ABSTRACT

Tuberculosis has been considered an occupational risk for health care workers since the 1930s. Over the past six decades, however, TB incidence and TB infection rates have dramatically decreased. This decline has been largely due to improved living conditions, nutrition and pharmaceutical treatment. Today, opinions about TB risk in the health care settings vary considerably and include the view that health workers are at no increased risk for TB infection compared to the general population.

TB screening programs have been operating in British Columbia long-term care facilities (LTCFs) since 1987. The primary interest of these programs has been to monitor the risk that employees of these health care facilities have. The purpose of this thesis is to evaluate these screening programs based on the following questions:

1. Is the TB incidence of LTCF employees higher than that of the general population who are similar in age, gender and ethnic origins?
2. Is TB infection rate of LTCF employees higher than that found in similar studies in other jurisdictions?
3. What are the costs of the screening program and how do these costs compare with the costs of treating active TB cases that would have occurred if the screening program had not been in place?

Analyses of the B.C. TB Control five year data has revealed that TB incidence of LTCF employees is not greater than the general population when age, gender and ethnic origin are controlled. An analysis of TB incidence rate by each ethnic group (immigrants, First Nations and other Canadians), revealed that the TB incidence rate in immigrants and
First Nations are 6 and 53 times, respectively, higher than Canadian born. Further, the TB incidence in each ethnic group is consistent with its corresponding population. These results suggest that TB is more related to birthplace than to working place.

The TB infection rate (21.9%) in British Columbia long-term care facility employees found in this study is in the mid-range of studies in other jurisdictions. When analysis was performed in each ethnic group, it was found that the infection rate in immigrants (52.3%, 95% CI is 3.23-3.58) and First Nations (46.3%, 95% CI is 2.49-3.61) are much higher than Canadian born (10.6%). However, the TB infection rate in adult care facility employees (24.6%) is not greater (95% CI is 0.87-1.0) than that of child care facility employees (17.6%) after adjusting for age, gender and ethnic origin. TB infection rate is also more related to birthplace than to the working place.

INH preventive therapy is provided to those who are found to be PPD positive to prevent the occurrence of active TB from TB infection. It was calculated that the cost of preventing of one TB case ($58,272) is much higher than the treatment of active TB ($10,304). From this perspective, this program should be stopped. However, considering the high TB infection rate in immigrants and First Nations, the TB screening program should target to these high risk groups to prevent the potential reactivation of TB.
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CHAPTER I

TUBERCULOSIS: A BACKGROUND

This chapter provides a basic introduction to the disease that is called tuberculosis. It covers, briefly and in non technical language, the etiology of the disease, its transmission, BCG vaccination, antibiotic chemotherapy, tuberculin skin testing and chemoprophylaxis.

Introduction

Tuberculosis (TB) is an ancient disease that was a scourge of humankind in many parts of the world. It has remained so in economically underdeveloped countries. TB is also referred to as mycobacterium tuberculosis (M. tuberculosis) since almost all causes of TB are now due to M. tuberculosis. The infection by M. tuberculosis occurs through inhalation of the tubercle bacillus which is dispersed through the air by sneezing, coughing, and talking of infectious TB patients. After the tubercle bacillus invades the human body, it can reside in most organs of the body and cause various kinds of TB. If the tubercle bacilli site is in the lungs and bronchi, it is referred to as pulmonary TB, representing 85% of all kinds of TB. Pulmonary TB is more infectious than other kinds of TB (Canadian Thoracic Society [CTS], 1996). If the site is in an organ other than the lungs or bronchi, it is referred to as extra-pulmonary TB. Thus, extra-pulmonary TB includes lymphatic TB, pleural TB, genitourinary TB, bone and joint TB, and tuberculous meningitis.

TB Infection and Active TB

When considering TB, it is important to distinguish between the concept of infection and disease. TB infection is the state in which the tubercle bacillus has become
established in the body. The infected individual has no symptoms, signs, nor roentgenographic abnormalities suggestive of TB, and bacteriologic studies are negative. On the other hand, TB disease is classified as clinical TB, a state in which an infected individual has an illness involving one or more organs of the body. The patient has symptoms and signs of active TB, abnormal roentgenograms, and positive bacteriologic studies (Table 1). Infection is usually defined by tuberculin skin test reactivity. Diagnosis

<table>
<thead>
<tr>
<th>Features Distinguishing Tuberculosis Infection from Pulmonary Tuberculosis Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Similarities:</strong></td>
</tr>
<tr>
<td>Tuberculosis organisms present in the body</td>
</tr>
<tr>
<td>Tuberculin skin test usually positive</td>
</tr>
<tr>
<td><strong>Differences:</strong></td>
</tr>
<tr>
<td>Chest X-ray</td>
</tr>
<tr>
<td>Specimens for mycobacteria (smears or cultures)</td>
</tr>
<tr>
<td>Symptoms</td>
</tr>
<tr>
<td>Infectious</td>
</tr>
<tr>
<td>A &quot;case&quot; of TB</td>
</tr>
</tbody>
</table>


of TB disease is usually established by finding mycobacteria on a smear or culture of appropriate body fluids. Smears of appropriate specimens for detection of mycobacteria are currently the fastest and easiest methods for early presumptive diagnosis of TB, but they are less sensitive and specific compared to cultures. Cultures are the definitive method for diagnosis of TB, but the testing process may take as long as 6 weeks.

**Transmission of TB**

TB is transmitted by airborne infection. When a source case coughs, sneezes, laughs, speaks, or sings, the aerosolized respiratory excretions are expelled from the nose
or mouth, and their water content evaporates rapidly leaving only a small residue of solid matter, the droplet nucleus, that includes the tubercle bacillus. The droplet nuclei reach the alveoli and may cause infection. The occurrence of infection depends on many factors.

These factors are grouped and summarized in Table 2.

Table 2
Factors Influencing Transmission of Tuberculosis

1. Source case
   a. Pulmonary versus non-pulmonary
   b. Extent of pulmonary disease
   c. Severity of cough
   d. Chemotherapy
2. Environmental factors & Circumstances of the exposure
   a. Concentration of organisms in the air
   b. Ultraviolet irradiation
   c. Proximity
   d. Duration
3. Host factors
   a. Previous tuberculosis infection
   b. Previous infection with nontuberculous mycobacteria
   c. Vaccination with Calmette-Guerin bacillus (BCG)
   d. Other clinical diseases which reduce cell-mediated immune system


TB transmission is defined as the mechanical act of transfer of *M. tuberculosis* from the source case to a potential new host. It depends on three conditions which are: the number of mycobacteria the source case produces; the environment shared with source case; and the host’s resistance to mycobacterium infection.

The number of mycobacteria produced by the source case is the first factor that affects TB infection. If both the environment shared with source cases and the host’s resistance are constant, a greater number of bacteria produced by the source case will increase the chance that the contacts will get infected. TB patients who have untreated
pulmonary TB and smear positive sputum transmit infection with significant frequency (CTS, 1996). However, individuals with TB infection and most TB patients do not produce a significant number of tubercle bacilli, they are not considered infectious (ATS/CDC, 1990).

The second condition that affects transmission is the environment shared with the source case. The conditions under which the exposure occurs determine, in part, the number of infectious particles inhaled. If the exposure is of long duration, and takes place under conditions that would be associated with a high concentration of droplet nuclei in the air, the likelihood that transmission will occur will be greater. However, in good living conditions, infection is unlikely to occur due to the dilution of infected air by ventilation, reducing the survival rate of most tubercle bacilli from the source case. It has been reported that improved living conditions were a major factor in the steady decrease of TB incidence and mortality long before antibiotic drugs were discovered (Grygier et al, 1994).

The third condition that determines TB transmission is the immune status of the host. In most individuals, the immune status is strong enough that most do not develop active disease when exposed. Further, both BCG vaccination and previous mycobacteria infection may increase the immune response, affording some protection against subsequent infection with *M. tuberculosis* (Koch-Weser, 1985; Palmer, 1966). But, other factors such as advancing age, malnutrition, diabetes, or HIV infection may cause defects in the cell-mediated immunity, increasing the risk of infection.
BCG Vaccine

The anti-tuberculosis vaccine is a suspension of live tubercle bacilli (M. bovis) that have been attenuated by laboratory cultivation on a special medium. This method was developed by Drs. Albert Calmette and Camille Guerin of France in 1920. To commemorate these two doctors, this vaccine is referred to as BCG (Bacilli Calmette-Guerin) vaccine. Evidence has suggested that BCG vaccination will result in a 60-80% decrease in the incidence of TB in a given population (Leulmo, 1982). It is also clear that the role of BCG is not to prevent infection, but rather to increase the host’s resistance, limiting the proliferation of tubercle bacillus to such a degree that clinical disease does not develop (Sutherland et al, 1979). However, since antibiotic chemotherapy has been administered to active TB patients, exogenous infection occurs infrequently, and TB incidence has dropped dramatically. Hence, BCG is no longer routinely used in the general population of developed countries.

Further, BCG vaccine can cause a false-positive reaction to the tuberculin skin test and the circumstances under which these reactions occur is detailed below in the section headed “The Tuberculin Skin Test”.

However, BCG is still recommended for the general population of developing countries by the World Health Organization (WHO) (WHO, 1982), since TB infection and incidence rates are still high in those countries.

Antibiotic Chemotherapy

While BCG vaccine is used to increase the host’s resistance to TB infection, antibiotic chemotherapy is used to kill the mycobacteria in the source case. When the drug
streptomycin (STM) was discovered, the treatment of active TB underwent a revolutionary change and, with the advent of even more effective drugs such as isoniazid (INH) and rifampin (RMP), the great majority of patients can be cured.

**Definition of TB Prevalence, Incidence and Mortality**

The measures of disease frequency used most frequently in epidemiology fall into two broad categories: prevalence and incidence. The prevalence of TB is calculated as the total number of TB patients in a defined population at a given point in time, divided by the total population investigated. On the other hand, TB incidence is defined as the number of new cases of TB that occur or are found during a specified period of time (annually in general), divided by the total population at risk.

TB mortality is calculated as the total number of deaths because of TB disease, divided by the total population investigated.

**The Epidemiology of TB**

At the beginning of this century, TB disease was the leading cause of death in the western world ("Canadian Discoveries", 1984). The most susceptible population was infants and young adults (Springett, 1952). But this mortality pattern has changed because of many factors which include improved living conditions, BCG vaccination, the availability of chest X-ray surveys, and the use of antibiotic chemotherapy in active cases. In Canada, the annual rate of new and reactivated cases of TB has dropped from 80/100,000 in 1938 to 7.1/100,000 in 1994. The mortality rate has declined from 55/100,000 to 0.4/100,000 in the same time period (Statistics Canada, 1996) (Figure 1). Not only has the incidence of TB decreased, but the population at risk has also changed.
Figure 1 Tuberculosis Morbidity & Mortality in Canada Between 1938 and 1994

Nowadays, this disease is largely found among seniors, First Nations, immigrants from areas with a high prevalence of TB, and socio-economically disadvantaged individuals (Canadian Thoracic Society [CTS], 1996).

The Tuberculin Skin Test

Although TB incidence and mortality rates have decreased dramatically, there continues to be a need to identify individuals with TB infection as candidates for INH preventive therapy, so that occurrence of active TB may be prevented. The tuberculin skin test has been adopted as a screening test.

Tuberculin (an impure extract derived from a culture broth in which tubercle bacilli had been grown) was first prepared by Koch in 1890 and he advocated its use for therapeutic purposes (Keers, 1978). However, it was later found that the reaction to tuberculin was of diagnostic rather than therapeutic importance. In 1934, Seibert made a simple protein precipitate of crude tuberculin, which she termed purified protein derivative (PPD). This purified preparation has become the preferred reagent for diagnostic purpose in most areas of the world and the current tuberculin skin test is also referred to as the PPD test.

Based on various studies of sanatorium patients and of large non-infected populations, Edward et al (1960) and Lester et al (1958) reported that the non-infected populations demonstrated a 0-5 mm induration in response to the PPD test and the sanatorium patients had a mean value of 16- to 17-mm reaction. Initially the accepted standard for the lower limit of a positive reaction was an induration of 5 mm (Lester et al, 1958). However, it was found that in many tropical climates, large segments of the
populations had skin test hypersensitivity to environmental mycobacteria (nontuberculous mycobacteria), producing cross-reactions with PPD manifested by small-sized tuberculin reactions (4-12 mm) (Edward et al, 1960). Recognition of the cross-reaction between antigens of nontuberculous mycobacteria led the American Thoracic Society (ATS, 1971) to recommend the adoption of 10 mm as the minimal size of induration defining a positive tuberculin skin test.

It should be noted that the tuberculin skin test is only an indicator of infection with tubercle bacilli. Both false-positive and false-negative reactions are encountered frequently.

BCG vaccination and nontuberculous mycobacterium infection are two major factors that cause false-positive PPD reactions. Menzies (1992) reported that, when BCG is given in infancy, it does not affect PPD reaction. However, for those vaccinated between 6 and 14 years, up to 25% had reactions larger than 10 mm without TB infection. A false-positive reaction may also be caused by nontuberculous mycobacterium infection (Grzybowski, 1974) since individuals with nontuberculous mycobacteria infection can produce cross-reactions with PPD.

Many factors may cause false-negative reactions. Age has been considered to be a problem in PPD testing for many years. Stead (1987) reported that today’s elderly had an infection rate of 80% in the 1930s when they were younger, but only 20-30% of them test positive today. Although the reason is not clearly understood, it is thought that the cell-mediated immune system is decreased in the elderly, so that the positive reactions may not
be reflected in the tuberculin skin tests. Hence, PPD testing is not recommended for screening an elderly population.

Some disease states that interfere with cell-mediated immune responses also cause a false-negative reaction. Common viral illnesses such as measles and the administration of live virus vaccines may cause a transient depression of tuberculin reactivity. Corticosteroids and immuno-suppressive drugs decrease tuberculin reactivity if the patient is on a sufficient dose for a long enough period of time (Bovornkitti, 1960). Malnutrition may cause defects in cell-mediated immunity. Further, advanced tuberculosis itself may cause diminished or absent tuberculin responsiveness. Finally, HIV infection may compromise the cell-mediated immune system and cause a false-negative reaction. It has been reported that 20% -30% of persons with known active TB without HIV infection and as many as 60% of persons with HIV infection have a false-negative reaction (Centre for Disease Control [CDC], 1990).

Although the tuberculin skin test is an imprecise diagnostic instrument, no better test has been developed. Recent developments in mycobacteriology based on radiometric methods and genetic probes specific for mycobacterial species may speed up the diagnosis of TB, but these methods have not been routinely used (CTS, 1996).

**INH Chemoprophylaxis**

Chemoprophylaxis, administered as the outcome of the tuberculin skin test, is defined by Hoeprich (1972) as a form of treatment for an infection which has not yet occurred, for an infection in the beginning stage, or for an asymptomatic subclinical state. Chemoprophylaxis is also referred to as preventive therapy.
The effectiveness of INH preventive therapy was first demonstrated by Ferebee and Mount (1962). Subsequent to this discovery, many clinical trials were performed in different countries. The protection rate of INH has been found to be between 60% and 100% (CTS, 1996). These results have contributed towards the goal “to eradicate TB by the year of 2010” (CDC, 1989). Nevertheless, side effects of INH have been identified and the use of INH preventive therapy has become limited by the counteraction of these effects.

**Side Effects of INH**. A serious side-effect of INH therapy is INH associated hepatitis or INH induced hepatitis. The United States Public Health Service (USPHS) reported the possibility of hepatitis in patients receiving INH as 1 per 100,000 under the age of 20; 300 between ages 20 and 35; 1,200 between ages 35 and 49; and 2,300 between ages 50 and 64 (Kopanoff et al, 1978). For those aged 64 years or older, the rate has been documented as 5,000/100,000 (Dutt et al, 1993). These results are summarized in Table 3.

<table>
<thead>
<tr>
<th>Age (yr.)</th>
<th>Hepatitis Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;20</td>
<td>rare</td>
</tr>
<tr>
<td>20-34</td>
<td>0.3%</td>
</tr>
<tr>
<td>35-49</td>
<td>1.2%</td>
</tr>
<tr>
<td>50-64</td>
<td>2.3%</td>
</tr>
<tr>
<td>&gt;=65</td>
<td>5.0%</td>
</tr>
</tbody>
</table>

Table 3
USPHS Study Recorded Possibility Of Hepatitis
Because INH associated hepatitis increases with age, the use of INH preventive therapy in the elderly is limited. This incorporated in ATS/CDC guidelines for INH preventive therapy (ATS/CDC, 1986).

Other side effects are less serious but more common. These include erythematous itchy rash, mental lethargy, arthralgia, peripheral neuropathy and optic neuritis. Although INH has not been found to be teratogenic, it is not routinely recommended for pregnant women, except for those who are HIV positive (CTS, 1996).

Candidates for INH Preventive Therapy. Balancing the risk of hepatic injury during the period of treatment and the potential lifelong benefit of preventive therapy, INH preventive therapy is recommended for (ATS/CDC, 1986): (a) individuals who are less than 35 years of age and have PPD positive reactions; and (b) individuals who are older than 35 with PPD positive reactions and have other risk factors which increase the risk of developing active TB. These risk factors include:

- close contacts
- newly infected persons or convertors
- past TB which has not been previously treated with adequate chemotherapy
- abnormal chest roentgenograms
- AIDS/HIV status
- other clinical conditions such as silicosis, diabetes mellitus, immunosuppressive therapy, and other conditions associated with substantial rapid weight loss or chronic undernutrition
HIV Infection and TB Disease

Since HIV infection seriously compromises the immune system, especially the cell-mediated immune system, TB disease is unusually high in the HIV positive population. In 1990, it was found in the United States that 4.3% of 152,441 AIDS cases were infected with TB. The results of HIV serological prevalence surveys in metropolitan TB clinics have shown that 11% of TB cases have HIV serological positive reactions (ATS, 1992). It is also indicated that, in the United States, from the 1950s to 1984, the rate of TB incidence was declining by 5 to 7% annually. However, from 1985 to 1991 the number of cases increased by 18%. The occurrence of TB among persons with HIV infection is a major factor contributing to this change in the decades-long pattern of decline in TB.

In Africa, the situation is even worse. By the end of 1993, 301,861 cases of AIDS, or 36% of the global total, had been officially reported to the World Health Organization (WHO) from Africa, a continent with less than 10% of the world's population (WHO, 1994). TB has become the greatest AIDS-related opportunistic infection. An autopsy study in Abidjan (Lucas, 1993) showed that TB was the cause of death in 32% of 247 HIV-positive patients. In Rwanda, among 370 HIV-positive patients surveyed, 22 (15%) were diagnosed as having active TB (Anglaret et al, 1995). Wilkinson and Moore (1995) investigated 297 patients diagnosed with TB in a rural district hospital in South Africa, and found that 107 (36%) were HIV positive. In these countries, the treatment of TB in HIV positive patients is not stressed because of the limited resources. As Reeve (1994, p 416) said, "HIV remains a terminal illness and the palliative treatment of HIV-related conditions must remain a low priority in African countries with limited health budgets."
a result, AIDS and related TB disease cause greatly increased adult mortality, reduced life expectancy, disrupted families, excessive demands on health care facilities, and reduced economic output (De Dock, 1994).

In Canada, there has been no evidence that the HIV epidemic has had a substantial impact on overall TB incidence rates. According to British Columbia data, less than 2% of TB cases are associated with HIV infection (CTS, 1996). However, with increasing number of HIV infections and AIDS, TB may be resurrected all over the world. This new trend poses a new problem for controlling TB disease.
CHAPTER II

TUBERCULOSIS IN BRITISH COLUMBIA

This chapter briefly reviews the history of the treatment of active TB, chest X-ray surveys and the tuberculin skin tests in British Columbia. A comparison of current TB status is made between general population and residential care in British Columbia.

The Tranquille Tuberculosis Society

In 1904, the Tranquille Tuberculosis Society was formed for the prevention and treatment of consumption, and the first sanatorium was built at Tranquille near Kamloops, British Columbia. Treatment of patients was based on rest, fresh air, exercise and good nutrition. In the beginning, this was a voluntary society. However, veterans returning from World War I increased the numbers of TB cases and strained the financial resources of the voluntary society. As a result, the management of Tranquille Sanatorium was taken over by the British Columbia government in 1919. Simultaneously, small scale clinical treatment of TB began in Vancouver.

The Division of British Columbia Tuberculosis Control, Ministry of Health

In 1935, the Division of British Columbia Tuberculosis Control of the Ministry of Health was established in Vancouver and the Tranquille TB Society was reorganized and moved to Vancouver to assist the new Division in terms of fund raising and public education (Ministry of Health, 1991). In the 1930s, British Columbia introduced assistance programs which were modeled after the province of Saskatchewan's free TB treatment program. In 1948, the federal government funded, through the National Health Grants
Act, the provision of free treatment of TB (Grygier, 1994). This led to the establishment of new sanatoria. In 1949 and 1952, two more sanatoria, Willow Chest Centre (WCC) and Pearson Hospital, were opened in Vancouver. At this time, sanatorium bed capacity reached its peak and subsequently the number of beds started to decrease (Table 4).

Table 4
Sanatorium population in British Columbia

<table>
<thead>
<tr>
<th>Year</th>
<th>Total population in British Columbia sanatoria</th>
</tr>
</thead>
<tbody>
<tr>
<td>1952</td>
<td>838</td>
</tr>
<tr>
<td>1955</td>
<td>615</td>
</tr>
<tr>
<td>1958</td>
<td>332</td>
</tr>
<tr>
<td>1961</td>
<td>244</td>
</tr>
<tr>
<td>1963</td>
<td>205</td>
</tr>
<tr>
<td>1964</td>
<td>163</td>
</tr>
</tbody>
</table>

Note. From “Annual Report”, by The Division of Tuberculosis Control, Province of British Columbia, 1965.

Over the 13 year period between 1952 and 1964 (corresponding roughly to the era of introduction of chemotherapy), the British Columbia sanatorium population dropped by over 500%. By 1958, Tranquille Sanatorium was closed and tuberculosis beds became centralized in the Vancouver area at the WCC, at the Pearson Hospital, and at the Essondale Mental Health Facility. This symbolized the transition of treatment from rural isolation to an urban general hospital setting.

As the bed capacity of sanatoria decreased, the efforts switched from passive treatment to active case-finding. In 1957, the Division of British Columbia TB Control launched a chest X-ray examination program across the province. Many early stage and asymptomatic patients were picked up in this campaign. This campaign was discontinued
in 1965 since community surveys were found to be no longer productive (Division of Tuberculosis Control, 1971).

As a result, the tuberculosis treatment facilities were closed or their functions changed. In 1964, operating rooms at the WCC were converted from TB surgical units to cardiac units and, in the same year, the full-time tuberculosis specialist stationed at Essondale was released. In 1996, the only chest clinics of the Division of TB Control across the province are located in WCC, New Westminster and Victoria, and only WCC provides in-patient services.

**Tuberculosis Chemotherapy in British Columbia**

By the mid-60s, tuberculosis treatment had become centralized in Vancouver and relied mainly on 18-24 month daily combination therapy (INH and p-aminosalicylic acid [PAS]). Patients remained in hospital for most of their treatment. This hospitalized drug therapy remained the treatment of choice until the 1970s. By the 1970s, RMP was recognized to be equally as effective as INH. Subsequently, RMP and INH short course daily chemotherapy were introduced as the out-patient treatment of choice at the WCC, replacing the long-course methods. In the 1970s, the WCC shifted from an in-patient centre for tuberculosis treatment to a mainly out-patient based treatment system. After 1979, RMP, INH and ethambutol short-course therapy administered for an average of 9 months became the standard treatment at the WCC.

**Tuberculosis screening program for the high risk groups**

Chest X-ray screening programs for TB were introduced in British Columbia as early as 1921 to screen First Nations populations. In 1944, X-ray examinations were
initiated as a screening method to identify active TB in Canadian immigrant applicants. In 1957, chest X-ray surveys were introduced for the general population. The purpose of these programs was to find active TB patients. Many asymptomatic TB patients were picked up in these programs and were treated with chemotherapy. Hence, TB incidence and infection rates decreased dramatically.

Current screening programs, introduced in the 1980s, use the tuberculin skin test. The use of the tuberculin skin test is based on the assumption that TB incidence and infection rates have decreased dramatically and the reactivation of early TB infection is the major cause of active TB. The major goal of this program is to identify individuals with TB infection, following which INH preventive therapy can be administered to prevent occurrence of active TB. The tuberculin skin test screening program is directed toward the populations at higher risk to contract TB than the general population. These populations include (CTS, 1996):

- close contacts of individuals with known or suspected active TB
- persons with a history of active TB, or with a chest X-ray suggestive of past TB, who have not received adequate therapy
- persons who are HIV positive
- foreign-born persons from areas with a high prevalence of tuberculosis
- aboriginal communities with high rates of tuberculosis
- the poor, especially the urban homeless
- alcoholics and intravenous drug users
- staff and residents of long-term institutions -- e.g., nursing homes, correctional facilities, and psychiatric institutions
• those with high-risk medical conditions, including chronic renal failure, diabetes mellitus, immunosuppressive therapy, and silicosis

• those at risk of occupational exposure to TB likely to be exposed to active cases of pulmonary tuberculosis. This includes health care workers

• those at risk of active TB who are employed in settings where they may infect infants, children, adolescents or the immunosuppressed

A tuberculin skin test screening program was initiated in British Columbia long-term care facilities (LTCFs) in 1987, concurrent with the publication of ATS/CDC guidelines of the TB screening program (ATS/CDC, 1986). However, this program has been questioned in recent years. In his presentation as the Director of TB Control to the 99th Meeting of Health Officers’ Council of British Columbia, Allen (1994) reported that TB incidence in residential care and correctional centres is not significantly greater than in the general population (Table 5). He suggested that the screening program may not ultimately be more efficient than passive case-finding since, although it may find cases earlier, the screening program is not likely to be justifiable as a case-finding procedure.

Table 5
The Comparison of TB Incidence Between Institutional And General Population

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of Surveyed</th>
<th>Number of active TB</th>
<th>Incidence (1/100,000)</th>
<th>Incidence of general population (1/100,000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1990</td>
<td>16,519</td>
<td>2</td>
<td>12.1</td>
<td>9.0</td>
</tr>
<tr>
<td>1991</td>
<td>16,717</td>
<td>1</td>
<td>6.0</td>
<td>8.6</td>
</tr>
<tr>
<td>1992</td>
<td>15,891</td>
<td>2</td>
<td>12.6</td>
<td>10.1</td>
</tr>
<tr>
<td>Total</td>
<td>49,127</td>
<td>5</td>
<td>10.2</td>
<td>9.2</td>
</tr>
</tbody>
</table>

Given this background, a more detailed study of the TB infection and incidence in British Columbia LTCFs is conducted as the basis for this thesis, and the objectives and methods are described in Chapter V.
CHAPTER III

TB SCREENING PROGRAMS IN LONG-TERM CARE FACILITIES

IN BRITISH COLUMBIA

According to the British Columbia Tuberculosis Screening Guidelines (Ministry of Health, 1992), all persons admitted to a licensed community care facility and all new employees of licensed community care facilities should be screened for tuberculosis.

Chest X-rays are administered to all newly admitted residents over the age of 60 to exclude active TB. The tuberculin skin test screening program is utilized for the residents who are under the age of 60 and all newly employed staff. The tuberculin skin test screening program is a three step process:

1. Tuberculin skin testing: A tuberculin skin test is the intracutaneous injection of 5 TU PPD (equivalent to 0.0001 mg of PPD protein contained in 0.1 ml of solution) in the volar surface of the forearm. The reaction is read 48-72 hours subsequent to the injection. A positive test is usually defined as greater than 10 mm of induration (erythema is not considered), 5-9 mm of induration is considered suspicious, and less than 5 mm is considered negative.

2. Chest X-rays: Chest X-rays are given to those who have more than 10 mm reactions. The purpose of the chest X-rays is to exclude active TB and to provide the baseline for chemoprophylaxis.

3. INH chemoprophylaxis: INH chemoprophylaxis is not mandatory for all the positive PPD reactions. According to Allen (1988), the Director of British Columbia TB
Control, patients meeting the indications for chemoprophylaxis (ATS/CDC, 1986) should be encouraged to accept this measure. However, the compliance and completion of the course should be taken into account. It is recommended:

- a 12 month treatment duration should be targeted. If there are problems with attitude or compliance or adverse effects, minimum 6 month treatment is recommended
- follow-up clinical visits must be made at least monthly
- biochemical monitoring: transaminase levels and close clinical monitoring are required each month for at least the first 3 months

After the initial screening test is done, routine re-testing of residents/employees is not carried out unless there are specific indications in an individual (e.g., abnormal chest X-rays compatible with tuberculosis) and specific local situations (e.g., institutions with high TB incidence and infection rate).

The screening model that has been described above is depicted in Figure 2.

The purpose of this study is to evaluate the tuberculin skin test screening program in LTCF employees. The specific purposes include the identification of TB incidence and infection rates, the determination of the unit cost of those with positive tuberculin tests who are recommended for INH preventive therapy, the determination of the cost of providing INH preventive therapy for preventing occurrence of active TB, and the comparison of those costs to the treatment of active TB cases. The time period of this study is from January 1, 1990 to December 31, 1994. The methods of this study is discussed in Chapter V.
Figure 2: The model of a tuberculin skin test screening program

- Employment PPD test
  - Positive reaction (≥ 10 mm)
    - Chest X-ray
      - INH preventive therapy
        - TB prevented
        - Active TB
      - No active TB
  - Negative reaction (<10 mm)
    - No further action required
    - Active TB
      - INH induced hepatitis
CHAPTER IV
LITERATURE REVIEW

This literature review focuses on studies of TB in elderly population, especially the elderly living in long-term care facilities and health care employees in various health settings.

TB in Long-Term Care Facility Residents

In Chapter I, it was observed that the present-day elderly lived in a time when more than 80% of persons were infected with TB. Some elderly individuals continue to harbor viable bacilli in dormant caseous and calcified lesions, and the cell-mediated immune status of the elderly decreases with age. Hence, persons with old dormant lesions may undergo reactivation of infection and become infectious. Approximately 95% of active TB in the elderly comes from reactivation of remote infection (Stead, 1967). Several factors may predispose the reactivation of dormant lesions in the elderly. These include insulin-dependent diabetes, poor nutrition, long-term corticosteroid therapy, and other debilitating diseases (Dutt et al, 1993). Further, persons who were never infected or who have outlived their bacilli may become infected because of reduced cell-mediated immune status. As a result, the elderly have a higher TB incidence rate than any other age group.

The elderly who live in long-term care facilities (LTCFs) may have greater TB incidence than those who live in the community. Residents in long-term care institutions
are less healthy and older, and live closer than community dwellers and, hence, have
greater chance of reactivation of infection or re-infection.

TB in older persons has characteristics that make it more difficult to diagnose than
in younger persons. Pulmonary TB commonly presents with symptoms of fever, weight
loss, cough, sputum, and debility. The latter four symptoms may occur in the elderly
without inciting significant apprehension, either in the patient or in the physician. They can
be explained by a variety of medical problems commonly encountered in the geriatric
population or they may simply be dismissed as part of aging. An abnormality observed on
a chest film may not be properly interpreted because of atypical roentgenograms. Further,
the overall decline in TB has resulted in a low index of suspicion among physicians. All
these factors may delay the diagnosis of TB in the elderly. Thus, the chance of TB
transmission may be increased.

Studies have shown that TB incidence in the elderly living in LTCFs is higher than
the elderly living in communities ("Tuberculosis--North Dakota", 1979; "Tuberculosis--
Oklahoma", 1980), but this was not considered a serious problem until Stead's widely
circulated seminal description of two outbreaks in Arkansas nursing homes (Stead, 1979,
1981). The first outbreak (Stead, 1979) was in a 230-bed facility where the index case was
a patient who had cavitary TB which had been misdiagnosed as lung cancer. Of the 172
residents at risk, 49 (28%) became strongly positive to PPD and three active cases
developed among these residents. Five members of the staff also converted. The second
outbreak was in a 240-bed nursing home in Arkansas (Stead, 1981). Results of the
investigation showed that the index case was a patient who had unrecognized TB for at
least 12 months. Forty-nine (30%) of 161 previously PPD negative residents became infected and eight (17%) acquired progressive primary TB. Of the employee group, 21 of 138 (15%) converted and one case of clinical TB occurred.

In the United States, the national data show that approximately 5% of persons over age 65 reside in nursing homes but account for 20% of the cases of TB, giving a case rate that is 4 times greater than that of elderly persons residing elsewhere (Stead, 1989). In Arkansas, 50% of all cases of TB reported from 1981 to 1983 were in persons over 65 years of age, an incidence of about 60/100,000. In nursing home residents, a reported incidence of 234/100,000 is four times greater than that of persons over 65 residing at home (Stead, 1985).

In a recent CDC sponsored survey from 29 states, the difference in TB incidence between community and LTCF elderly has declined (Hutton, 1993). Of 15,379 TB cases reported, 8% of the 4,919 cases among the elderly occurred among the elderly living in nursing homes. The incidence of TB among nursing home residents was 39.2/100,000 person years, whereas the incidence of TB among elderly persons living in the community was 21.5/100,000. The elderly living in the LTCFs has 1.8 times greater TB incidence than other elderly. These results, however, did not take into account confounding variables such as age, gender and ethnic origins.

Canadian studies have indicated that LTCF residents are not at an increased risk to contract active TB. MacArthur (1992) compared the TB incidence in the institutional elderly (30.6/100,000) with community dwellers (25.2/100,000) in the province of Alberta after controlling for confounding variables (age, gender and ethnic origins). He concluded
that the LTCF elderly are not at increased risk of tuberculosis (RR = 1.22, 95% confidence interval is [0.74-1.70]). A ten-year retrospective survey in the province of Saskatchewan also reported no increase in tuberculosis incidence among the elderly in chronic care homes (Hoeppner, 1987). In Canada, the national data for 1993 indicated that TB incidence in the elderly is 14.6/100,000 and only 6% of the 494 cases in the elderly occurred among the residents of LTCFs (Statistics Canada, 1993).

**TB in Health Care Employees**

TB infection has been considered an occupational risk for health care workers for many years (Amberson, 1936; Barrett-Connor, 1979; Bow, 1937; Daniel, 1948; Heimbeck, 1936; Levine, 1968). Daniel (1948) reported that, in a survey of over 5,000 nurses, 80% of them had positive tests at the time of entry to the hospitals. Among those who initially had negative results, 54-80% converted to positive in the first year. The incidence of TB among all nurses was about twice that among control populations of the same sex and age. Bow (1937) reported that the incidence of TB among Saskatchewan nursing students was 1.3%, 8 times greater than other students of the similar age. Amberson (1936) had similar results, finding a rate of 1.7% TB incidence in student nurses, nearly 6 times greater than other professional women with a 0.3% annual rate in the same age.

For these high risk groups, it was found that TB incidence among persons with initial positive PPD tests was much lower than those with negative PPD tests. Heimbeck (1936) in Norway reported that, among 200 students who already had PPD positive reaction before the time of entry into nursing school, in a three years follow-up, three
students developed active TB, a rate of 1.5%. Among the students who had negative results, 95% of them converted to positive and 48 of 220 (22%) developed active TB during 3 years of training. Hyge (1947) had similar findings showing that 41 of 105 (59%) tuberculin skin test-negative students developed TB after exposure to an infectious teacher. Of 130 classmates who had tested positive before exposure to their infectious teacher, only 2 (1.5%) developed TB. These studies not only suggested that there were high exogenous infection rates in these students, they also showed that previous TB infection provided protection from re-infection.

Since the 1980s, a number of studies have shown that health care workers have no increased risk of contracting TB (Aitken, 1987; Burrill et al, 1985; Raad et al, 1989). Aitken (1987) divided all hospitals in Washington State into three groups: those with no TB patients, those with smear-positive TB patients, and those with smear-negative TB patients being admitted. The conversion rate of employees in these three categories of hospitals was not significantly different in statistical terms and the conversion rate was not greater than the general population.

Raad et al (1989) compared a psychiatric hospital without a known TB case with a general hospital that had admitted unsuspected TB cases. He found that the conversion rate of employees in both hospitals was not related to the number of unsuspected TB patients admitted but was proportional to the incidence of TB in their surrounding communities. It was also found that the majority of skin test convertors at the general hospital had little or no contact with patients.
Burrill (1985) and co-workers analyzed 11 years of data from British Columbia and found that the TB incidence in female nurses across all health settings was similar to that in other women after adjusting for age and birthplace. It was also reported that the nurses who had positive tuberculin skin tests were found to be 4 times as likely to contract active TB as the nurses having negative results when they started their training. This suggests that the likelihood of becoming infected with tubercle bacilli has diminished appreciably, and more TB comes from reactivation of remote infection than from exogenous infection.

**Tuberculosis and Birthplace**

As TB is still epidemic in some developing countries, immigrants from such areas may have a high infection rate before they come to the countries like Canada. Even if infection rate is low in the developed countries, these immigrants bring TB infection with them and tend to reactivate to active TB and have a greater TB incidence than the general population. Rosenberg and coworkers (1993) reported that the infection rate in foreign born nursing home employees is 42%, nearly 4 times that of Canadian born employees, who have a 12% infection rate. Burrill et al (1985) found that the TB incidence among nurses born in Asia was 12 times greater than other Canadian born nurses. It appears that the occurrence of the disease has more to do with the prevalence of TB in the country of origin than the place of current employment (Ashley, 1971; Berman, 1981; Price, 1987).

**The Social Determinants of Tuberculosis**

This review of the literature has covered the microbiological etiology of tuberculosis, the emergence of antibiotic therapies, the development of immunization
agents and their application as population screening tests, and the epidemiology of the
disease in terms of its distribution in populations around the world.

While this review has described the vulnerability of specific populations to the
disease, it has not done justice to the social and economic factors that have contributed to
the emergence of the disease as a major cause of death in the world since early times,
especially in the late 18th and early 19th centuries (McKeown, 1976, p 84), to the decline
of the disease in the developed countries, to the continuing prevalence of the disease in the
developing countries, and to the recrudescence of the disease in recent years in Western
countries.

The dramatic decline in mortality due to tuberculosis in England and Wales has
been elegantly captured by McKeown in Figure 3, adapted from his book entitled “The

Figure 3: The Trend of Mortality from Respiratory TB
in England and Wales Between 1938 and 1970

Francisco: Academic Press
Modern Rise of Population” (1976). This figure clearly shows that the decline in mortality preceded the identification of the bacillus and the introduction of chemotherapy. Why this occurred is attributed by McKeown to the social and economic changes that resulted from the Industrial Revolution. These changes had a dramatic impact on the living circumstances of the former "peasantry" and even factory workers and miners were able to enjoy improved nutrition and better housing, water, and sanitation. These living circumstances, unsatisfactory as they might have been by modern standards, were the factors that contributed to the decline in mortality from tuberculosis over the decades.

The relative contribution of chemotherapy and immunization has been at the "tail end" of decline and, while the contribution has been dramatic in reducing mortality and incidence of the disease, the gains have been at the margin after the social and economic factors had taken their effect (McKeown, 1976, p 101).

It is perhaps ironic that it is those very same social and economic factors have begun to take their toll in this last decade of the twentieth century. The re-emergence of the disease is taking place among the groups and populations that share the living circumstances of people in the Western world 150 years ago. The gains that have been made in the living circumstances of the poor and marginalized appear now to be being lost as populations of homeless people emerge in an apparently affluent society that has failed to provide appropriate supports. Further, those who have had difficulty in making their way in a predominately white and western society such as blacks, Latin American and the aboriginal peoples find themselves further marginalized and trapped in unfavorable lifestyles that include the use of drugs, alcohol, cigarettes as well as inadequate nutrition

This has been further compounded in the modern world by the emergence of "new diseases" (such as HIV/AIDS) that compromise the immune system, leaving a foothold for tuberculosis. Inner city populations already vulnerable because of their living circumstances, now find themselves with rising incidence of HIV infection that in many cases will lead to death from tuberculosis.

The social "safety net" that Canada has in place may have provided some protection from a replication of the increase in the incidence of TB in the US. But the country cannot be complacent since its vulnerable populations such as the aboriginal, the numbers of homeless (especially the elderly), the inner city problems of drug use, and continuing waves of immigrants from countries in which TB is still endemic, create a situation in which there will be an escalation in emergence of TB. The study reported in this thesis focuses on a vulnerable population, the staff of long term care facilities, and represents an attempt to not only to review a current monitoring program, but to restate the increased need for public health vigilance.
CHAPTER V

RESEARCH QUESTIONS, STUDY DESIGN, AND VARIABLES

This chapter covers the research questions, subjects, sources of data, variables and analytical methods. It states the assumptions that have been made in analyzing the costs of British Columbia TB screening program in long-term care facilities (LTCFs).

Research Questions

Based on the screening model described in Chapter III, three research questions are formed:

1. Is TB incidence of LTCF employees higher than that of the general population who are similar in age, gender and ethnic origins?

2. Is TB infection rate of LTCF employees higher than that found in similar studies in other jurisdictions?

3. What are the costs of the screening program and how do these costs compare with the costs of treating active TB cases that would have occurred if the screening program had not been in place?

Population Screened

The population defined in this study is comprised of all LTCF employees who entered employment in British Columbia during the study time period from January 1, 1990 to December 31, 1994 (last complete data available). LTCFs refer to those facilities which are funded and licensed by the Department of Continuing Care. These facilities include both adult care and child care.
Sources of Data

The medical records of each newly employed member and all ward admissions were downloaded from the Division of British Columbia TB Control database into four new files: demographics; tuberculin skin test; ward admissions; and chemoprophylaxis/active cases. The data were downloaded in ASCII format and converted to dBASE files for the purpose of analysis.

**Variables contained in file.** For all the newly employed staff, the following variables were obtained:

- population at risk type (adult vs. child care)
- gender
- birthday
- birth country
- aboriginal status
- date of arrival in Canada
- date of skin test administered
- reaction of the skin test (mm)
- date of skin test reading

If the files showed that a screened employee had taken INH preventive therapy, the following variables were obtained:

- reasons for starting INH preventive therapy
- date of starting INH preventive therapy
- date of stopping INH preventive therapy
• reasons for stopping INH preventive therapy
• occurrence of INH-induced hepatitis
• total days of taking INH preventive therapy

For all active TB patients, the following variables were obtained:

• date of diagnosis
• methods of diagnosis
• sites and types of active TB
• treatment of active TB

For all hospitalized TB patients, the following variables were extracted:

• date of admission to hospitals
• date of discharge from hospitals
• total days of hospitalization

**Calculation of TB Infection and Incidence Rate**

**TB infection rate.** TB infection rate is calculated as the total number of positive PPD reactions, divided by the total number of employees screened in the study time period.

**TB incidence rate.** To calculate the TB incidence rate, the numerator is the total number of TB cases that were reported in the study time period. The denominator is defined in term of “person-years” in order to capture the fact the population “at risk” is characterized by various lengths of employment. “Person-years” at risk was defined by using the number of FTE employees of LCTF’s during the period of study. The Department of Continuing Care, Ministry of Health stated that the number of employees expressed as full time equivalents
(FTEs) was 9,500, a figure that was in steady state during the five year study period. The figure of 9,500 was multiplied by 5 to derive the “person years” at risk.

Statistical Tests of Differences in Rates

To test for the statistical differences in TB infection rates among various ethnic origins, between adult and child care employees, TB incidence rates between LTCF employees and British Columbia general population, chi-square (χ²) statistical tests were used, and confidence intervals (CI) were calculated (Hennekens et al, 1987).

Program Costs

Unit Cost of screening program. The costs of the screening program were compiled based on the advice of Dr. John Farley, former Director of British Columbia TB Control Clinics.

In the present study, only the direct costs of the medical procedures and tests related to the screening program were included. These costs encompass the following two components of the screening program:

• screening cost: cost of tuberculin skin test and cost of chest X-ray
• cost of INH preventive therapy including consultation, liver function tests (three times for the first three months), follow-up visits on a monthly basis (12 months), and drugs (INH and B6 for 12 months). Since no INH-induced hepatitis occurred in the review of the employees files, costs associated with this side effect were excluded.

The various cost elements are detailed in Table 6.
It needs to be emphasized that various overhead, indirect, and "opportunity costs" are not included in this cost analysis. Such costs include those associated with the administration and direction of the program, maintenance of data files, and employees' loss of time at work when attending for follow-up and treatment. The total costs attributed to the program in the present analysis is, therefore, conservative.

Table 6
Unit Costs For Screening And Routine Isoniazid Prophylaxis.

<table>
<thead>
<tr>
<th>Items</th>
<th>Costs $</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tuberculin skin testing</td>
<td>7.65</td>
</tr>
<tr>
<td>Chest X-ray, PA and lateral</td>
<td>37.69</td>
</tr>
<tr>
<td>INH preventive therapy</td>
<td></td>
</tr>
<tr>
<td>Liver function tests 4.77 X 3 (SGPT, SGOT, T.Bili)</td>
<td>13.31</td>
</tr>
<tr>
<td>Medical consultation X 1</td>
<td>118.59</td>
</tr>
<tr>
<td>Clinic costs per visit, 34.00 X 12</td>
<td>408.00</td>
</tr>
<tr>
<td>Drug costs, for one year</td>
<td></td>
</tr>
<tr>
<td>Isoniazid, 300mg, orally, daily</td>
<td>26.10</td>
</tr>
<tr>
<td>Pyridoxine, 12.5 mg, orally, daily</td>
<td>6.06</td>
</tr>
<tr>
<td>Subtotal</td>
<td>572.06</td>
</tr>
</tbody>
</table>

Note: From "British Columbia Medical Service Fee Schedule" by Medical Service Commission, British Columbia, 1993.

Total Cost of Screening Program. The total cost of the tuberculin skin test screening program itself (i.e. excluding the costs of treating TB cases) encompasses the initial screening costs to identify possible cases and the costs of INH preventive therapy (Adhikari, 1995; Yuan, 1995).

(1) Total cost of initial screening

- total cost of PPD tests = number of employees screened multiplied by the unit cost of each PPD test
- total cost of X-rays = number of employees who have PPD positive reactions multiplied by the unit cost of chest X-ray
(2) Total costs of INH preventive therapy

- number of employees who take INH multiplied by the cost of treatment of one TB infection with INH. It should be noted that the number of employees taking INH includes all those who started an INH regimen, whether or not they completed the full course. No adjustment was made for the lower drug costs that would be incurred by "drop-outs" since the cost of clinical and chest X-ray follow-up would still be incurred.

**Estimation of Occurrence of Active TB from TB Infection**

The number of active TB cases prevented by INH preventive therapy is calculated based on the following assumptions:

- for those who have PPD positive reactions but do not take INH preventive therapy, it is assumed that 5% will develop active TB in their lifetime (Stead, 1995)

- for those who take INH preventive therapy less than 6 months, INH protection is considered to be negligible (Grzybowski et al, 1976). Therefore, the same rate of the development of active TB as those who do not take INH is used for this group

- for those who have PPD positive reactions and take more than 6 months of INH preventive therapy, 90% of those 5% who would otherwise have developed active TB will be prevented (CTS, 1996; Fitzgerald et al, 1990)

Hence, the number of active TB cases prevented by INH is calculated as the number of persons who finish INH preventive therapy multiplied by 5% and 90%.

The number of individuals finishing INH preventive therapy is calculated as the total number of individuals prescribed INH multiplied by the compliance rate.

**A Comparison of Current, Standard and Ideal Screening Programs**

As described above, the costs of the B.C. program under review are based on the total number of employees, the number of employees who have positive PPD reactions, the number of employees who take INH preventive therapy, and the actual compliance rate.
The costs of programs are also calculated for two additional scenarios, a "standard" program and "ideal" program. These programs are defined as follows.

A standard program is defined as one in which the number of LTCF employees with PPD positive reactions who proceed to take INH preventive therapy is based on the ATS/CDC (1986) recommendations and Stead’s study (1985).

According to ATS/CDC recommendations, individuals over 35 years old with other factors that increase the risk of developing active TB are recommended for INH preventive therapy. Based on Stead’s report (1985), 14% of employees who are over 35 years old have other factors increasing their risk of developing active TB. Further, all those less than 35 years old with positive PPD reactions are recommended for INH preventive therapy.

It is assumed that the compliance rate in the standard program is the same as in the current program.

The costs of an ideal program is based on the assumptions of a standard program except that the compliance rate is assumed to be 100%.

**Costs for treatment of active TB**

In order to compare the cost of the screening program and the INH preventive therapy with the potential cost of the treatment of an active TB case that may have occurred if the screening program had not been in place, algorithms were constructed for the hypothetical costs of active TB treatment programs.

The cost of treating an active TB case was calculated using an outpatient model, an inpatient model and the cost of follow-up of contacts for an index case.
Costs for treatment of outpatients. The costs include: routine chest X-rays (three times which occur at the beginning, middle and end of treatment), sputum smear, culture and antibiotic sensitivity (three times), baseline CBC, ESR and liver function tests (three times), medical consultation, follow-up clinical visits and drugs (INH, RMP and Pyridoxine for 9 months, and Ethambutol for the first two months) (Table 7).

Table 7
Costs For Treatment Of An Outpatient During A Nine-Month Period

<table>
<thead>
<tr>
<th>Items</th>
<th>Costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical examinations and various tests</td>
<td></td>
</tr>
<tr>
<td>Chest X-ray (PA and lateral) 37.69 X 3</td>
<td>113.07</td>
</tr>
<tr>
<td>Sputum smear, culture, and sensitivity (39.02 X 3)</td>
<td>117.06</td>
</tr>
<tr>
<td>Antibiotic sensitivity (13.16 X 3)</td>
<td>39.48</td>
</tr>
<tr>
<td>CBC, ESR</td>
<td>17.36</td>
</tr>
<tr>
<td>Liver function tests (4.77 X 3)</td>
<td>14.31</td>
</tr>
<tr>
<td>Medical consultation</td>
<td>118.59</td>
</tr>
<tr>
<td>Clinical visit monthly, 34.00 X 9</td>
<td>306.00</td>
</tr>
<tr>
<td>Drug cost</td>
<td></td>
</tr>
<tr>
<td>Isoniazid, 300mg daily X 9 months</td>
<td>19.31</td>
</tr>
<tr>
<td>Rifampin, 600mg daily X 9 months</td>
<td>380.65</td>
</tr>
<tr>
<td>Ethambutol, 1,200mg orally, daily X 2 months</td>
<td>56.41</td>
</tr>
<tr>
<td>Pyridoxine, 12.5mg, orally, daily X 9 months</td>
<td>4.48</td>
</tr>
<tr>
<td>Total</td>
<td>1186.72</td>
</tr>
</tbody>
</table>

Costs for inpatients. The major costs of hospitalized patients include hospitalization and daily physician visits. According to the Division of Tuberculosis Control data (1994), the average length of hospitalization is 29 days. The per diem cost of hospitalization are stated to be $575.00, a figure that includes “hotel” costs and routine drug and testing costs. Since other tests, such as gastric washing, sputum induction and fiberoptic bronchoscope, are not routinely performed, charges for these procedures have not been included.
Table 8
Major Costs For Treatment Of A Hospitalized Patient For 29 Days

<table>
<thead>
<tr>
<th>Items</th>
<th>Costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospitalization for 29 days, $575.00/day</td>
<td>16675.00</td>
</tr>
<tr>
<td>Daily medical visit for 29 days, $21.62/visit</td>
<td>626.98</td>
</tr>
<tr>
<td>Total</td>
<td>17301.98</td>
</tr>
</tbody>
</table>

Costs for follow-up of contacts with an index case. These costs include those related to the testing of contacts, the initiation of INH preventive therapy, and the treatment of contacts if they develop active TB. According to Fitzgerald et al (1990), each contact requires two physician evaluations, two clinical visits, and one tuberculin skin test. Based on national data from the United States, each index case precipitates 6.56 contacts who are given a tuberculin skin test, 1.5 chest X-rays are performed on infected contacts, and INH preventive therapy is administered for one year to 0.8 contacts. Each case also results in 0.06 additional cases requiring treatment (Snider et al, 1986). The calculations of costs for clinical examinations and treatment of contacts are listed in Table 9.

Table 9
Costs for follow-up of contacts with index case

<table>
<thead>
<tr>
<th>Items</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physician costs per contact (2 X 34.00)</td>
<td>$68.00</td>
</tr>
<tr>
<td>Clinic costs per visit ($21.62 X 2)</td>
<td>$43.24</td>
</tr>
<tr>
<td>Mantoux skin test</td>
<td>$7.65</td>
</tr>
<tr>
<td>Subtotal</td>
<td>$119.89</td>
</tr>
<tr>
<td>6.50 contacts/case (6.6 X 119.89)</td>
<td>778.29</td>
</tr>
<tr>
<td>1.5 chest X-rays/case ($37.69 X 1.5)</td>
<td>56.54</td>
</tr>
<tr>
<td>0.8 INH preventive therapy administered</td>
<td>457.65</td>
</tr>
<tr>
<td>0.06 new cases of TB treated</td>
<td>557.36</td>
</tr>
<tr>
<td>Total</td>
<td>1850.84</td>
</tr>
</tbody>
</table>
Total cost of treatment of an active TB case. The total costs of treatment of a patient without hospitalization include the cost of treatment as an outpatient ($1,186.72) and the cost of follow-up of contact cases ($1,850.84) as shown in Table 7 and Table 9, respectively.

The total cost for a TB patient treated in an outpatient basis, therefore, is $3,037.56.

The total costs for treatment of a patient with 29 days of hospitalization include the cost of hospitalization ($17,301.98) and the cost of follow-up of contact cases ($1,850.84) as shown in Table 8 and Table 9, respectively. Since hospitalized patients continue their treatment on an outpatient basis after discharge, it is necessary to add in the costs of the out-patient treatment as shown in Table 7. These costs have not been adjusted for the tests and drugs that may have been administered in the hospital stay.

The total cost for a hospitalized patient is, therefore, $20,339.54.

Average cost for treatment of an active TB case. In order to arrive at an average cost for a patient treated for TB, “weighted” for whether the patient is hospitalized or not, the hospitalization experience of B.C. was used. These costs again do not include indirect and opportunity costs. According to B.C. TB Control (1994), 42% of active TB patients are hospitalized with the remaining 58% treated on an outpatient basis. Using the total costs attributed to hospitalized and outpatient patients respectively, the weighted cost for the treatment of a TB patient is calculated as follows:

\[(58\% \times $3,037.56) + (42\% \times $20,339.54) = $10,304.39.\]
CHAPTER VI

RESULTS: TB INFECTION AND INCIDENCE RATES IN LTCF EMPLOYEES

In this chapter, the demographic characteristics, TB infection and incidence rates among LTCF employees in the period 1990-94 are presented. These rates are compared among foreign born, First Nations and other Canadian born individuals and also between adult and child care facilities.

The actual incidence of TB in British Columbia and in LTCFs in the province is included in this chapter.

The infection rates tabulated in this chapter are used as the basis for the calculation of the costs of the screening program, the follow-up treatment with INH, and treatment of TB cases. The results of these calculations are shown in Chapter VII.

The Demographic Characteristics of the Screened Population

Between January 1, 1990 and December 31, 1994, 17,571 individuals started to work in British Column LTCFs. Among them, 49 did not have pre-employment tuberculin skin tests and 544 had tests but no result recorded in the files. Gender or and country of birth were missing in the files of other 392 individuals. These subjects are excluded from this study. Totally, 16,586 complete records were available for analysis.

The demographic characteristics of the screened populations are summarized in Table 10. For all screened employees, the mean age is 35 years, with a standard deviation of 11 (M=35, SD=11). The gender proportion of female to male employees across all the groups is 5 to 1, approximately. Among the different ethnic groups, the age proportions are similar, the mean
age in foreign born individuals is 38 with standard deviation (SD) of 11, First Nations 36, with SD of 11, and Canadian born 34 with SD of 11.

<table>
<thead>
<tr>
<th>Number of Female Employees</th>
<th>Foreign Born</th>
<th>First Nations</th>
<th>Canadian Born</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3,707</td>
<td>178</td>
<td>9,871</td>
<td>13,756</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Number of Male Employees</th>
<th>Foreign Born</th>
<th>First Nations</th>
<th>Canadian Born</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>730</td>
<td>27</td>
<td>2,073</td>
<td>2,830</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Total Number of Employees</th>
<th>Foreign Born</th>
<th>First Nations</th>
<th>Canadian Born</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>4,437</td>
<td>205</td>
<td>11,944</td>
<td>16,586</td>
</tr>
</tbody>
</table>

| Mean Age & (SD)          | 38(11)       | 36(11)        | 34(11)        | 35(11) |

**TB Infection Rate**

The results showed that 3,657 subjects have positive reactions, and the overall infection rate is 21.9% (Table 11). In the different ethnic groups, however, the rates vary.

<table>
<thead>
<tr>
<th>Number of Number of PPD</th>
<th>Crude Rate (%)</th>
<th>Adjusted Rate (%)</th>
<th>Adjusted RR*</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canadian born</td>
<td>11,944**</td>
<td>1,243</td>
<td>10.6</td>
<td>14.6</td>
</tr>
<tr>
<td>Foreign born</td>
<td>4,437</td>
<td>2,319</td>
<td>52.3</td>
<td>49.7</td>
</tr>
<tr>
<td>First Nations</td>
<td>205</td>
<td>95</td>
<td>46.3</td>
<td>43.8</td>
</tr>
<tr>
<td>Total</td>
<td>16,586</td>
<td>3,657</td>
<td>21.9</td>
<td>25.5</td>
</tr>
</tbody>
</table>

*RR stands for relative risk
**include 381 subjects who were born in the United States of America.

Foreign born and First Nations individuals, respectively, have 5 and 4.5 times greater infection rate than Canadian born. Direct age and gender standardization based on 1991 census of British Columbia was carried out. The rates in foreign born (RR=3.4, 95% CI is [3.23-3.58])
and First Nations individuals (RR=3.0, 95% CI is [2.49-3.61]) were significantly greater than that of Canadian born.

The infection rate among each age and ethnic group is shown in Figure 4.

Figure 4 The Comparisons of TB Infection Rates Among Ethnic Groups by Age
For all employees, the infection rate increases with age. For foreign born individuals, the infection rate increases with age until the 35-44 age group when the infection rate becomes stable. This pattern is complicated, since many factors affect PPD tests, such as BCG vaccination status, immigration date and country of origin (Adhikari et al, 1995; Yuan et al, 1995). For First Nations persons, the infection pattern is similar to foreign born, but the sample size is small and may not be reliable. For Canadian born individuals, the infection rate increases with age until 64 years of age, with a drop after 65, since individuals over 65 may revert to negative reactions (Stead, 1987).

Foreign born individuals were classified into 5 subgroups based on geographic areas of origin (Table 12): Africa; Asia-Oceania; Latin America (South and Central America);

<table>
<thead>
<tr>
<th>Country Group</th>
<th>Number of Employees</th>
<th>Number of PPD Positive</th>
<th>Crude R.(%)</th>
<th>Adjusted RR*</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa</td>
<td>190</td>
<td>96</td>
<td>50.5</td>
<td>3.24</td>
<td>2.69-3.90</td>
</tr>
<tr>
<td>Latin America</td>
<td>301</td>
<td>180</td>
<td>59.8</td>
<td>2.86</td>
<td>2.44-3.35</td>
</tr>
<tr>
<td>Asia &amp; Oceania</td>
<td>2,004</td>
<td>1,171</td>
<td>58.4</td>
<td>3.91</td>
<td>3.68-4.16</td>
</tr>
<tr>
<td>Eastern Europe</td>
<td>416</td>
<td>291</td>
<td>70.0</td>
<td>4.31</td>
<td>3.86-4.81</td>
</tr>
<tr>
<td>Western Europe</td>
<td>1,526</td>
<td>581</td>
<td>38.1</td>
<td>2.60</td>
<td>2.37-2.85</td>
</tr>
<tr>
<td>Total</td>
<td>4,437</td>
<td>2,319</td>
<td>52.3</td>
<td>3.40</td>
<td>3.23-3.58</td>
</tr>
</tbody>
</table>

* the RRs were calculated based on the Canadian born.

Western Europe, and Eastern Europe. Western Europe was defined as the United Kingdom, Ireland, Iceland, Denmark, Norway, Sweden, Germany, Netherlands, Belgium, France, Switzerland, Greece, Italy, Spain and Portugal. All other European countries were defined as Eastern Europe. Immigrants as a whole have significantly greater infection rate (52.3%, 95%
CI is [3.23-3.58]) than Canadian born individuals, and each subgroup also has a higher infection rate when compared to the Canadian born individuals. The infection rates, however, are different among the different origins. Immigrants from Western Europe (38.1%, 95% CI is [2.37-2.85]) have the lowest infection rate, but those from Eastern Europe (70.0%, 95% CI is [3.86-4.81]) have the highest infection rate in all the immigrant groups.

The comparison of TB infection rate between child care facility employees and adult care facility employees is shown in Table 13. TB infection rate in child care facility employees is lower than adult care facility employees. After adjusting for age, gender and ethnic origin, however, child care facility employees do not have significantly lower infection rate (RR = 0.93, 95% CI is [0.87-1.0]) than adult care facility employees.

<table>
<thead>
<tr>
<th>Table 13</th>
<th>The Comparison Of TB Infection Rate Between Adult Care And Child Care Facility Employees</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of tests</td>
</tr>
<tr>
<td>Adult care</td>
<td>10,516</td>
</tr>
<tr>
<td>Child care</td>
<td>6,070</td>
</tr>
<tr>
<td>Total</td>
<td>16,586</td>
</tr>
</tbody>
</table>

**TB Incidence Rate**

Between 1990 and 1994, 1,574 active TB cases were diagnosed in British Columbia. Of these, 5 occurred in LTCF employees. The incidence of TB in LTCF employees is shown in Table 14. The crude TB incidence in LTCF employees and the general population is 10.5/100,000 and 9.6/100,000 respectively. There is no significant difference between these two rates (RR = 1.1, 95% CI is [0.46-2.64]). For a more accurate comparison, indirect
standardization was used based on the 1991 census of British Columbia population. After adjustment for age, gender and birthplace, there is still no significant difference in these two groups (RR = 1.03, 95% CI is [0.40-2.32]).

Table 14
TB Incidence Rate Among LTCF Employees And Community Individuals 
(Crude And Adjusted Rates)

<table>
<thead>
<tr>
<th></th>
<th>Person-years</th>
<th>Number of TB</th>
<th>Rate (1/100,000)</th>
<th>Crude RR</th>
<th>95% CI</th>
<th>Adjusted RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>LTCF employees</td>
<td>47,500</td>
<td>5</td>
<td>10.5</td>
<td>1.1</td>
<td>0.46-2.64</td>
<td>1.03</td>
<td>0.40-2.32</td>
</tr>
<tr>
<td>General population</td>
<td>16,362,850</td>
<td>1,569</td>
<td>9.6</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>16,410,350</td>
<td>1,574</td>
<td>9.6</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

TB incidence in each ethnic group was also calculated (Table 15). Although foreign born and First Nations employees together represented 28% of the population, they accounted for 80% of the total TB cases. The TB incidence in foreign born and First Nations persons are
7 and 54 times, respectively, greater than Canadian born. The relative risk of TB in foreign born employees to foreign born community individuals, First Nations employees to First Nations community individuals and Canadian born employees to Canadian born community individuals are 0.88, 3.26 and 1.07, respectively. These results must be interpreted with caution, since the number of cases in each subgroup is small.

TB incidence rate in adult care and child care facility employees is shown in Table 16. TB incidence of adult care (10.1/100,000) is similar to the rate of child care facility employees (11.3/100,000), which implies that TB transmission in adult care is negligible. However, as the sample is small, no statistical analysis was carried out.

<p>| Table 16 |
| TB Incidence Rate In Adult And Child Care facility employees |</p>
<table>
<thead>
<tr>
<th>Person-years</th>
<th>Number of TB cases</th>
<th>Rate (1/100,000)</th>
<th>Crude RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult care</td>
<td>29,871</td>
<td>3</td>
<td>10.1</td>
</tr>
<tr>
<td>Child care</td>
<td>17,719</td>
<td>2</td>
<td>11.3</td>
</tr>
<tr>
<td>Total</td>
<td>47,500</td>
<td>5</td>
<td>10.5</td>
</tr>
</tbody>
</table>

Of the 5 TB cases in the LTCFs, 2 of them are pulmonary TB (40%) and 3 are extra-pulmonary TB (60%). The pulmonary TB rate in the LTCF employees is one-half of the general population, which has a rate of 70-75% (Division of TB Control, 1994). Since pulmonary TB is more infectious than extra-pulmonary, from this aspect, the risk of TB transmission in the LTCFs is lower than the general population. Further, the sputum smears of all 5 TB cases in LTCF employees are negative, only one case has a positive culture, reinforcing the conclusion that the risk of TB transmission is not significant.
CHAPTER VII

RESULTS: COSTS AND COST IMPLICATIONS OF THE TB SCREENING PROGRAM IN LTCFS IN BRITISH COLUMBIA

In this chapter, the costs of the screening program, the follow-up treatment with INH, and the treatment of TB cases are calculated. The costs of the actual, “standard,” and “ideal” programs are compared.

The Outcome of the Screening Program

As shown in Chapter VI, 3,657 employees were recorded as having positive PPD reactions in the five years 1990 - 94. Of this number, 236 (6.5%) were prescribed INH preventive therapy to prevent occurrence of active TB from TB infection.

At the time that the data were obtained, sufficient time had not elapsed for 57 cases who had begun INH therapy in 1994 to complete their course of treatment. For this reason, the compliance rate was based on the experience of 1990-93 with the assumption that the compliance rate for the 1994 cases would have been similar.

Compliance rate. Between 1990 and 1993, 179 employees were administered INH preventive therapy and 115 finished the treatment, giving a compliance rate of 64% (115/179). The compliance rate varies, however, by diagnostic status as shown in Table 17. Individuals who had inactive TB have the greatest compliance rate (100%). The contacts who had positive PPD reactions had the lowest rate (40%).

The reasons for non-compliance as recorded in the files are shown Table 18. It was found that 36% stopped taking the drug because of drug reactions. Twenty-two percent did not co-operate with treatment and another 34% stopped taking INH for unknown reasons.
Table 17
The Comparison Of Compliance Rate Among Various Candidates For Preventive Therapy (1990-1993)

<table>
<thead>
<tr>
<th>Reason for preventive therapy</th>
<th>Number of prescribed</th>
<th>Number of finished</th>
<th>Compliance rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inactive TB</td>
<td>11</td>
<td>11</td>
<td>100.</td>
</tr>
<tr>
<td>Contact and PPD positive</td>
<td>5</td>
<td>2</td>
<td>40</td>
</tr>
<tr>
<td>Convertor</td>
<td>20</td>
<td>15</td>
<td>75</td>
</tr>
<tr>
<td>PPD positive</td>
<td>129</td>
<td>79</td>
<td>61</td>
</tr>
<tr>
<td>Misdiagnosis</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>TB with chest X-ray change</td>
<td>12</td>
<td>7</td>
<td>58</td>
</tr>
<tr>
<td>PPD positive with HIV positive</td>
<td>1</td>
<td>1</td>
<td>100</td>
</tr>
<tr>
<td>Total</td>
<td>179</td>
<td>115</td>
<td>64</td>
</tr>
</tbody>
</table>

Table 18
The Various Factors of Causing Incomplete INH Preventive Therapy (1990-1993)

<table>
<thead>
<tr>
<th>Reasons</th>
<th>Number</th>
<th>Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lost follow-up</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Not co-operative</td>
<td>14</td>
<td>22</td>
</tr>
<tr>
<td>Drug reaction</td>
<td>23</td>
<td>36</td>
</tr>
<tr>
<td>Left province</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Not known</td>
<td>22</td>
<td>34</td>
</tr>
<tr>
<td>Total</td>
<td>64</td>
<td>100</td>
</tr>
</tbody>
</table>

The Actual Costs of British Columbia TB Screening Program

The total costs of the British Columbia screening program were calculated using the costs of the various tests, procedures and drugs as shown in Chapter V applied to the number of employees screened, the number of employees who had positive PPD reactions, and the number of employees who took INH preventive therapy. The following process represents the detailed calculation of the various costs.
Total costs of the screening program

(1) total cost of tuberculin skin test:

\[ \$7.65 \times 16,386 \text{ (number of complete tests)} = \$125,353 \]

(2) cost of chest X-ray:

\[ \$37.69 \times 3,657 \text{ (number of positive PPD)} = \$145,146 \]

(3) total screening cost:

\[ (1) + (2) = \$263,185 \]

(4) total cost of INH preventive therapy:

\[ \$572.06 \times 236 \text{ (number prescribed INH)} = \$135,006 \]

(5) total cost of the screening program:

\[ (3) + (4) = \$398,191 \]

Number of Cases Prevented by the Screening Program

(6) Number of employees completing INH therapy:

\[ 236 \times \text{compliance rate of 64\%} = 151 \]

(7) number of active TB cases prevented:

(a) \[ 151 \times 5\% \text{ (estimated rate of TB occurrence)} = 7.55 \]

(b) \[ 7.55 \times 90\% \text{ (estimated rate of protection by INH)} = 7 \]

Costs attributed to the Prevention of One TB Case

These total costs of the program provide the basis for calculating the costs that can be attributed to the prevention of a case of TB occurring in this screened population using assumptions detailed in Chapter V (pp. 38)

(8) screening cost for preventing one TB case:

\[ \text{screening cost/number of TB cases prevented} = \$263,185 / 7 = \$38,732 \]

(9) cost of INH preventive therapy for preventing one TB case:

\[ \text{INH therapy cost/TB cases prevented} = \$135,006.16 / 7 = \$19,868 \]
(10) total cost for preventing one TB case:

\[
\text{total cost of screening program/TB cases prevented} = \frac{398,191}{7} = 58,600
\]

The above results have been summarized in Table 19.

---

Table 19
The Cost of TB Screening Program in the Current Program

<table>
<thead>
<tr>
<th>Items</th>
<th>Costs/Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost of tuberculin skin test</td>
<td>$125,353</td>
</tr>
<tr>
<td>Cost of chest X-ray</td>
<td>$145,146</td>
</tr>
<tr>
<td>Total screening cost</td>
<td>$263,185</td>
</tr>
<tr>
<td>Cost of INH preventive therapy</td>
<td>$135,006</td>
</tr>
<tr>
<td>Total costs of the program</td>
<td>$398,191</td>
</tr>
<tr>
<td>Number of employees completed INH</td>
<td>151</td>
</tr>
<tr>
<td>Number of TB case prevented</td>
<td>7</td>
</tr>
<tr>
<td>Screening cost for preventing one TB case</td>
<td>$38,732</td>
</tr>
<tr>
<td>Cost of INH preventive therapy for preventing one TB case</td>
<td>$19,868</td>
</tr>
<tr>
<td>Total cost for preventing one TB case</td>
<td>$58,600</td>
</tr>
</tbody>
</table>

Comparison of the Cost of Preventing One Case with the Cost of Treating One Case of TB

While the total cost of preventing one case of active TB based on the cost figures that have been attached the B.C. program and the "yield" of bringing cases to preventive INH therapy is $58,600, the cost of treating one active case of TB was shown to be $10,304 ("weighted" cost based on hospital and outpatient treatment) as shown in Chapter V(pp.42).

Calculation of the Costs of Standard and Ideal Programs

As described in Chapter V, a standard program assumes that the number of employees taking INH preventive therapy will be based on the ATS/CDC (1986) recommendations and Stead's study (1985). These assumptions are applied to the outcome of
the B.C. screening program. Table 20 shows that the number of candidates who would be eligible under these assumptions would be 1,545.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Number of PPD positive</th>
<th>Number of INH candidates</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;35</td>
<td>1201</td>
<td>1201</td>
</tr>
<tr>
<td>≥35</td>
<td>2456</td>
<td>2456 x 14% = 344</td>
</tr>
<tr>
<td>Total</td>
<td>3657</td>
<td>1545</td>
</tr>
</tbody>
</table>

Assuming that 1,545 cases begin INH therapy, that the compliance rate of 64% found in the B.C. experience applies, and using the cost figures of the B.C. program, Table 21 shows that the costs of preventing one TB case are $5,915 for screening and $19,863 for INH therapy in the standard program. The cost of INH therapy is three times greater than the screening cost. However, the total cost of preventing one case is $25,778. When comparing to the actual program, increasing number of INH candidates decreases the costs for preventing one TB case.

<table>
<thead>
<tr>
<th>Items</th>
<th>Standard Condition</th>
<th>Ideal Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost of tuberculin skin test</td>
<td>125,353</td>
<td>125,353</td>
</tr>
<tr>
<td>Cost of chest X-ray</td>
<td>145,146</td>
<td>145,146</td>
</tr>
<tr>
<td>Total screening cost</td>
<td>$263,185</td>
<td>$263,185</td>
</tr>
<tr>
<td>Cost of INH preventive therapy</td>
<td>$883,833</td>
<td>$883,833</td>
</tr>
<tr>
<td>Total costs of the screening program</td>
<td>$1,147,018</td>
<td>$1,154,332</td>
</tr>
<tr>
<td>Number of employees finished INH</td>
<td>989</td>
<td>1,545</td>
</tr>
<tr>
<td>Number of TB cases prevented</td>
<td>45</td>
<td>70</td>
</tr>
<tr>
<td>Screening cost for preventing one TB case</td>
<td>$5,915</td>
<td>$3,785</td>
</tr>
<tr>
<td>Cost of INH preventive therapy for preventing one TB case</td>
<td>$19,863</td>
<td>$12,712</td>
</tr>
<tr>
<td>Total cost for preventing one TB case</td>
<td>$25,778</td>
<td>$16,497</td>
</tr>
</tbody>
</table>
When the calculations are expanded to the ideal program in which it is assumed that the compliance rate is 100%, the screening cost for preventing one TB case is $3,785; the cost of INH preventive therapy for preventing one TB case is $12,712, nearly 4 times greater than the screening cost. The total cost for preventing one case ($16,497) is 1.5 times more than the cost of treatment of one active TB case. Compared to the standard program, the increasing compliance rate decreases the screening cost and the cost of INH preventive therapy for preventing one active TB case, and the total cost of this program for preventing each active TB case decreases.

However, while the data from the ideal program emphasize the impact that compliance has on unit costs, it is unrealistic to expect that 100% compliance can be achieved since INH side-effects are a significant cause for cessation of therapy. In the present study of LTCF employees, 36% of cases dropped out because of drug reactions, while the Division of Tuberculosis Control (1994) reports 14% with drug reactions in its treatment of cases in the general population.

The comparisons among the current, standard and ideal programs imply that:

(a) to reduce the cost of preventing active TB cases, more employees who have positive PPD reactions should be encouraged to take INH preventive therapy.

(b) the compliance rate of INH preventive therapy should be stressed.
CHAPTER VIII
DISCUSSION AND RECOMMENDATIONS

The purpose of the present study was to review the British Columbia TB screening program in long-term care facility (LTCF) employees based on 5 years of data (from January 1, 1990 to December 31, 1994). In this Chapter, the findings showed in Chapter VI & VII are discussed and interpreted. Specifically, TB infection rate, the use of INH preventive therapy and TB incidence rate are discussed and related to findings in other jurisdictions. The cost of this screening program compared to the outcome of the screening program are discussed. Finally, policy recommendations and future studies are suggested.

British Columbia TB Database and Its Limitations

Since the reporting of TB infection and disease is mandatory and screening is done only by the Division of TB Control, the British Columbia TB Control database represents a record of all PPD tests and all diagnosed TB cases in British Columbia. The large size of the population of LTCF employees screened in the present study provides a basis for a reliable estimate of the TB infection rate in this population and for the comparisons of rates among various subgroups. When the TB incidence rate is calculated and compared for each subgroup in the population, however, the numbers are small precluding standardization and statistical analysis.

In the present study, less than 6% (985/17571) of cases had one or more missing variables and were deleted for the purpose of analysis. Since there is no reason to believe
that these cases are different than the population from which they are drawn, it is not believed that any bias has been introduced.

Discussion of TB Infection Rate

Screening methods and PPD results. In British Columbia, the one-step tuberculin skin test is used for screening. However, the two-step skin test is also used in some jurisdictions, as recommended by the American Geriatrics Society (1988). Different screening methods may affect the results. The two-step test produces 6% more positive reactions than the one-step tuberculin skin test (Rosenberg et al, 1993). However, false-positive reactions may also be observed in persons infected with nontuberculous mycobacteria or vaccinated with BCG (Rosenberg et al, 1993; Thompson et al, 1979). A comparison of the observed British Columbia rates of TB infection with other jurisdictions, therefore, should be made cautiously.

Overall TB infection rate. TB infection rate of 21.9% among British Columbia LTCF employees is in the mid-range of the 4.6-47% reported in the literature (Barry, 1987; Bass, 1981; Brennen, 1988; Gross, 1986; Halperin, 1992; Price, 1987; Rosenberg et al, 1993; Simon, 1983; Thompson et al, 1979; Valenti, 1982; Welty, 1985). This wide range of reported TB infection rates is related to variance in ethnic composition, age and gender in the population screened and to the methods of screening used. In general, the higher the percentage of immigrants from countries where TB is still epidemic, and the more recent the immigration, the higher the infection rate. Rosenberg et al (1993) studied nursing home employees in Manitoba and found that foreign born subjects were more than twice as likely to have tuberculin skin test positive reactions as Canadian born subjects.
(60%, 95% CI is [2.5-11.4]). Also, a tuberculin skin test positive reaction is inversely related to the duration of time elapsed since arrival in Canada (Menzies et al, 1992; Rosenberg et al, 1993). The older the population, the higher the infection rate. It has also been found that the higher proportion of males in the population, the higher the infection rates, although the reason for this is not clear (Gerald et al, 1990).

**TB infection in Canadian born employees.** The infection rate in the Canadian born employees of 10.6% was shown to be significantly lower than foreign born (52.3%) and First Nations (46.3%). The infection rate in Canadian born individuals increases with age to 64 years old and then drops, consistent with Stead’s finding (Stead, 1987). It is probable that lower cell-mediated immune status among the elderly contributes to a higher false-negative reaction rate. For comparison, TB infection rate in Canadian born employees in British Columbia LTCFs is lower than the study in Manitoba with rate of 23.8% (Rosenberg et al, 1993). This may be explained partly by the age difference between these two populations. The mean ages in British Columbia and Manitoba LTCF employees are, respectively, 35 (SD=11) and 41 (SD=13). The difference can also be attributed to the small sample size (n=126) and its an urban population in the Manitoba study, which had a higher infection rate (Gerald et al, 1990).

**TB infection in First Nations employees.** Among the First Nations employees, the overall infection rate is 46.3%. It is believed that they have a high infection rate because they were not exposed to TB until contact with settlers from the Old World and the population has not yet developed a strong immune status. As a result, TB is epidemic in
this population (Gerald et al, 1990). Further, BCG vaccination is widely used in this population and may overestimate the infection rate.

**TB infection in foreign born employees.** In foreign born group, immigrants (52.3%) from different parts of the world have a significantly greater TB infection rate than Canadian born individuals (10.6%). These differences are related to the TB infection and incidence rates in the countries of origin (Menzies, 1992). These differences are also dependent on age, immigration time and whether or not BCG vaccination has been administered. It has been reported that the younger the immigrants come to Canada, the lower the infection rate (Menzies, 1992). If age is constant, the longer they stay in Canada, the lower the infection rate, representing either waning immune memory or the death of residual tubercle bacilli from remote infection (Stead et al, 1987).

As discussed in Chapter I, since BCG vaccination and non-mycobacterium infection may cause false-positive reaction of PPD test, the high rate of BCG vaccination and the high non-mycobacterium infection rate in some developing countries may overestimate the TB infection rate in these groups.

For comparison, TB infection rate in the immigrant group in the present study is also in the mid-range of 32-80% reported in other studies (Blum, 1993; Menzies, 1992; Nolan, 1988; Passes, 1982; Quillan, 1990).

**Comparison of TB infection rate between adult and child care facility employees.** When the TB infection rate between adult care and child care facility employees is compared, it is found that the adult care facility employees have a higher infection rate (24.6%) than the child care (17.6%). However, after adjusting for age, gender and ethnic
origin, the difference is not significant (RR=0.93, 95% CI is [0.87-1.0]). This supports the conclusion that employees working in the adult care facilities are not at increased risk of TB infection compared to the child care employees.

Discussion of TB Incidence Rate

It was calculated that the TB incidence rate in LTCF employees (10.5/100,000) is not greater (RR = 1.03, 95% CI is [0.40-2.32]) than the general population (9.6/100,000). This can be interpreted to mean that the LTCF employees are not at higher risk than the general population of developing active TB. Second, TB incidence in adult care facilities (10.1/100,000) is similar to the rate in child care facilities employees (11.3/100,000). This implies that neither residents of adult care facilities have greater risk of transmission of TB to the employees nor employees of adult care facilities have greater risk of transmission of TB to the residents than the child care facilities. Third, it was also found that the TB incidence rate is more related to the country of origin and ethnic groups than where they are working. The incidence rates in foreign born and First Nations individuals are, respectively, 7 and 42 times higher than other Canadian born individuals. Fourth, TB incidence in each ethnic group is consistent with its corresponding general population. The relative risk of TB in foreign born employees to foreign born community individuals, First Nations employees to First Nations community individuals and Canadian born employees to Canadian born community individuals are 0.88, 3.26 and 1.07, respectively. These results also indicate that TB is more related to the country of birth rather than place of employment (Ashley, 1971; Berman, 1981; Price, 1987).
It should be noted that in this study TB incidence rate in LTCF residents was not calculated, further research is needed to evaluate the TB incidence in LTCF residents and the relationship with that of LTCF employees.

**INH Preventive Therapy**

INH preventive therapy was administered to those persons who had positive PPD reactions in order to prevent occurrence of active TB. Of 3,657 employees who had positive PPD reactions, 6.5% (236) were prescribed INH. This rate of prescription of INH is much lower than the CDC/ATS recommendations (CDC/ATS, 1986). Based on these recommendations and Stead’s study (1985), it was calculated that 42.2% (1,545/3,657) should take INH. The reasons for the low INH administration rate in the British Columbia screening program attributed by the former director of TB Control clinics, Dr. John Farley (personal communication, November, 1996) to the following factors:

- the patients’ unwillingness to take INH, since they feel they are healthy and do not need treatment
- the long-term treatment (12-month on daily basis) of INH preventive therapy requires a substantial commitment that may be difficult to make
- doctors may be reluctant to prescribe INH preventive therapy because of the potential side effects of INH

Of 236 employees who began to take INH, 64% completed the treatment. The compliance rate appears to be related to the status of TB infection. Patients with inactive TB and TB infection with positive HIV had 100% compliance rates reflecting their expected annual risk of developing TB of 1 in 190 and 1 in 12 respectively (Ministry of
Health, 1991). The lowest rate (40%) was found in contacts with positive reactions, a group that has a low risk of developing active TB (5% for a lifetime).

Among the individuals who did not finish INH, 22% did not comply with the treatment and another 36% with unknown reasons were lost to follow up. The results suggested that enhanced follow up of INH preventive therapy may be needed to improve the compliance rate.

Analysis of Program Costs

As it was discussed in Chapter V, the costs of the screening program was based on the medical procedures and various tests (e.g., cost of tuberculin skin testing, chest X-ray, various lab tests and drug treatment). Indirect costs such as those associated with the administration and direction of the program, maintenance of data files, and employees’ loss of time at work when attending for follow-up and treatment were not included. If the indirect cost is included, the costs of screening program and treatment of active TB patients would be increased. Specially, the “opportunity” costs for inpatients would be increased dramatically. Hence, the cost gap between the screening program and treatment of active TB cases is narrower than shown in the present study.

Further, the assumptions made about the lifetime risk of TB and the protection rate of INH affect the costs attached to the outcome of TB screening program. In the present study, 5% of TB occurrence of lifetime risk among those who have positive PPD reactions without INH and 90% INH protection to those who finished INH preventive therapy were used. In fact, for estimation of lifetime risk of TB, the reported range was between 0.9% and 10% (Comstock, 1975; CTS, 1994; Kopanoff, 1978; Tsevat, 1988). However, it is
widely stated that, if not treated, 5% of tuberculin converters will develop active TB within 1 or 2 years and that another 5% will develop it later in life (Stead, 1995). For the British Columbia TB screening program, only a one-step test is administered and no further tests are required, so a positive reaction of the tuberculin skin test is defined as a reactor not as a convertor. It is therefore reasonable to use 5% estimation. The ninety percent of INH protection which was used in calculation is in the mid-range of the 70-100% reported in the other studies, and is consistent with the CTS recommendation rate (CTS, 1996). However, different estimations of lifetime risk of TB and INH protection rate would affect the cost of TB screening program. The higher the estimation of lifetime risk of developing active TB from TB infection and the higher the INH protection rate used, the less the cost for preventing one case of active TB in the screening program.

Costs and Benefits

It was calculated that $58,600 was spent to prevent one active TB. If he/she were not screened and administered INH preventive therapy, the cost of treatment of one active TB case, on average, would have been $10,304.

When the costs of the actual program is expanded to hypothetical standard and ideal programs, the costs of these screening programs for preventing one TB case ($25,778 and 16,497, respectively) are lower than the actual program. These results showed that increasing number of employees with positive PPD reactions taking INH and increasing compliance rate reduce the cost of preventing each active TB case.

Although this study was not intended to be a full cost efficiency or cost benefit analysis, the dramatic cost difference between the screening program and the treatment of
active TB cases that are potentially prevented supports that, at first sight, the program is not cost effective. But the method used to calculate costs were based only on direct screening, medical costs, future work is needed to expand this research into a cost effective/cost benefit study.

Nevertheless, taking another approach, MacArthur (1992) reported that a common rule of thumb in TB screening program is that screening is cost-efficient when the disease incidence is greater than 100/100,000 people. Given a 10.5/100,000 TB incidence rate in British Columbia LTCF employees, it would need a ten-fold increase in TB incidence in this population to satisfy this screening criterion.

While the low incidence rates of TB infection and disease in this population and the cost of the screening program suggest that the program may not be currently justified, the ethnic heterogeneity of the LTCF employee population with TB infection rates of 52.3% and 46.3%, and incidence rates of 21.4/100,000 and 163/100,000 for foreign born and First Nations, respectively, there appears to be a need for sustained vigilance particularly in these two subgroups.

**Recommendations and Policy**

1. The data related to the rate of TB infection, the incidence of TB disease and the costs of the screening program as calculated in the present study strongly indicate that the Division of British Columbia TB Control should consider whether the present screening program should be continued.

2. The data suggest that it would be more cost effective to limit the screening the high risk groups which were identified in this study as First Nations and immigrants.
within the larger population.

3. Comparing the low rate (6.5%) of prescription of INH to those who had positive PPD reactions in the screening program with the rate (42.2%) calculated base on the CDC/ATS recommendations (CDC/ATS, 1986) and Stead’s study (1985), the recommendations from ATS/CDC and CTS (1996) should be followed to increase the effectiveness of the screening program.

4. Considering the reasons of stopping INH preventive therapy, 21.9% did not comply with the treatment and another 36% with unknown reasons were lost to follow up, enhanced follow up programs are required to increase the compliance rate.

Future Research

1. A cost effective /cost benefit analysis should be conducted to evaluate the tuberculin skin test screening program. Direct and indirect costs should be included.

2. Although it is impossible to calculate TB infection rate for LTCF residents, since chest X-ray screening program is mainly performed in this group, TB incidence should be investigated and compared to the surrounding communities.

3. A cost of chest X-ray screening program should also be evaluated.
References


