17	Sudan	SDN	n/a	2	6	60	72	80	97	99	99	82	91
18	Syrian Arab Republic	SYR	n/a	0	48	58	78	100	100	100	100	100	100
19	Tunisia	TUN	n/a	0	n/a	0	100	100	100	100	100	100	100
20	United Arab Emirates	ARE	n/a	n/a	n/a	n/a	0	20	100	20	100	20	20
21	West Bank and Gaza Strip	WBG	n/a	0	n/a	0	n/a	100	100	n/a	100	100	100
22	Yemen	YEM	3	15	50	52	n/a	89	97	98	98	98	93
Total			17	21	26	39	67	85	87	81	95	92	94

Table 14. Whole country (A) and DOTS (B) new smear-positive case detection rate, for 1995-2005 by year

A) Whole country new smear-positive case detection rate (%) -> Total for 1995 - 2005 by year

S/N	Countries	Ab	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
1	Afghanistan	AFG	n/a	n/a	3	8	8	13	21	29	28	36	44
2	Bahrain	BAR	11	20	14	16	14	15	15	12	11	50	77
3	Djibouti	DJI	n/a	96	100	84	74	63	57	52	48	42	42
4	Egypt	EGY	43	51	56	52	56	49	49	56	58	62	63
5	Iran (Islamic Republic of)	IRN	46	49	53	54	59	58	61	61	62	62	64
6	Iraq	IRQ	59	184	141	150	161	51	55	58	52	46	43
7	Jordan	JOR	102	95	84	74	74	67	75	73	88	70	63
8	Kuwait	KWT	66	59	77	66	60	61	56	69	68	85	66
9	Lebanon	LBN	45	50	60	70	63	72	71	70	70	79	74
10	Libyan Arab Jamahiriya	LBY	n/a	90	n/a	n/a	146	111	n/a	136	146	174	178
11	Morocco	MAR	92	93	92	90	91	88	86	91	93	93	101
12	Oman	OMN	96	121	120	120	90	122	111	116	85	127	108
13	Pakistan	PAK	3	2	n/a	13	5	3	9	13	17	27	37
14	Qatar	QAT	33	27	24	43	33	29	41	34	52	36	47
15	Saudi Arabia	ASU	n/a	n/a	38	36	37	35	37	36	37	37	36
16	Somalia	SOM	19	36	39	39	43	47	56	60	64	79	86
17	Sudan	SDN	35	34	40	36	37	40	35	31	32	34	35
18	Syrian Arab Republic	SYR	37	44	38	42	41	42	42	41	45	47	42
19	Tunisia	TUN	96	80	n/a	101	93	101	103	90	84	86	82
20	United Arab Emirates	ARE	n/a	n/a	n/a	n/a	11	26	23	18	24	18	19
21	West Bank and Gaza Strip	WBG	3	7	n/a	2	n/a	10	8	n/a	4	1	2
22	Yemen	YEM	46	53	58	60	66	68	60	52	47	43	44
Total			36	56	47	53	58	53	49	54	55	61	62

B) DOTS new smear-positive case detection rate (%) -> Total for 1995 - 2005 by year

S/N	Countries		1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
1	Afghanistan	AFG	n/a	n/a	3	8	8	13	21	29	28	36	44
2	Bahrain	BAR	n/a	n/a	n/a	n/a	14	15	15	12	11	50	77
3	Djibouti	DJI	n/a	96	100	84	74	63	57	52	48	42	42
4	Egypt	EGY	44	1	11	17	31	45	49	56	58	62	63
5	Iran (Islamic Republic of)	IRN	42	n/a	12	35	56	58	61	61	62	62	64
6	Iraq	IRQ	n/a	n/a	n/a	5	13	51	55	58	52	46	43
7	Jordan	JOR	102	n/a	n/a	74	74	67	75	73	88	70	63
8	Kuwait	KWT	n/a	n/a	n/a	n/a	60	61	56	69	68	85	66
9	Lebanon	LBN	45	n/a	n/a	n/a	63	72	71	70	70	79	74
10	Libyan Arab Jamahiriya	LBY	n/a	n/a	n/a	n/a	146	111	n/a	136	146	174	178
11	Morocco	MAR	92	93	92	90	91	88	86	91	93	93	101
12	Oman	OMN	n/a	121	120	120	90	122	111	116	85	127	108
13	Pakistan	PAK	1	2	n/a	4	2	3	5	13	17	27	37
14	Qatar	QAT	33	27	24	43	33	29	41	34	52	36	47
15	Saudi Arabia	ASU	n/a	n/a	n/a	n/a	21	35	37	36	37	37	36
16	Somalia	SOM	n/a	29	39	39	43	47	56	60	64	79	86
17	Sudan	SDN	n/a	2	1	27	28	32	30	31	32	34	35
18	Syrian Arab Republic	SYR	n/a	n/a	8	20	27	40	42	41	45	47	42
19	Tunisia	TUN	n/a	n/a	n/a	n/a	93	101	103	90	84	86	82
20	United Arab Emirates	ARE	n/a	n/a	n/a	n/a	n/a	26	23	18	24	18	19
21	West Bank and Gaza Strip	WBG	n/a	n/a	n/a	n/a	n/a	10	8	n/a	4	1	2
22	Yemen	YEM	2	8	30	37	51	54	52	47	45	41	41
Total			36	17	20	27	47	52	46	54	55	61	61

Table 15. DOTS (A) and Non-DOTS (B) treatment success, for 1994-2004 by year

A) DOTS treatment success (%) -> Total
Applied Time Period: from 1994 to 2004

S/N	Country	Ab	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004
1	Afghanistan	AFG	n/a	n/a	n/a	45	33	87	86	84	87	86	89
2	Bahrain	BAR	n/a	n/a	n/a	n/a	13	95	73	87	88	97	82
3	Djibouti	DJI	n/a	75	77	76	79	72	62	78	82	73	80
4	Egypt	EGY	52	n/a	81	82	87	87	87	82	88	80	70
5	Iran (Islamic Republic of)	IRN	n/a	n/a	87	84	83	82	85	85	85	84	84
6	Iraq	IRQ	n/a	n/a	n/a	n/a	83	85	92	89	91	85	85
7	Jordan	JOR	90	n/a	n/a	n/a	92	88	90	86	89	87	85
8	Kuwait	KWT	n/a	n/a	n/a	n/a	n/a	66	69	73	55	62	63
9	Lebanon	LBN	89	n/a	n/a	n/a	73	96	92	91	91	92	90
10	Libyan Arab Jamahiriya	LBY	n/a	n/a	n/a	n/a	68	67	n/a	n/a	61	62	64
11	Morocco	MAR	86	90	88	89	88	88	89	87	89	86	87
12	Oman	OMN	n/a	84	87	91	86	95	93	90	92	90	90
13	Pakistan	PAK	74	70	n/a	67	66	70	74	77	77	75	82
14	Qatar	QAT	83	81	72	79	84	74	66	60	75	73	78
15	Saudi Arabia	ASU	n/a	n/a	n/a	n/a	57	66	73	77	76	79	82
16	Somalia	SOM	n/a	86	84	90	88	88	83	86	89	90	91
17	Sudan	SDN	n/a	n/a	n/a	70	65	81	79	80	78	82	77
18	Syrian Arab Republic	SYR	n/a	n/a	92	88	88	84	79	81	87	88	86
19	Tunisia	TUN	n/a	n/a	n/a	n/a	91	91	91	90	92	91	90
20	United Arab Emirates	ARE	n/a	n/a	n/a	n/a	n/a	n/a	74	62	79	64	70
21	West Bank and Gaza Strip	WBG	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	100	80	50
22	Yemen	YEM	n/a	66	78	81	80	79	75	80	80	82	82
Total			22	25	34	43	64	75	73	74	83	81	80

B) Non-DOTS treatment success (%) -> Total
Applied Time Period: from 1994 to 2004

S/N	Country	Ab	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004
1	Afghanistan	AFG	n/a	n/a	n/a	n/a	n/a	84	84	n/a	n/a	n/a	n/a
2	Bahrain	BAR	n/a	n/a	21	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
3	Djibouti	DJI	n/a	62	50	76	81	81	n/a	n/a	n/a	n/a	n/a
4	Egypt	EGY	n/a	n/a	83	82	81	87	n/a	n/a	n/a	n/a	n/a
5	Iran (Islamic Republic of)	IRN	95	80	77	67	59	60	n/a	n/a	n/a	n/a	n/a
6	Iraq	IRQ	n/a	92	n/a	85	n/a	n/a	n/a	n/a	n/a	n/a	n/a
7	Jordan	JOR	51	71	73	71	70	n/a	n/a	n/a	n/a	n/a	n/a
8	Kuwait	KWT	n/a	91	73	65	n/a	n/a	n/a	n/a	n/a	n/a	n/a
9	Lebanon	LBN	64	65	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
10	Libyan Arab Jamahiriya	LBY	65	n/a	n/a	n/a	20	n/a	n/a	n/a	n/a	n/a	n/a
11	Morocco	MAR	n/a	n/a	54	56	64	83	n/a	n/a	n/a	n/a	n/a
12	Oman	OMN	93	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
13	Pakistan	PAK	96	79	26	36	66	69	53	n/a	n/a	n/a	n/a
14	Qatar	QAT	46	61	66	58	n/a	n/a	62	n/a	n/a	n/a	n/a
15	Saudi Arabia	ASU	n/a	n/a	n/a	89	n/a	n/a	n/a	n/a	n/a	n/a	n/a
16	Somalia	SOM	n/a	n/a	n/a	n/a	93	n/a	n/a	n/a	n/a	n/a	n/a
17	Sudan	SDN	n/a	100	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
18	Syrian Arab Republic	SYR	40	52	47	55	47	58	59	57	78	73	76
19	Tunisia	TUN	n/a	n/a	n/a	n/a	91	91	91	90	92	91	90
20	United Arab Emirates	ARE	n/a	n/a	n/a	n/a	n/a	n/a	74	62	79	64	70
21	West Bank and Gaza Strip	WBG	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	100	80	50
22	Yemen	YEM	n/a	66	78	81	80	79	75	80	80	82	82
Total			25	37	29	37	34	31	23	13	20	18	17

Appendix C: Figures

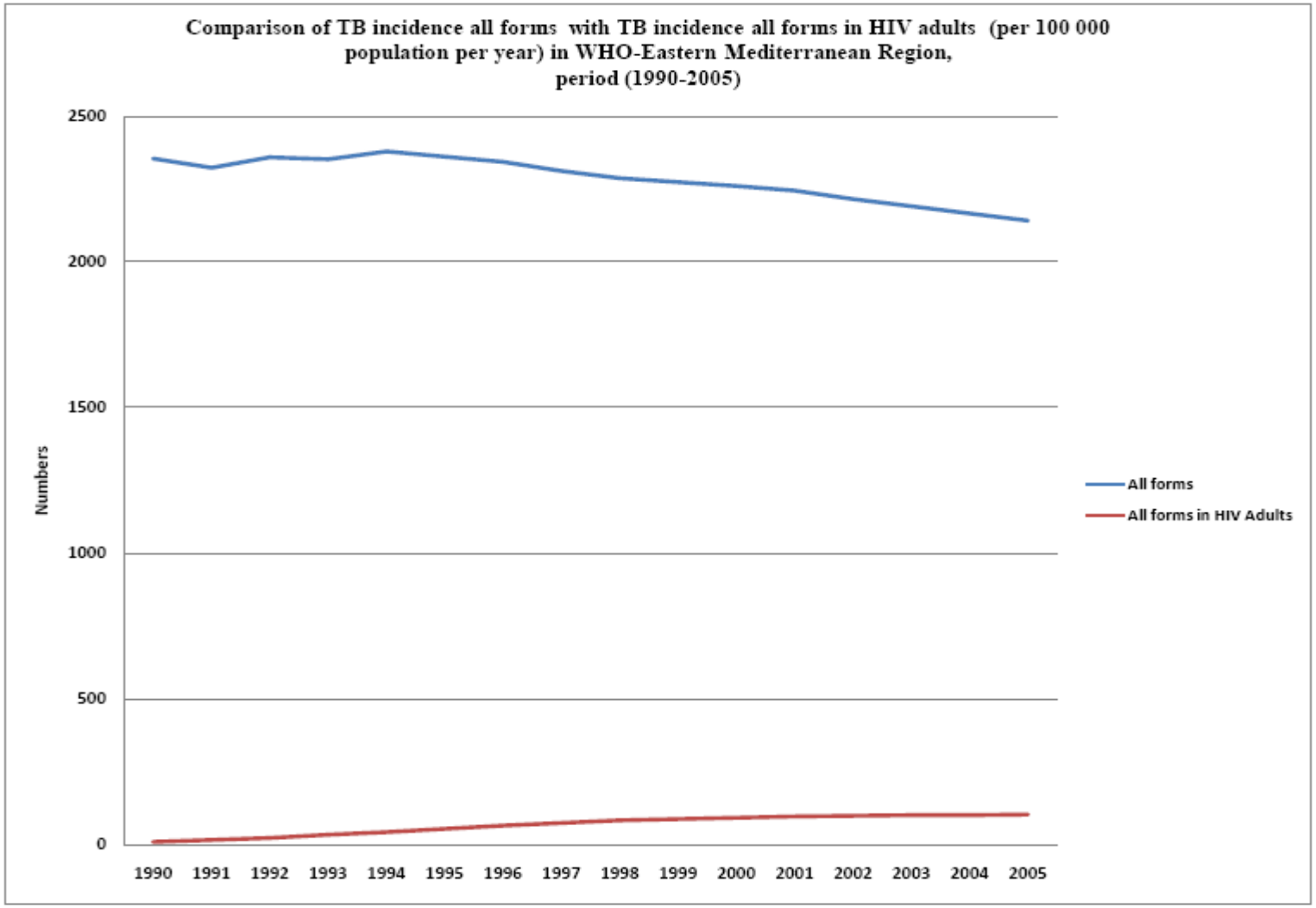


Figure 9. Comparison of TB incidence, all forms with TB incidence, all forms in HIV+ adults in EMR for 1990 and 2005 by year

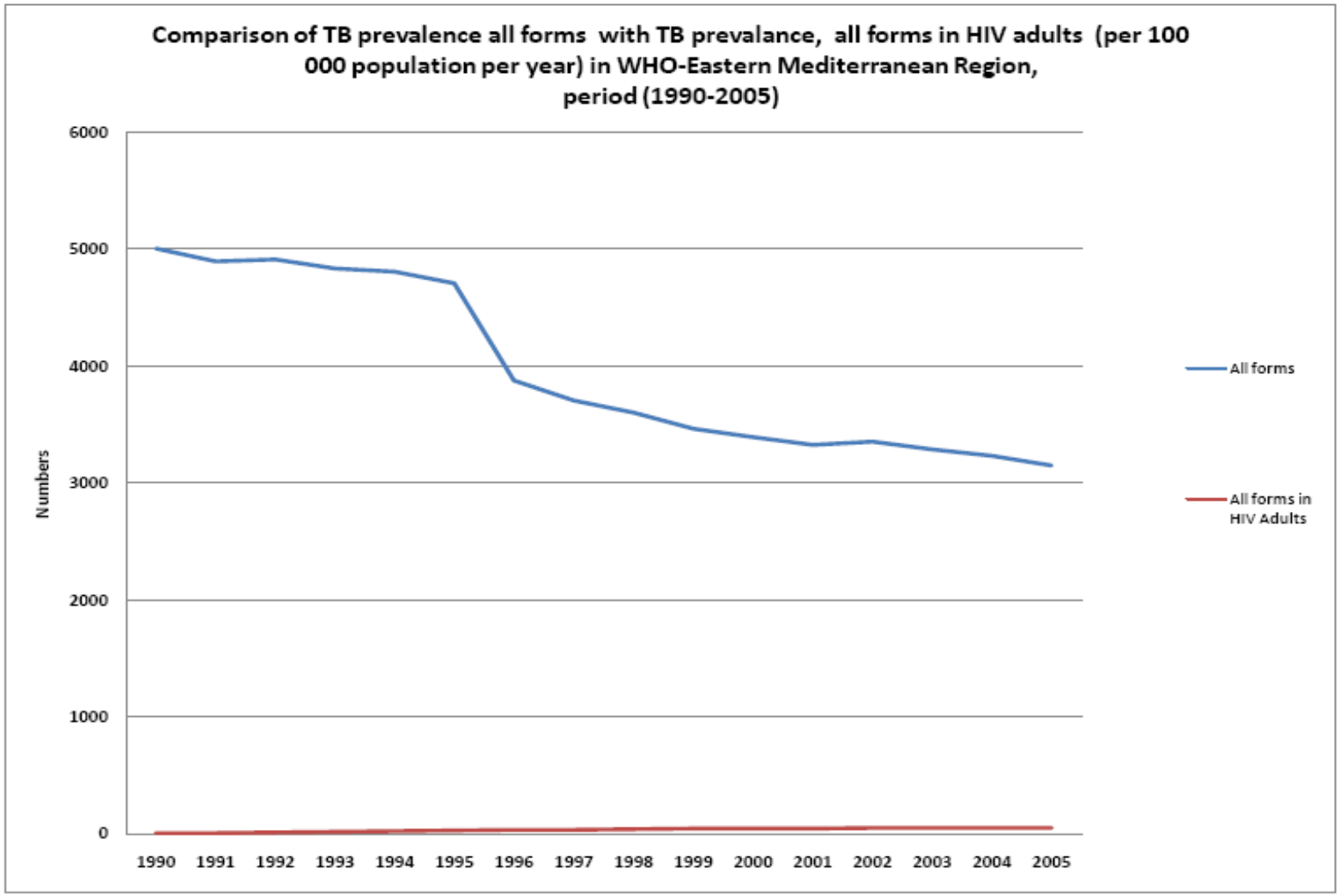


Figure 10.Comparison of TB prevalence, all forms with TB prevalence, all forms in HIV+ adults in EMR for 1990 and 2005 by year

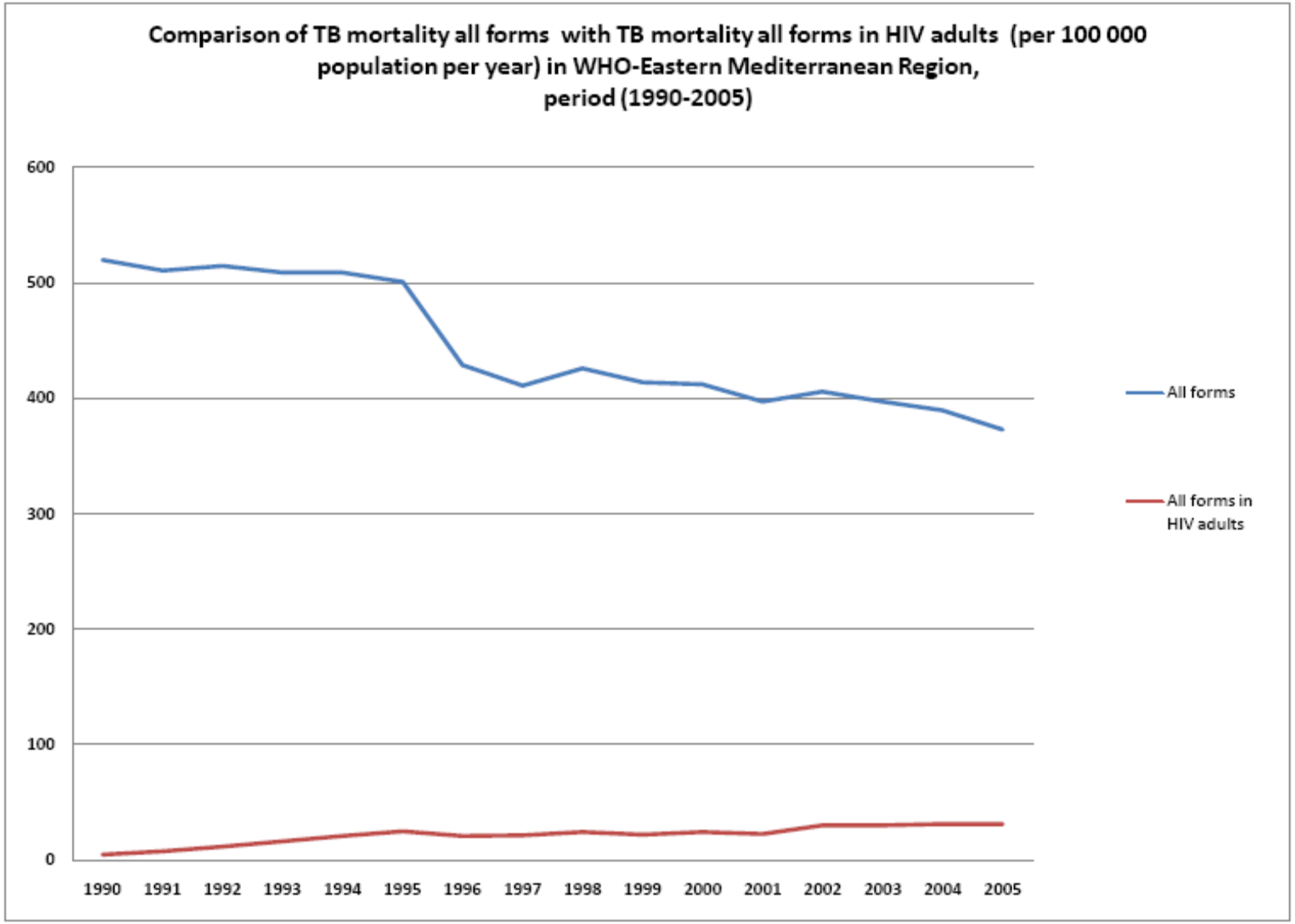


Figure 11.Comparison of TB mortality, all forms with TB mortality, all forms in HIV+ adults in EMR for 1990 and 2005 by year

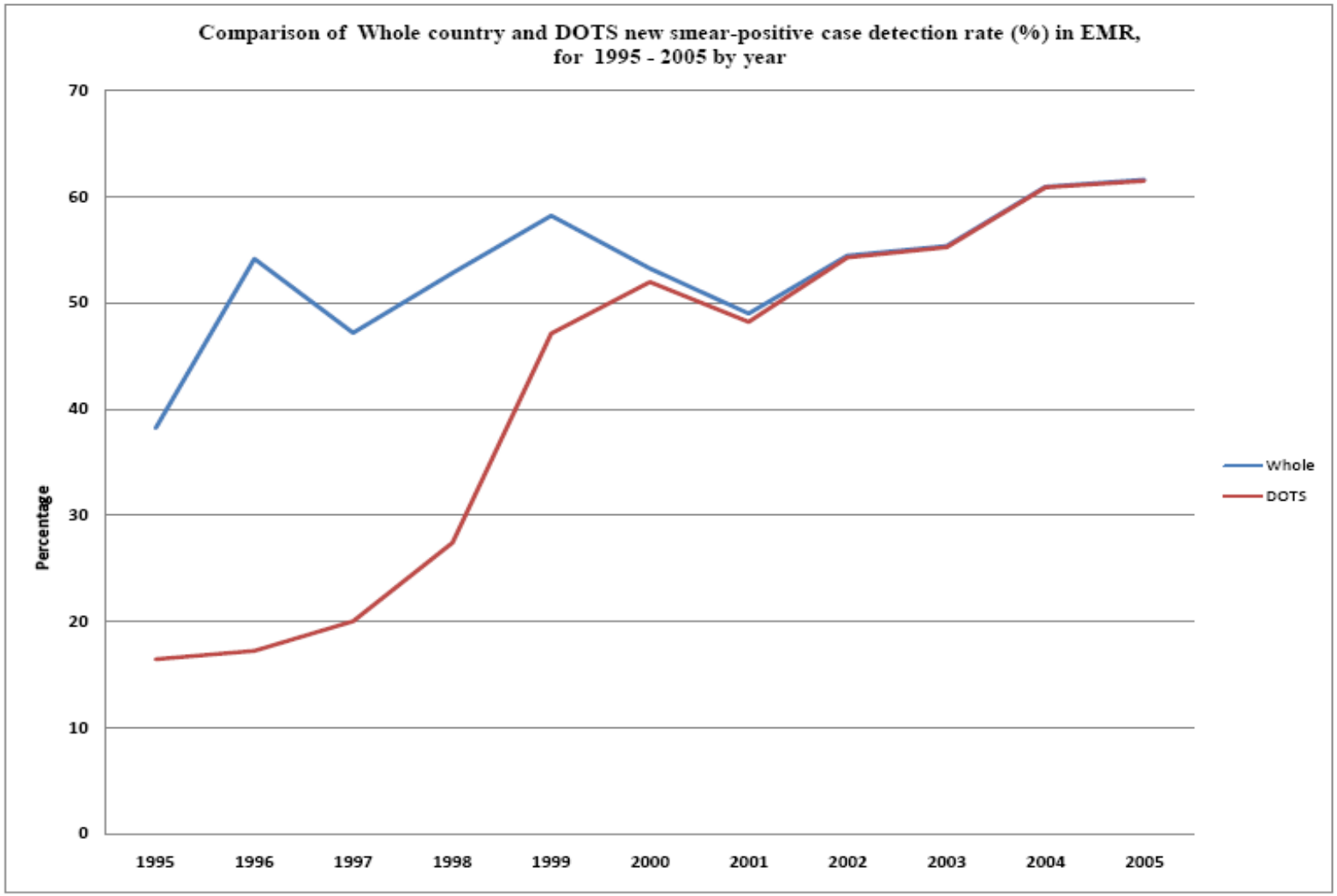


Figure 12.Comparison of DOTS and Whole country new smear positive case detection rates in EMR for 1995 and 2005 by year

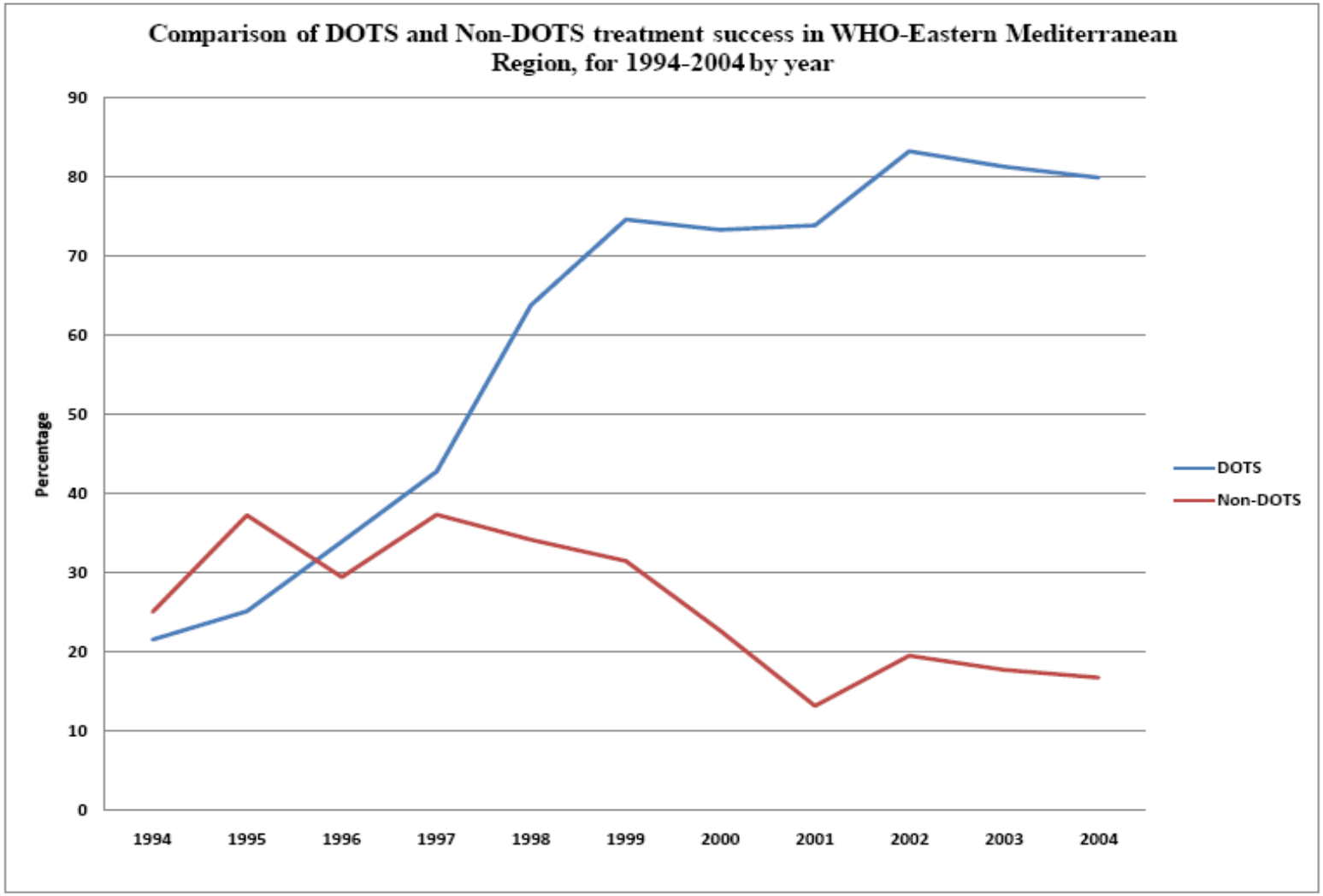


Figure 13.Comparison of DOTS and Non-DOTS treatment success rates in EMR for 1994 and 2004 by year

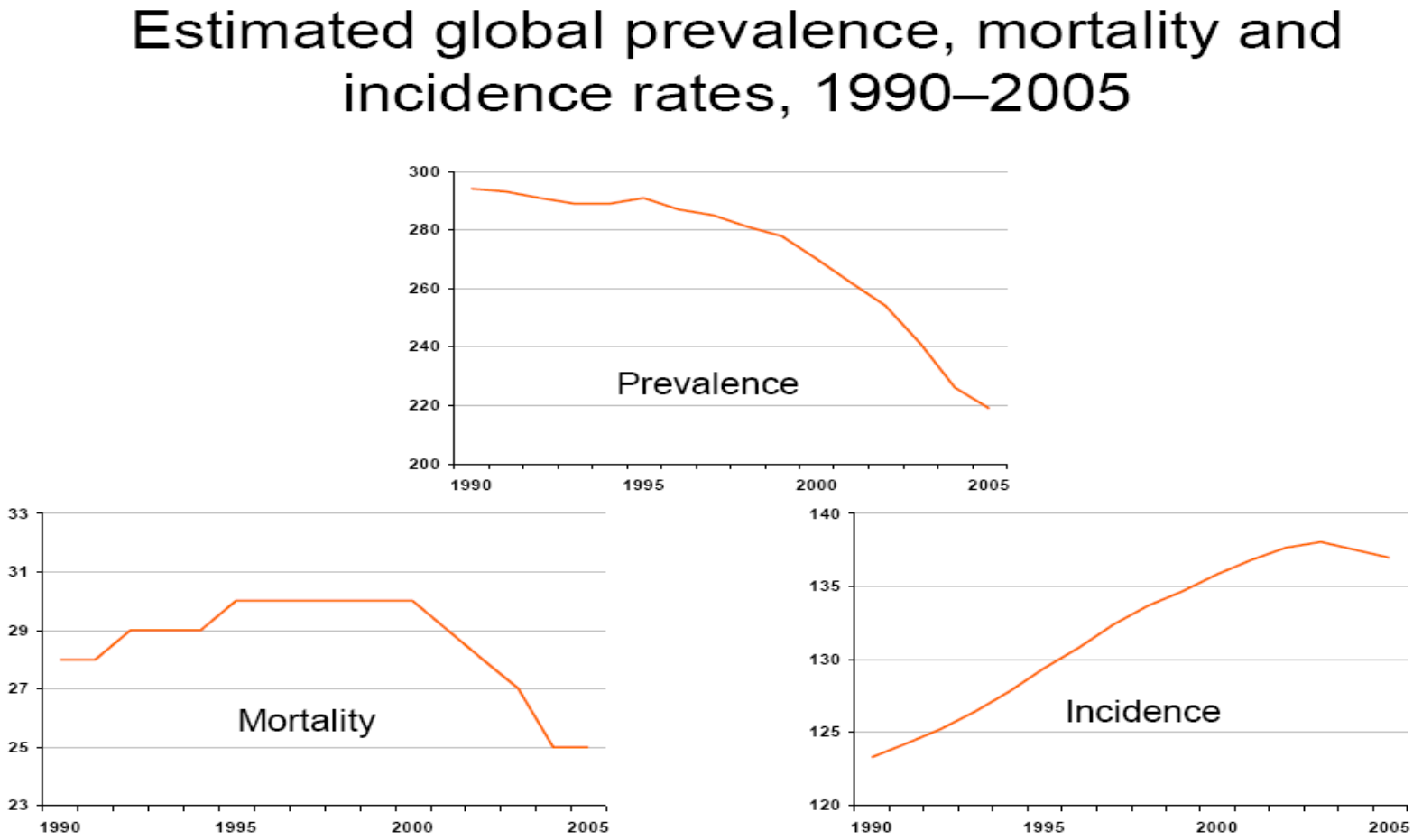


Figure 14. Estimated Global TB incidence, prevalence and mortality rates, 1990-2002 (22)

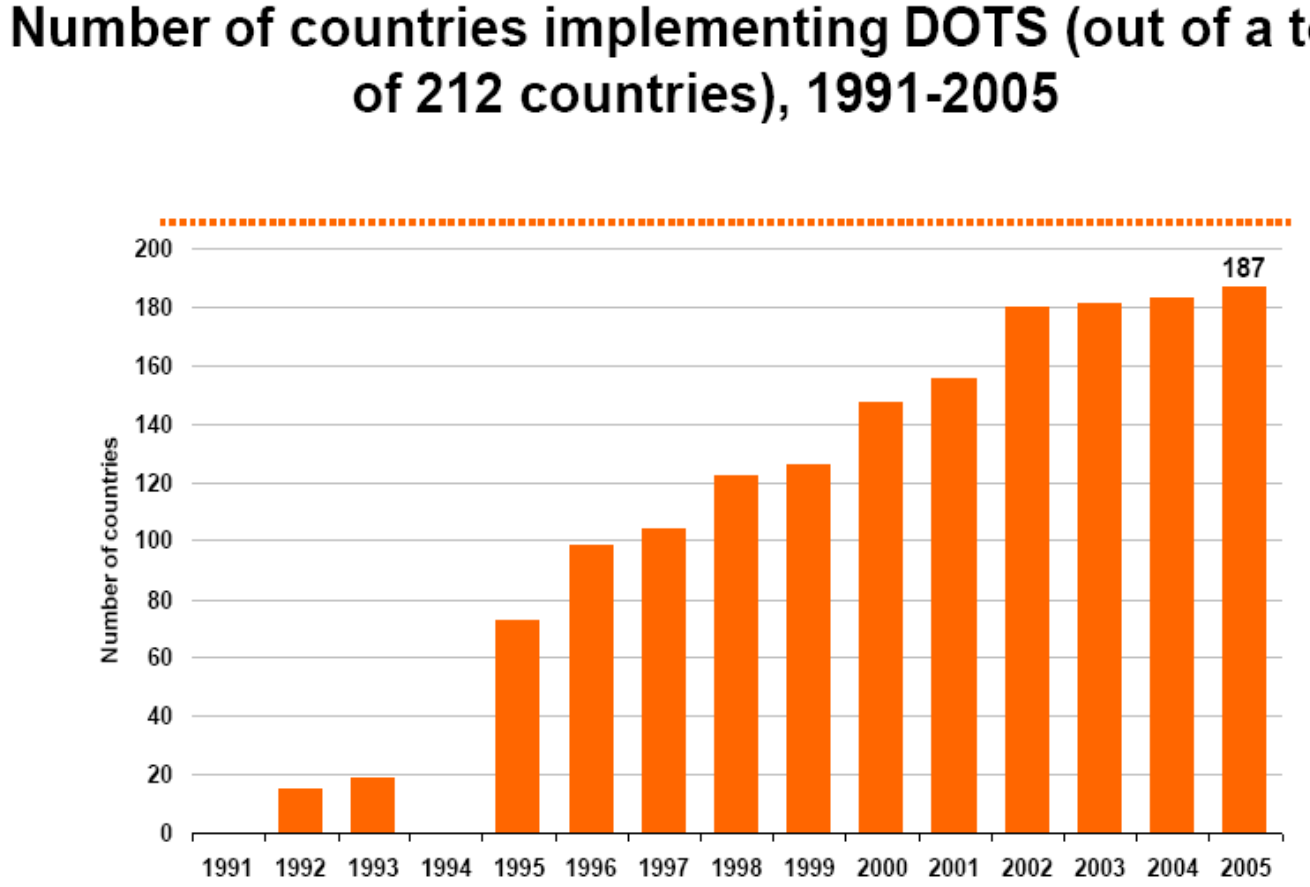


Figure 15. Number of countries implementing DOTS, 1991-2005 (22)

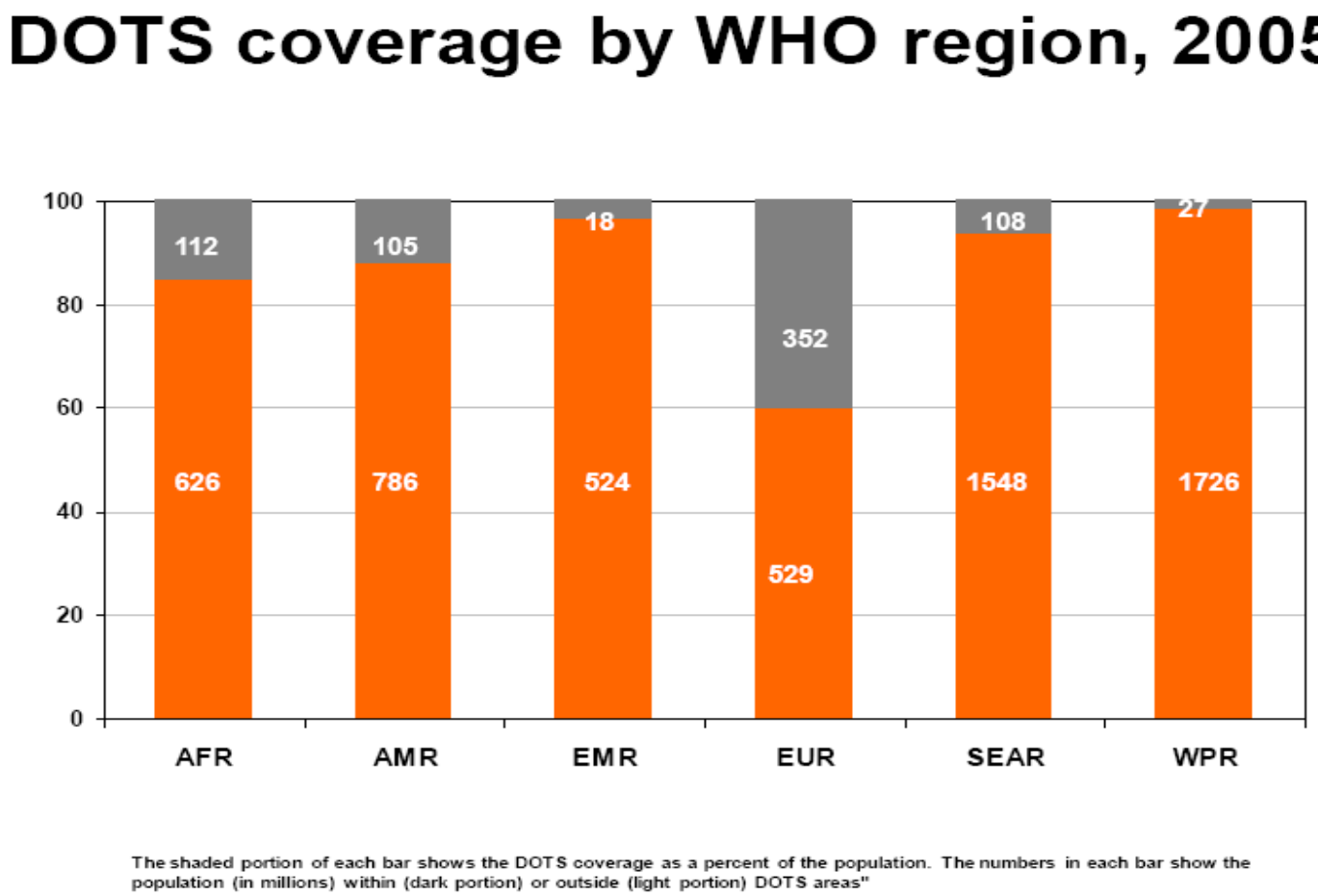


Figure 16. DOTS Coverage by WHO Region, 2005 (22)

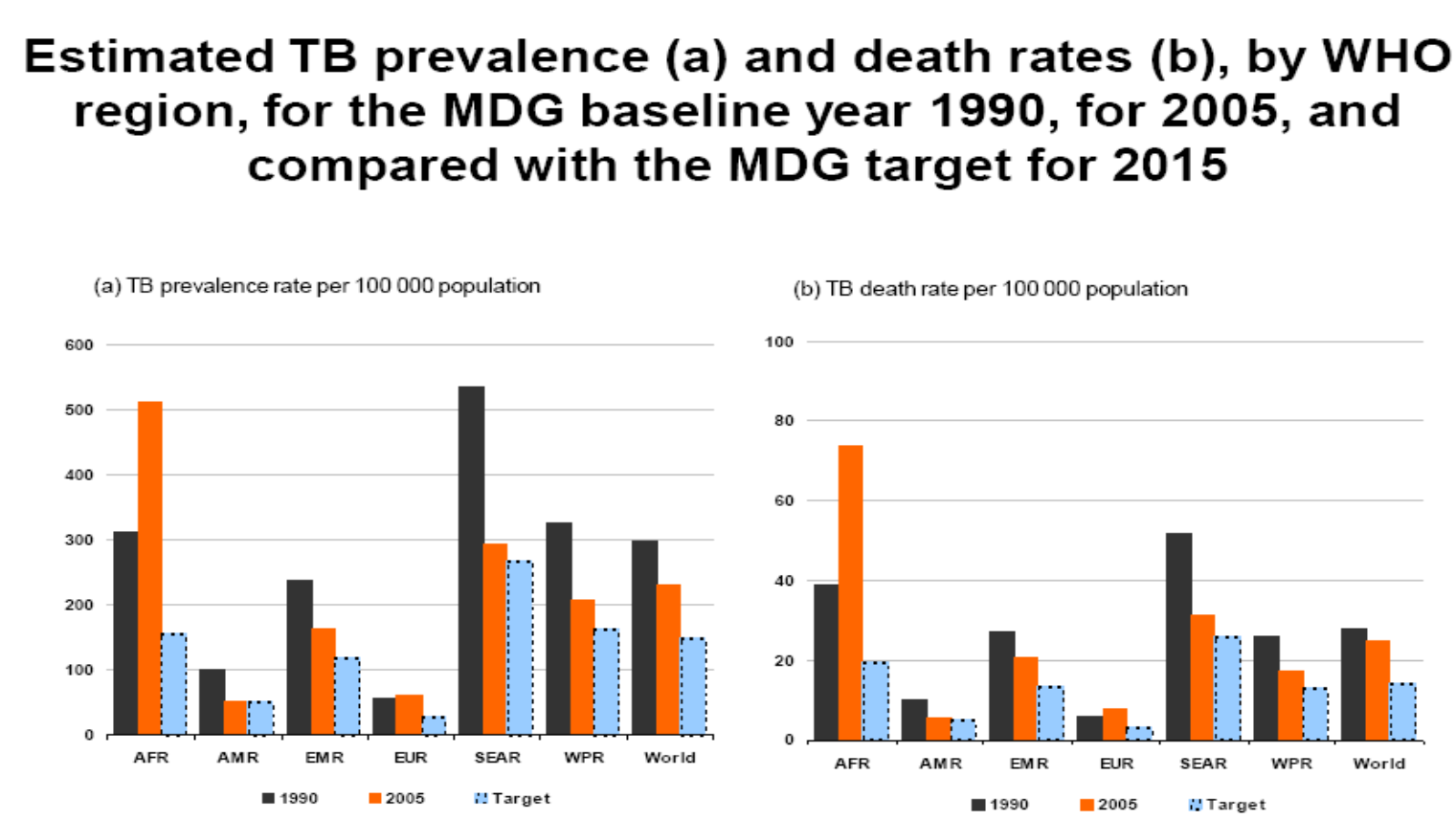


Figure 17. Estimated TB prevalence (a) and death (b) rates, by WHO regions, for MDGs baseline year 1990, for 2005, and compared with the MDGs targets for 2015 (22)

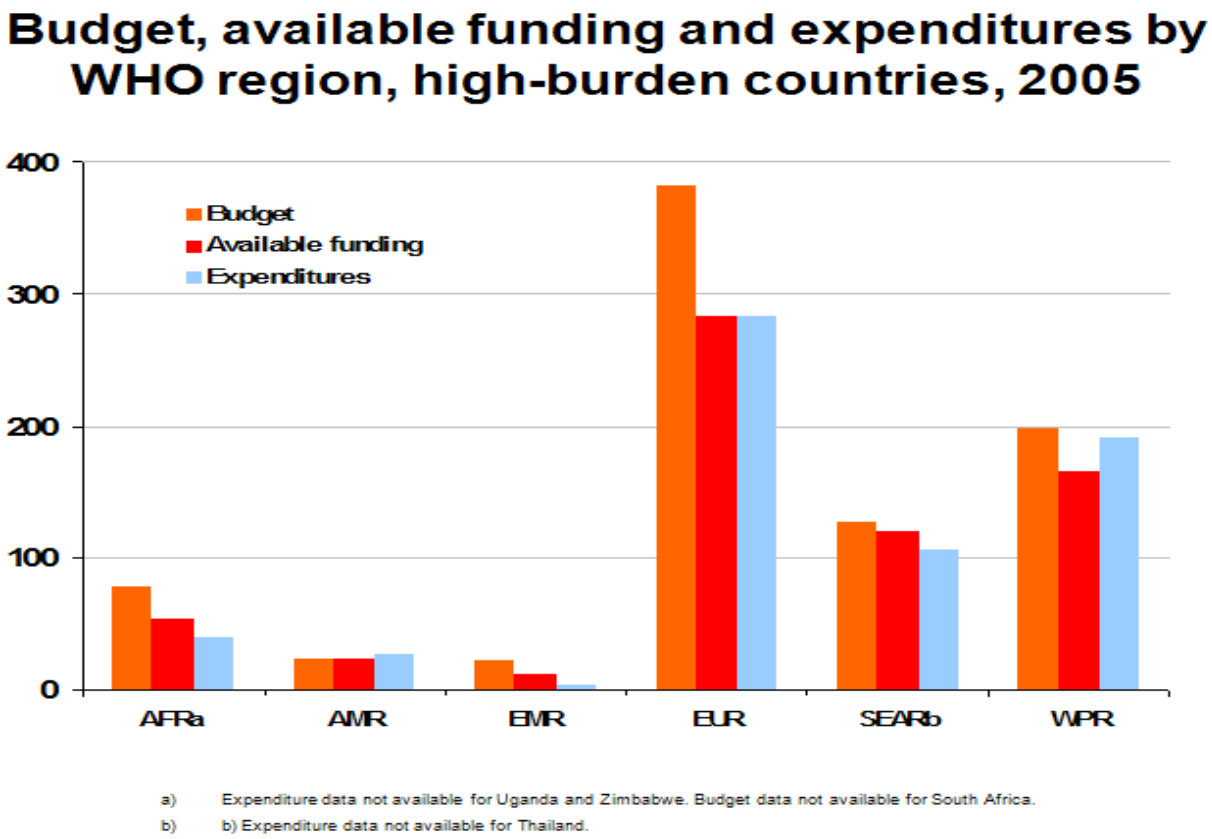
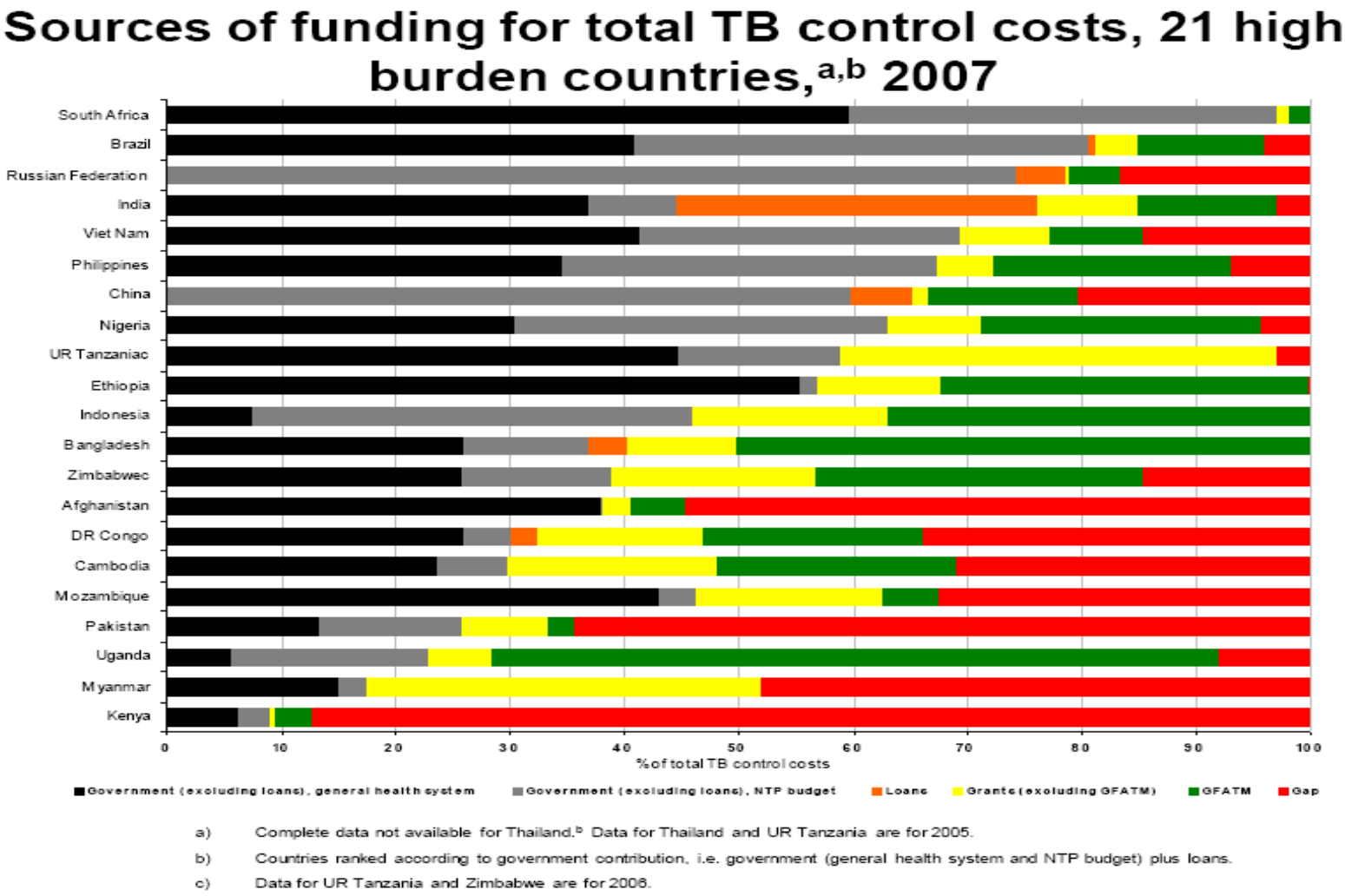


Figure 18. Budget, available funding and expenditures by WHO region, high-burden countries, 2005 (22)



a) Complete data not available for Thailand.[b] Data for Thailand and UR Tanzania are for 2005.

b) Countries ranked according to government contribution, i.e. government (general health system and NTP budget) plus loans.

c) Data for UR Tanzania and Zimbabwe are for 2006.

Figure 19. Sources of funding for total TB control costs, 21 high-burden countries, 2007 (22)

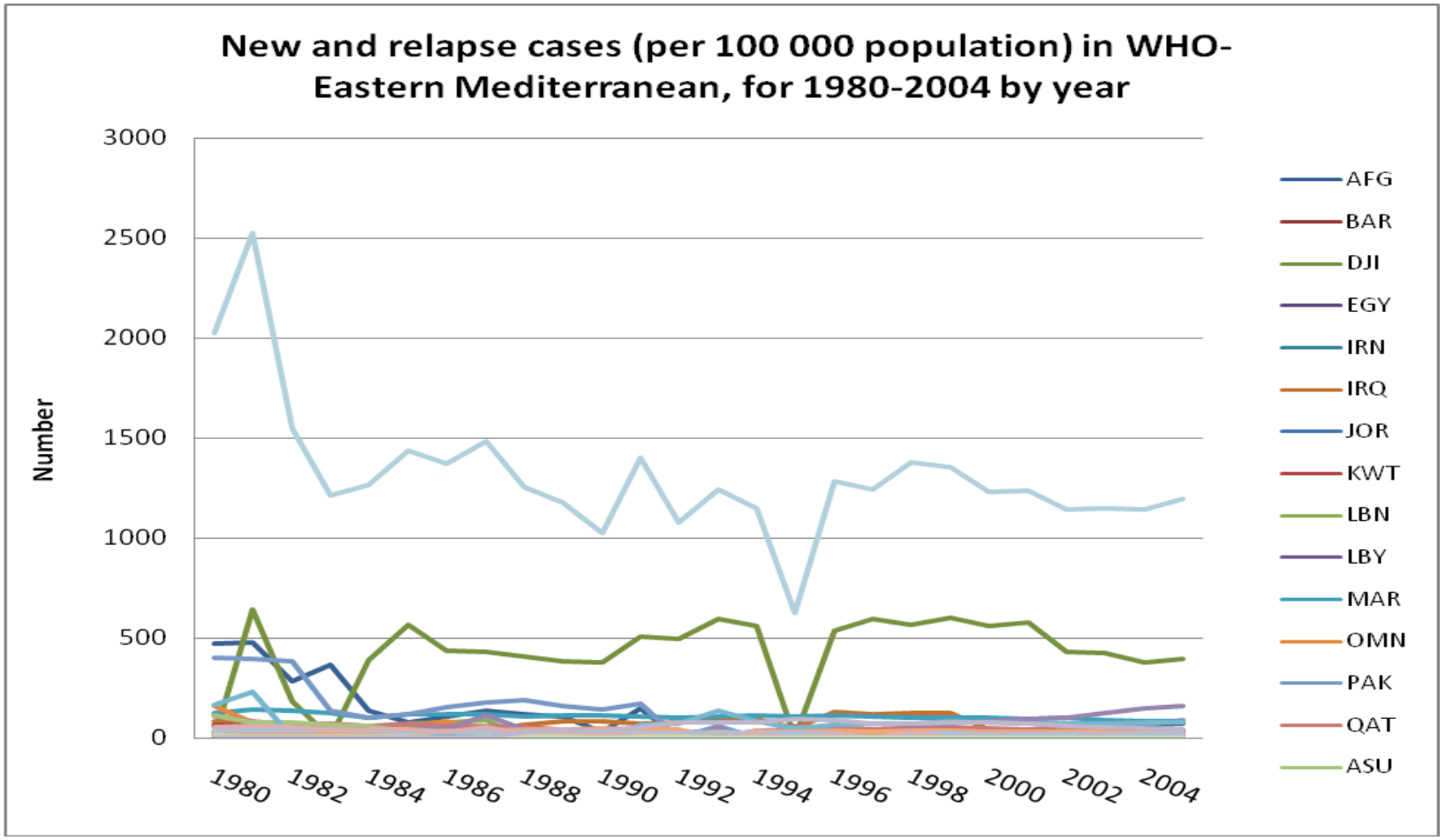


Figure 20. New and relapse cases (per 100000 populations in WHO Eastern Mediterranean, for 1980-2004 by year

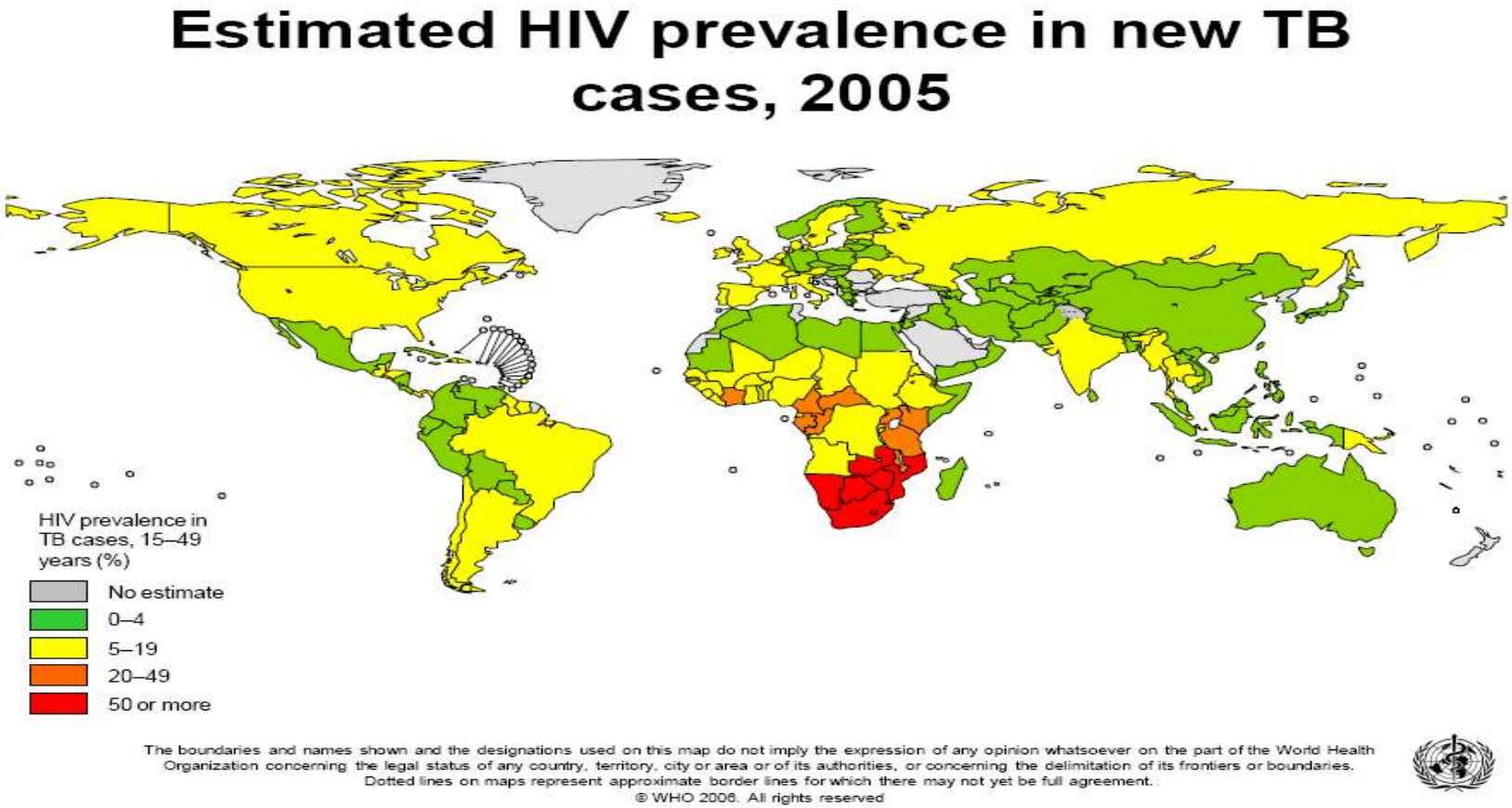


Figure 21. Estimated HIV prevalence in new TB cases, 2005 (22)

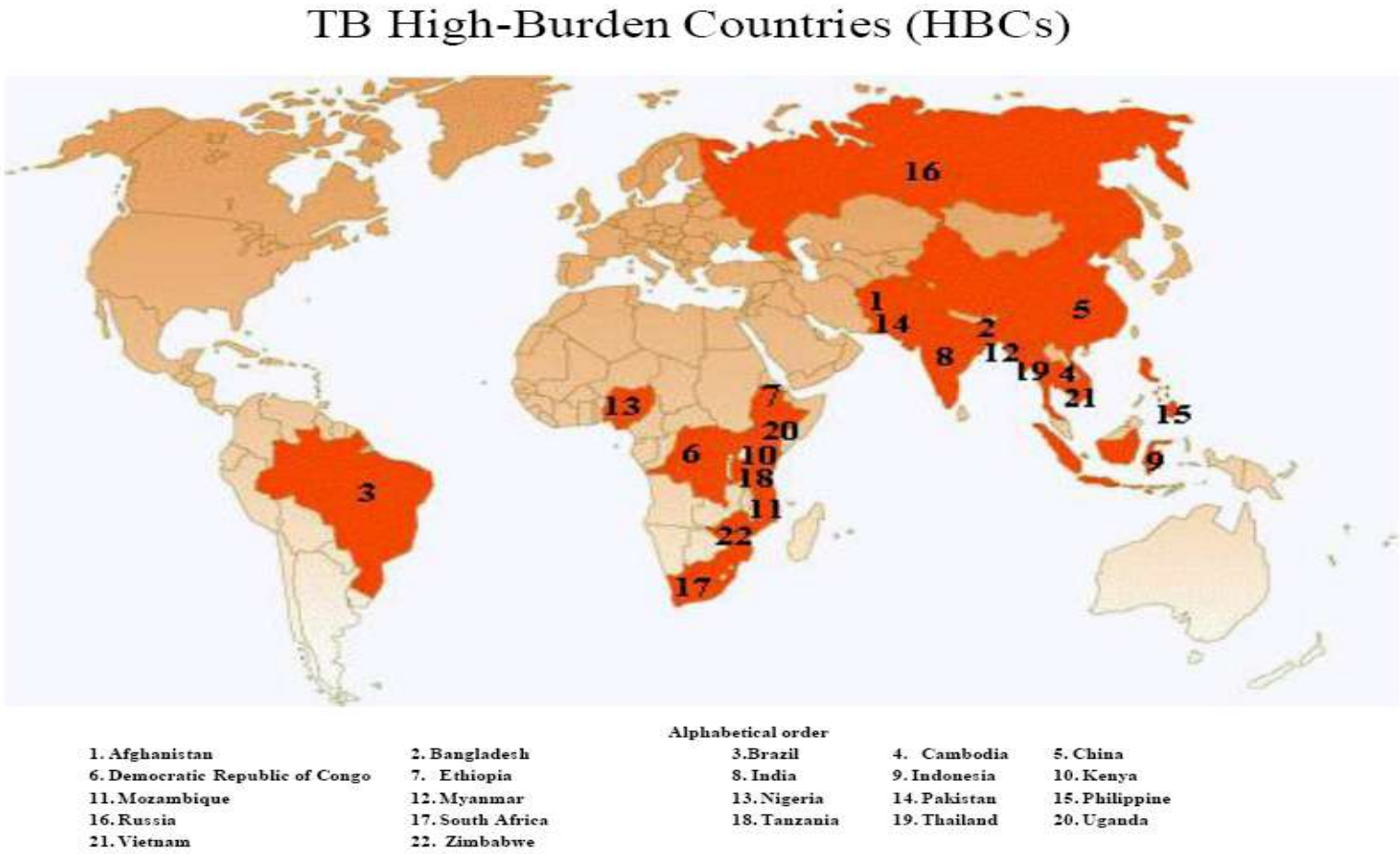


Figure 22. TB high-burden Countries (109)

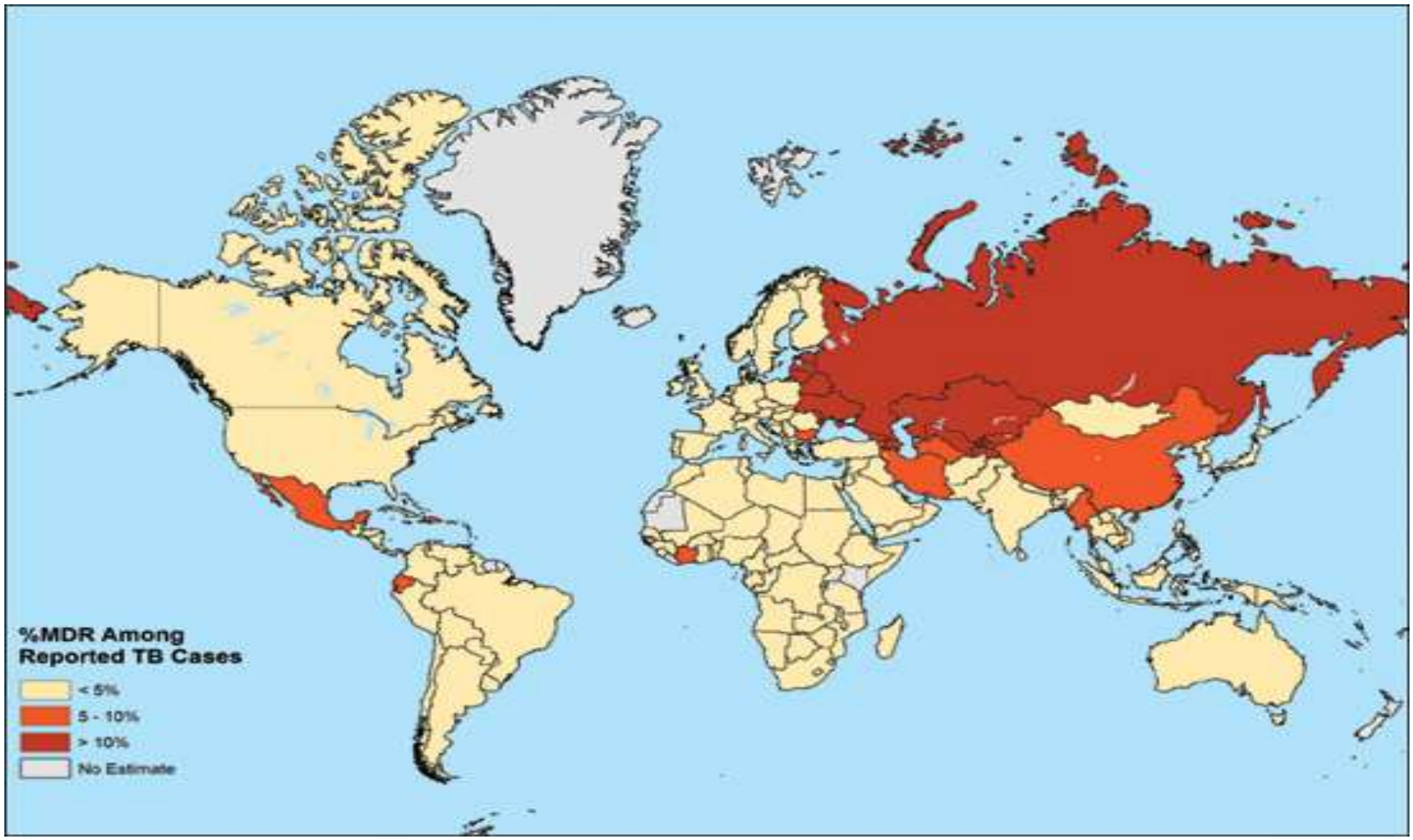


Figure 23. Percentage of MDR-TB among reported TB cases (111)

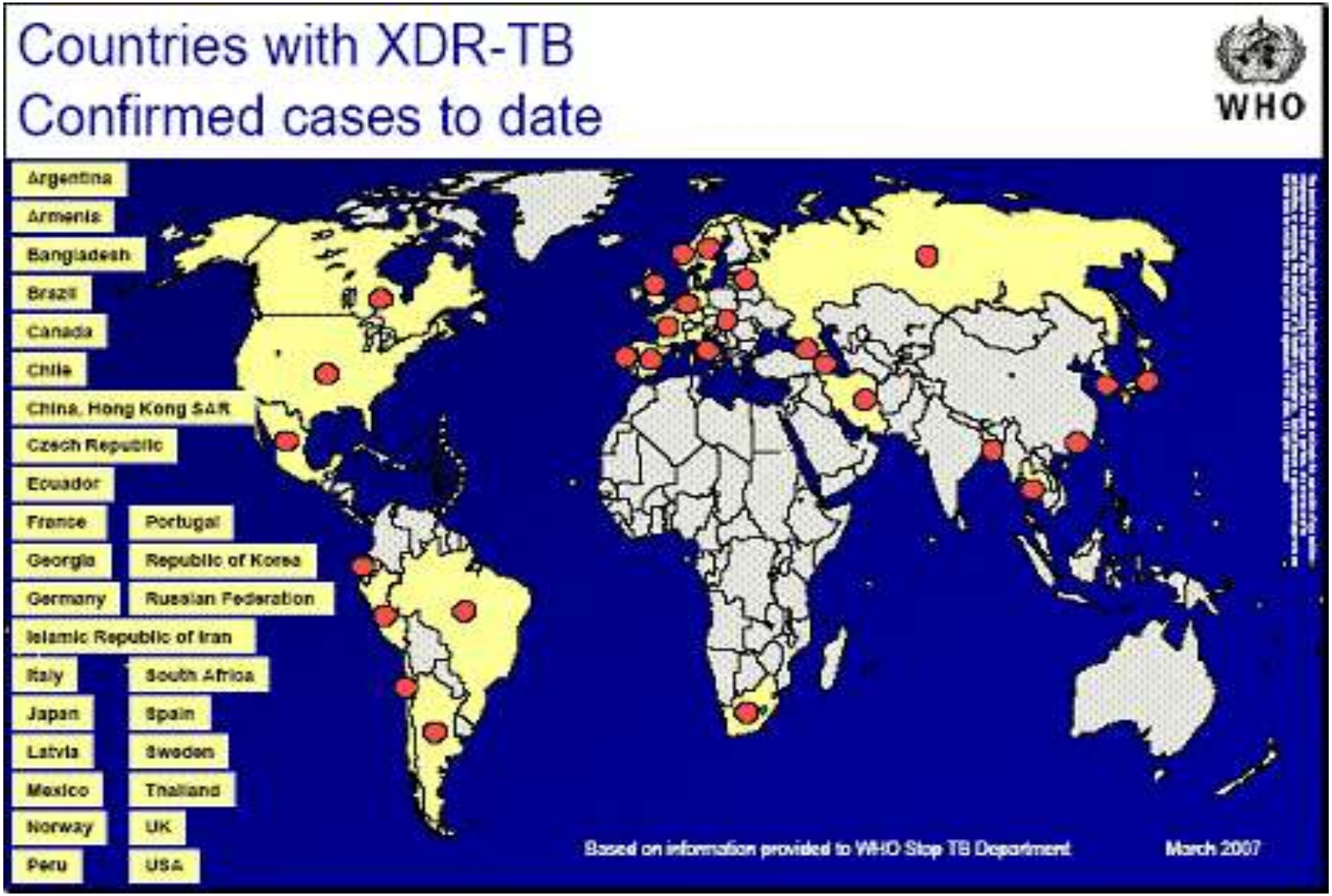


Figure 24. Countries with XDR-TB confirmed cases to date (110)

Appendix D

Glossary:

TB terminology

Directly Observed Therapy, Short-course (DOTS) is a proven approach to TB control that comprises political commitment with increased and sustained financing; case detection through quality-assured bacteriology; standardized treatment with supervision and patient support; an effective drug supply and management system; and a monitoring and evaluation system and impact measurement. Pursuing high-quality DOTS expansion and enhancement is the first component of the WHO-recommended Stop TB Strategy (21, 106).

DOTS coverage: "The percentage of the national population living in areas where health services have adopted DOTS" (21).

Tuberculosis detection rate under DOTS (percentage): "The proportion of estimated new smear-positive cases of TB detected (diagnosed and then notified to WHO) by DOTS programs provides an indication of the effectiveness of national TB programs in finding and diagnosing people with TB. The case-detection rate is calculated as the number of new smear positive cases notified divided by the number of new smear positive cases estimated for that year, expressed as a percentage" (21).

Tuberculosis treatment success under DOTS (percentage): "The proportion of new smear-positive TB cases registered under DOTS in a given year that successfully completed treatment, whether with or without bacteriological evidence of success ("cured" or "treatment completed" respectively)" (21)**.**

Directly Observed Treatment (DOT): "A trained and supervised person observes the patient swallowing the medication" (21).

DOTS-Plus: "The adaptation of DOTS to respond to MDR- TB" (106).

Targets for TB control established by the 44th World Health Assembly (1991): "To cure 85% of the sputum smear-positive TB cases detected and to detect 70% of the estimated new sputum smear-positive TB cases" (21).

Drug susceptibility testing (DST): "Determining in a culture of Mycobacterium tuberculosis the anti-TB drugs that are effective against that particular sample"(106).

Green Light Committee (GLC): "A committee established under the Working Group on DOTS-Plus for MDR-TB, which reviews applications from potential DOTS-Plus pilot projects to determine their compliance with guidelines for access to concessionally priced second-line anti-TB drugs"(106).

Millennium Development Goals (MDGs): "Time-bound and quantified targets for addressing various dimensions of development, adopted by world leaders at the United Nations Millennium Summit in 2000" (106).

Practical Approach to Lung Health (PAL): "A comprehensive, symptom-based approach to the management of patients with respiratory symptoms within the primary health care system"(106).

Public-private mix (PPM) DOTS: "A comprehensive approach to involve all relevant health care providers (public and private) in providing effective TB services"(106).

Disability-adjusted life year (DALY): "A health gap measure that combines the time lived with disability and the time lost due to premature mortality" (106).

Stop TB strategy: "The new WHO-recommended strategy for TB control elaborated in 2006 that encompasses and goes beyond the DOTS strategy" (106).

TB/HIV: "The interaction between the epidemics of TB and HIV (sometimes refers to TB patients who also have HIV infection)" (106).

TB burden: is defined as TB incidence, prevalence and mortality in this study.

TB Notification: "the process of reporting diagnosed TB cases to WHO; the data collected by this process. This does not refer to the systems in place in some countries to inform national authorities of cases of certain "notifiable" diseases. Annual case notifications (and other data on program performance) are collected by WHO via an annual data collection form, distributed to national TB control programs through WHO regional and country offices" (107).

Definitions of TB cases

Tuberculosis suspect: "Any person who presents with symptoms or signs suggestive of TB, in particular cough of long duration" (21).

Case detection: "Activity of identifying infectious cases, mainly among adults attending an outpatient health facility for any reason with cough for 2 or 3 weeks or more, through sputum smear examination" (21).

Case of tuberculosis: "A patient in whom tuberculosis has been bacteriologically confirmed, or has been diagnosed by a clinician" (21).

New sputum smear-positive TB case: "The revised definition of a new sputum smear-positive pulmonary TB case is based on the presence of at least one acid fast bacilli (AFB+) in at least one sputum sample in countries with a well functioning external quality assurance (EQA) system" (21).

Pulmonary tuberculosis, sputum smear negative (PTB-): "Case of pulmonary tuberculosis which does not meet the above criteria for smear positive TB. Diagnostic criteria should include: at least three sputum smear examinations negative for AFB; and radiographic abnormalities consistent with active pulmonary TB; and no response to a course of broad-spectrum antibiotics; and a decision by a clinician to treat with a full course of anti-tuberculosis chemotherapy; or positive culture but negative AFB sputum examinations"(21).

Extra-pulmonary tuberculosis: "Tuberculosis of organs other than the lungs: e.g. pleura, lymph nodes, abdomen, genito-urinary tract, skin, joints and bones, meninges etc. Diagnosis should be based on one culture positive specimen, or histological or strong clinical evidence consistent with active extra-pulmonary tuberculosis, followed by a decision by a clinician to treat with a full course of anti-tuberculosis chemotherapy. A patient diagnosed with both pulmonary and extra-pulmonary tuberculosis should be classified as a case of pulmonary tuberculosis"(21).

All forms: "pulmonary (smear-positive and smear-negative) and extra-pulmonary TB" (107).

HIV+ adults: "Percentage of adults 15–49 who are HIV infected" (107).

New Case: "Patient who has never had treatment for TB or has taken anti-tuberculosis drugs for less than one month" (21).

Relapse: "A patient previously declared cured but with a new episode of bacteriologically positive (sputum smear or culture)" (21)

Treatment outcomes for smear positive pulmonary TB patients

Cured: "A patient who was initially smear-positive and who was smear-negative in the last month of treatment and on at least one previous occasion" (21).

Completed treatment: "A patient who completed treatment but did not meet the criteria for cure or failure. This definition applies to pulmonary smear-positive and smear-negative patients and to patients with extra-pulmonary disease"(21).

Died: "A patient who died from any causes during treatment" (21).

Failed: "A patient who was initially smear-positive and who remained smear-positive at month 5 or later during treatment" (21).

Defaulted: "A patient whose treatment was interrupted for 2 consecutive months or more"(21).

Transferred Out: "A patient who transferred to another reporting unit and for whom the treatment outcome is not known"(21).

Successfully Treated: "A patient who was cured or who completed treatment"(21) .

Sociopolitical and health terms

Gross Domestic Product (GDP): "A measure of the size of economies, reported here in million current US dollars. GDP is the total market value of all final goods and services

produced in a country in a given year, equal to total consumer, investment, and government spending" (105).

The Political Stability and Absence of Violence Indicator: " A measure of perceptions of the likelihood that the government will be destabilized or overthrown by possibly unconstitutional and/or violent means, including domestic violence and terrorism." Low scores in this variable indicate that citizens cannot count upon continuity of government policy or the ability to peacefully select and replace those in power. Values are indexed to have a mean of zero and a standard deviation of one index unit. Positive scores indicate better governance and 99% of the values fall between 2.5 and -2.5" (105). This variable was recorded to dichotomous variable of bad governance (0) and good governance (1). The negative values got bad governance (0) and the positive values got good governance (1).

Access to improved sanitation: "measures the total proportion of the population with access to improved sanitation facilities, expressed as a percentage. Improved sanitation includes any of the following excreta disposal facilities: connection to a public sewer, connection to a septic tank, pour-flush latrine, simple pit latrine, ventilated improved pit latrine, pit latrine with slab, and composting toilet. Improved sanitation facilities are more likely to be sanitary than unimproved facilities, but are not a direct measure of 'basic' sanitation--facilities which are "considered the lowest-cost options for safe, hygienic and convenient facilities that prevent the user and his or her immediate environment from coming into contact with human excreta. A poor water supply and sanitation system can lead to a number of diseases, including diarrhea, intestinal worms, and cholera. Examples

of an unimproved sanitation system include: open pit latrines, public or shared latrines, service or bucket latrines (where excreta are manually removed), hanging latrines, flush to elsewhere (street, yard, open sewer, ditch, river, etc.), and no facilities" (100).

Government expenditure on health: "A percent of total expenditure on health is the percentage of total health expenditures attributable to the national government" (100).

National poverty rate: "The percentage of a country's population living below the country's established national poverty line" (100).

Adults and children living with HIV: "An estimate of the total number of adults (aged 15 years and older) and children (aged 0-14) infected with HIV, whether or not they have developed symptoms of AIDS, alive at the end of the year specified" (100).

Adult Literacy Rate: "Though it varies across countries, the adult literacy rate is usually defined as the percentage of the population aged 15 years and over who can both read and write, with comprehension, a short, simple statement regarding their everyday life. Literacy data can be used to assess gender, age-group, and geographic patterns of illiteracy within each country, as well as the achievement of national literacy programs and policies. According to the United Nations Educational, Scientific, and Cultural Organization (UNESCO), "These estimates reflect the performance of the national education system, as well as the quality of the human resources within a country in relation to their potential for growth, contribution to development, and quality of life." Adult literacy correlates with GNP per capita, life expectancy, fertility rates, infant mortality, and urbanization" (100).

Population density: "The number of persons per square kilometer of land area. This dataset is calculated by WRI using population data from the United Nations Population Division and total land area data from FAOSTAT" (100).

Physicians per 100,000 people: "Include graduates of a faculty or school of medicine who are working in any medical field (including teaching, research and practice) per 100,000 individuals. This is an indicator of the presence of health personnel in a country" (100).

Malnutrition: "Underweight children under five years, moderate and severe, an indicator of child malnutrition, refers to the proportion of children under 5 whose weight-for-age is below minus 2 standard deviations (for moderate underweight) or below minus 3 standard deviations (for severe underweight) from the median weight-for-age of an international reference population recognized by the World Health Organization (WHO). The values presented here, reported by the United Nations Children Fund (UNICEF), include both moderately and severely underweight children"(100).

Income: "Economies are divided according to 2006 GNI per capita, calculated using the World Bank Atlas method. The groups are: low income, $905 or less; lower middle income, $906 - $3,595; upper middle income, $3,596 - $11,115; and high income, $11,116 or more"(104). According to WB, developing economic countries are defined as countries with low and middle income and developed economic countries are defined as countries with high income and these two recent definitions were used in this study" (105).