

# Public health aspects of Tuberculosis

Montreal TB Course October 30, 2009



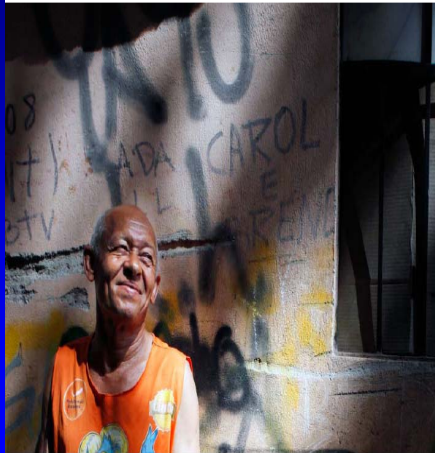
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Jewish General Hospital, McGill University

## Outline

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- Burden and epidemiology of TB globally and in Canada
- Principles of TB control globally and in low TB incidence countries
- Targeted LTBI screening and treatment programs: Barriers and challenges

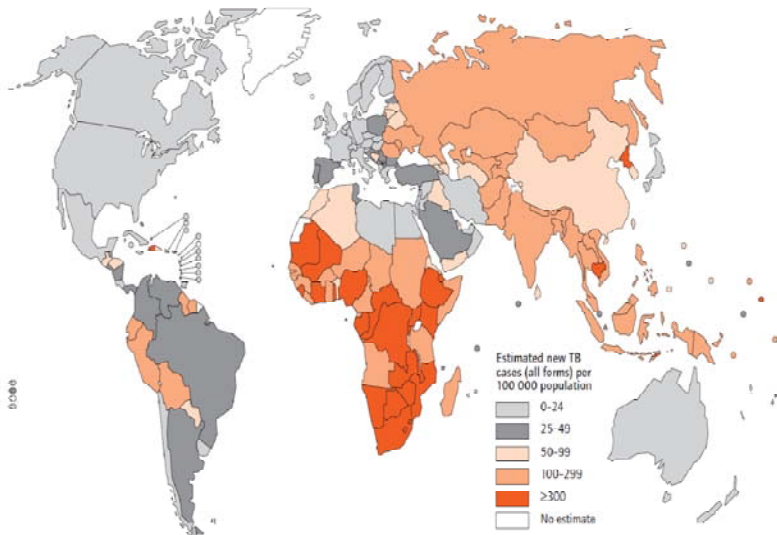
**CAN YOU IMAGINE  
A WORLD WITHOUT TB?  
WE CAN.**



Stop TB Partnership

- One third of the world's population is infected with TB
- 9.27 million new people develop active TB per year
  - >95% of these cases occur in developing countries
  - 82% of these cases occur in Africa and Asia
  - occur in those 15-54 yr in their prime productive years.
- Is the 2<sup>nd</sup> leading infectious cause of death in adults after HIV.
- Kills 1.7 million people per year, 98% in low income countries
- 1.8 million people fail to get access to TB treatment every year.

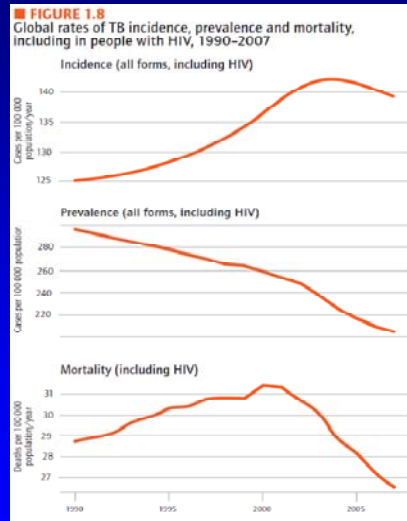
**FIGURE 1.2**  
Estimated TB incidence rates, by country, 2007



WHO 2009

## Global Burden of TB

- Prior to the HIV era (before the 1980s) the risk of infection declined by 1-5% / year in most developing countries
- Between mid 1980s and 2004 this trend was reversed by the HIV epidemic in Africa and multi-drug resistance in Eastern Europe.
- Since 2004 rates have begun to decrease again, but slowly ~1% per year in 5 of 6 world regions and stable in Eastern Europe.
- Despite decreasing rates, the total number of new number of cases of TB increases each year due to the population growth.



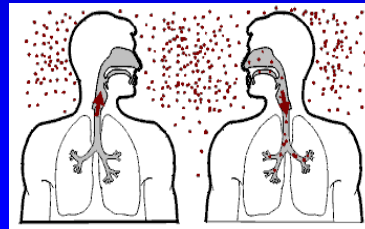
WHO Global TB Control Report 2009

## Transmission of *M. tuberculosis*

- Spread by droplet nuclei produced by those with pulmonary TB when they cough, talk or sing
- The infectiousness of the individual increases with degree of smear positivity of the sputum
- Transmission is more likely to occur with prolonged exposure in a closed poorly ventilated setting.
- An untreated person can infect 10-15 people in a year

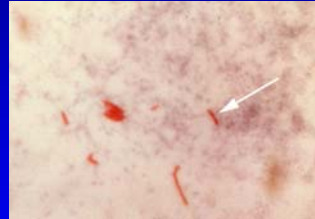


WHO Stop TB Photo Gallery



## TB Pathogenesis

- 10% of latently infected persons with normal immune systems develop TB at some point in their lifetime
- The risk of developing TB is greatest within the first 1-2 years of infection. Thus 1-2% of close contacts will have active TB at the time of diagnosis of the index case
- Certain medical conditions ie those that cause immunosuppression increase risk that TB infection will progress to TB disease eg. HIV



## Principles of TB Control

### Three priority strategies:

- Identify and treat all persons with TB disease (detect 70% and treat 85%)
- Identify contacts of persons with infectious TB; evaluate and offer chemoprophylaxis
- Test high-risk groups for LTBI; offer therapy as appropriate



## Global TB Control Efforts

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- 1993 WHO declared TB to be a Global emergency
- 1995 DOTS launched by WHO
- 1999- STOP TB Partnership started with 6 partners (IUATLD, WHO, KNCV, ALA/ATS, World Bank)
- Global Plan to STOP TB 2006-2015 in line with Millennium Development Goals



## The Global Plan to Stop TB 2006-2015

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1. High-quality DOTS expansion
2. Address TB/HIV, MDR-TB and other challenges
3. Contribute to health system strengthening
4. Engage all providers
5. Empower people with TB and their communities
6. Enable and promote research

2006 WHO, STOP TB Partnership. The STOP TB strategy

## Stop TB Goals and Data 2007

### Goals

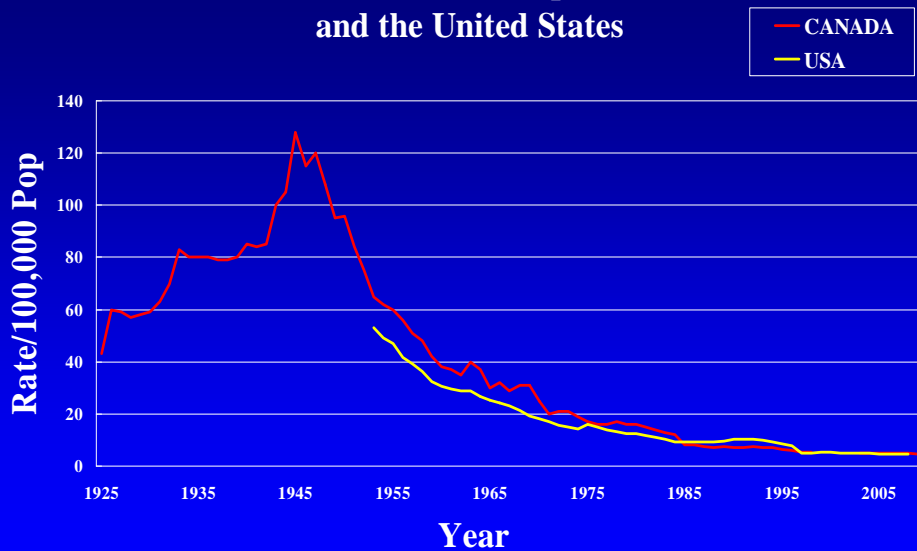
1. Incidence of TB should be falling by 2015 (MDG)
2. TB prevalence and death rates should be halved by 2015 vs rates in 1990.
3. At least 70% of incident smear positive cases should be Dx and Tx
4. At least 85% of these cases should complete Tx.

### Data 2007

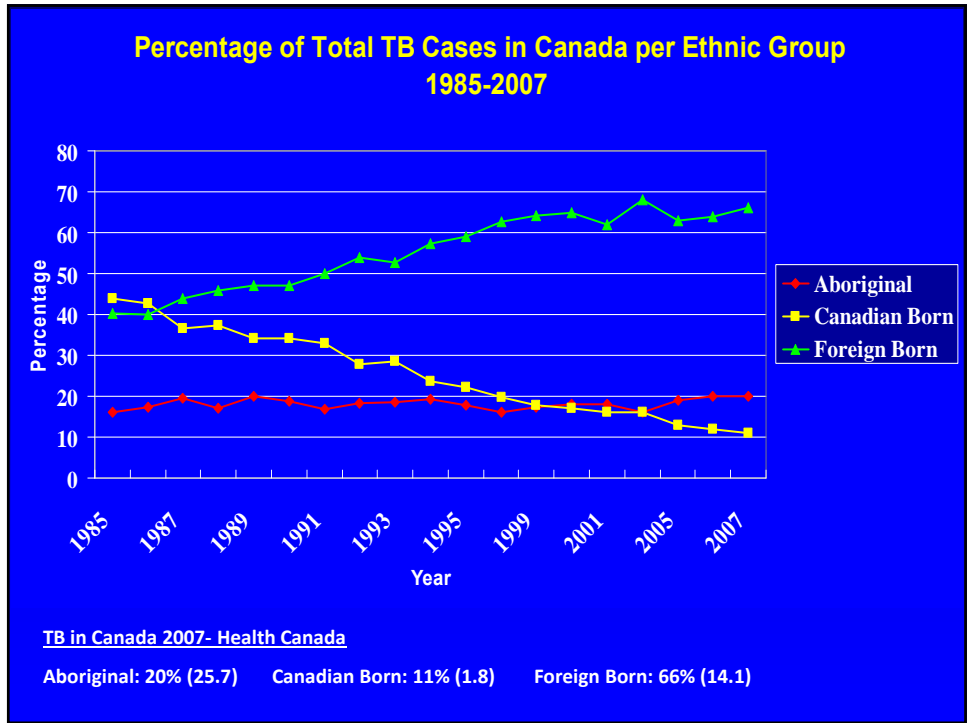
1. Incidence has been falling since 2004
2. The prevalence and death rates will be halved in at least 3 of 6 WHO regions by 2015 but will not be achieved globally.
3. The case detection rate was 63% in 2007
4. The treatment success rate reach 85% in 2006

WHO Global TB Control Report 2009

## Tuberculosis Rates/100,000 Population in Canada and the United States



Source: Health Canada Tuberculosis Report 1996, PHAC TB Report 2000, 2002, 2004 2005, 2006.  
 CDC- Trends in Tuberculosis Incidence-United States, MMWR 53 (10) 2004, MMWR 54 (10) 2005, MMWR 56 (11) 2007



- ## Priorities for TB Control in Canada
- Early diagnosis and treatment of person with active TB
  - Identify contacts of persons with infectious TB to identify secondary cases of TB and offer chemoprophylaxis to TST positive close contacts without TB
  - Targeted TST screening and LTBI treatment for high-risk groups for reactivation ie those with underlying medical conditions and young recently arrived immigrants from TB endemic countries.
- Canadian TB Standards 6<sup>th</sup> Ed 2007

## Risk of Reactivation of LTBI

- Risk is determined by the prevalence of LTBI and the presence of underlying risk factors that increase the risk of reactivation.
- Persons with a positive TST from low TB incidence countries have a 0.1% risk of reactivation per year and thus a 5-10% lifetime risk of developing active TB.
- This risk increases with recent transmission (extrapolated from studies of contacts) 1-2% have active TB at time of screening with the highest risk of TB in the first year after exposure and decreases to baseline 5-10 years after exposure.
- Certain underlying medical conditions increase the risk of reactivation by several fold.

Watkins IJTL 2000;4(10):895-903

**Table 2: Relative Risk of Developing Active TB in the Presence of Underlying Medical Conditions**

Condition	Relative Risk (RR)	Reference
<b>HIGH RISK (RR&gt;15)</b>		
Acquired immunodeficiency syndrome (AIDS)	110-170	183,184
Human immunodeficiency virus (HIV) infection	10-110	185-187
Transplantation (related to immunosuppressant)	20-74	183,185
Leukemia, lymphoma	1.0-35	186,187
Sarcosis	1.5-33	183,182
Chronic renal failure requiring hemodialysis	1.6-25	183,180
Carcinoma of head and neck	16	181
Recent TB infection ( $\leq$ 2 years)	15	182,183
Abnormal chest x-ray – fibronodular disease	6-19	184,188
Intravenous drug abuse	3.2-19.2	187,188
Transmission of infection per active case, No.	3.2-13	185,186
<b>INTERMEDIATE RISK RR=1.3-5</b>		
Previously healed TB	5.2	181,182
Treatment with glucocorticoids	4.9	182
Tumor necrosis factor (TNF)-alpha inhibitors	1.5-4	184,185
Prolonged corticosteroid therapy	1.0-5.1	180,188
Diabetes mellitus (all types)	2.0-4.1	187,188,189
Chronic renal failure	2.4	187
Underweight ( $<$ 90% ideal body weight; for most persons this is a body mass index $\leq$ 20)	1.6-3	183,184
Weight loss $\leq$ 10% below ideal body weight	1.8-2.1	183,184
Young age when infected (0-4 years)	2.2-5	185
Cigarette smoker (1 pack/day)	2-3	186
Abnormal chest x-ray – granuloma	2	186,187
Gastrectomy	1.3-5.0	188,189
<b>LOW RISK RR=1 *</b>		
Infected person, no known risk factor, normal chest x-ray ("low risk reactor")	1	181

\*Incidence of developing active TB of 0.1%/yr



## Canadian Guidelines for Targeted LTBI Screening

### High Priority for LTBI Screening

- Close contacts of active TB cases
- HIV positive individuals
- Persons with an history of untreated active TB or an abnormal CXR (inactive TB)
- Individuals in the Post-Landing Surveillance program
- Aboriginal communities with high rates of TB
- The poor esp the urban homeless
- Staff and residents of long-term care and correctional facilities
- Health care workers with risk of occupational exposure to active TB

Canadian TB Standards 6<sup>th</sup> Ed 2007

## Canadian Guidelines for Targeted LTBI Screening

### Consider for LTBI Screening

- Persons with medical conditions that increase the risk of TB reactivation
- Children <15 years of age from a TB endemic country that have arrived <2 years previously.
- Individuals >15 years of age from a TB endemic country with a known recent contact with TB or medical conditions that increase the risk of TB reactivation.
- Individuals working in settings with populations at risk for active TB ie childcare workers, works with HIV+
- Substance abuse
- Travellers to TB endemic countries and with high risk exposure or high risk underlying conditions.

Canadian TB Standards 6<sup>th</sup> Ed 2007

## TB in Close Contacts

- 1-2% of close TB contacts have active TB at the time of diagnosis of the index case and 50% are TST positive
- Close contacts are at greatest risk of developing active TB within the first 1-2 years of infection and therefore are a priority for LTBI treatment
- This is a routine part of case management of active TB cases by public health.



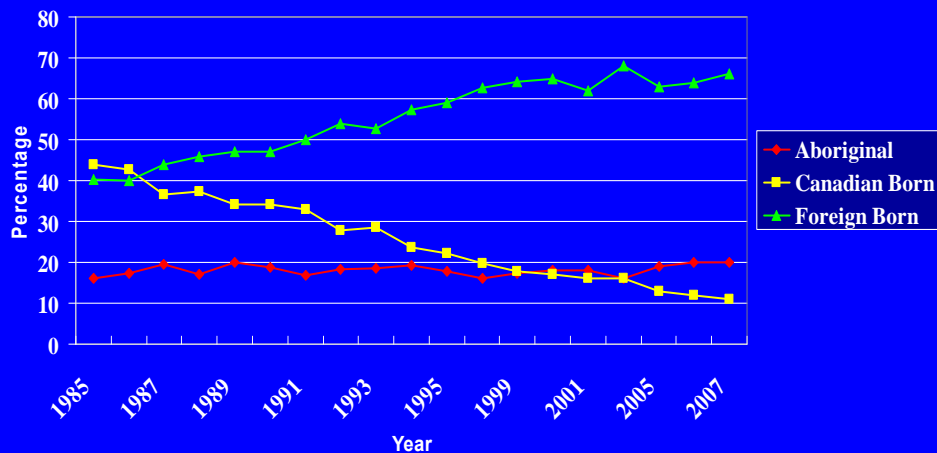
## Targeting those with medical conditions that increase the risk of TB reactivation

- HIV
- Immunosuppression such as organ transplant, hematologic malignancy, chemotherapy, steroids, anti-TNF
- Fibrosis or granuloma on CXR
- IV Drug Use
- Diabetes, renal failure and dialysis
- Underweight

## Underlying Medical Conditions

- It is unclear what proportion of all TB cases have an underlying medical problem.
- It is also unclear the proportion of those at risk are screened and offered LTBI
- There are no organized programs to screen and give LTBI to these groups
- Depends on the treating physicians to screen and offer LTBI

Percentage of Total TB Cases in Canada per Ethnic Group  
1985-2007



TB in Canada 2007- Health Canada

Aboriginal: 20% (25.7)    Canadian Born: 11% (1.8)    Foreign Born: 66% (14.1)

# Global Migration

- The total number of immigrants has more than doubled in the past 40 years

1960	75M
2000	175 M
2050	230 M

Migrating Populations 1960-1975



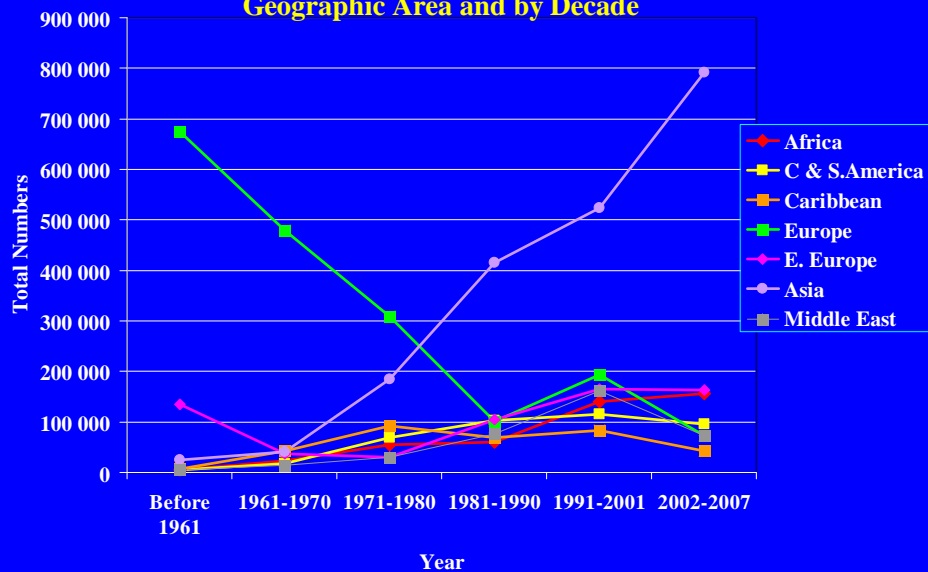
Source: Population Action International 1994

Migrating Populations, 1990-2000



Sources: Population Action International 1994, International Organization for Migration, 2003

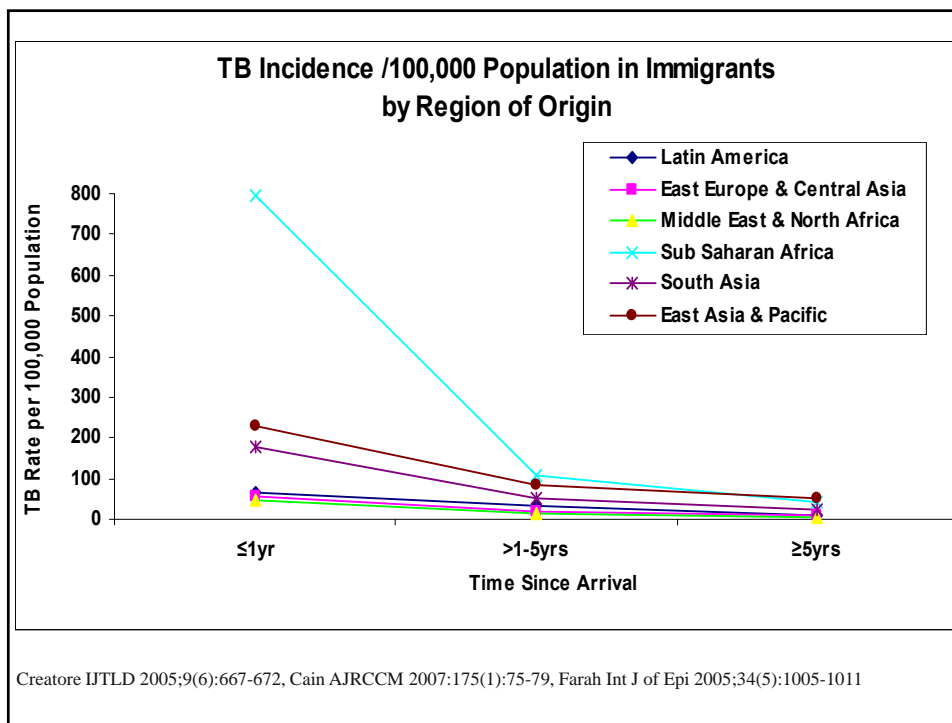
Total number of immigrants admitted to Canada per Geographic Area and by Decade

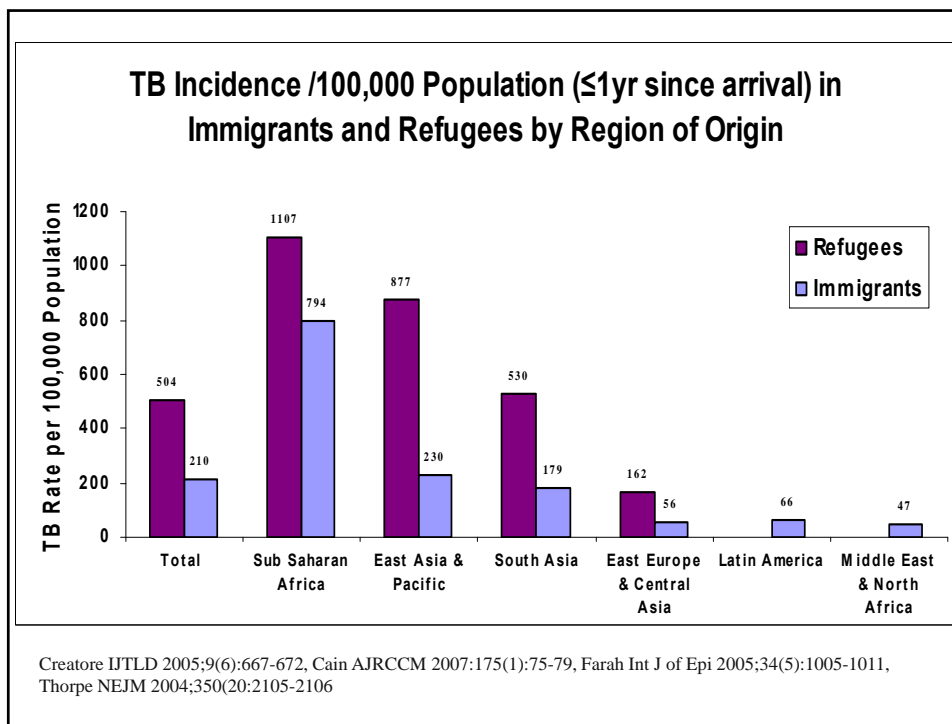


Source: Statistics Canada, Census Nation Tables 2001 and 2006

## Characteristics of TB in Foreign-Born Individuals after Immigration to Industrialized Countries

- The proportion of TB cases due to foreign-born individuals in all industrialized countries has increased over the past 20 years . In Canada 17% in 1970 to 65% in 2006.
- The highest rates of TB are seen in immigrants from countries with the highest burden of TB globally
- The greatest risk of developing TB in the foreign-born occurs in the first year after arrival but ~50% of cases occur in the first 5 years after arrival.
- Risk of reactivation remains elevated lifelong
- Refugees are 2-3 fold greater risk of reactivation compared to immigrants





## Pre Landing Screening and Post-Landing Surveillance for TB

- All individuals > 11 years of age that apply for permanent residency, those claiming refugee status, and students and workers staying for >six months are screened with a CXR
- Those with an abnormal CXR are required to have three sputum examinations (smear and culture) and if found to have active TB must be treated and prove that they have negative smears and cultures prior to entry to Canada.
- All individuals with previously-treated TB or inactive TB must be monitored after arrival to Canada in the Post-Landing Surveillance (PLS) Program.

## Efficacy of Pre-Landing Screening and PLS

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- The pre landing CXR screening and PLS has relatively low impact on TB control in Canada and other strategies are needed.
- Of those screened <1% are found to have active TB and 3-5% (8,000-13,000 individuals/year) are found to have inactive TB.
- Only account for a small proportion of all cases of FB TB (8% in Alberta; 5-17% in Quebec; 12-13% in the US).

## Post Landing Screening

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- In all domestic screening programs (school-based, targeted immigrant/refugee or contact tracing) only 11-30% of those at risk for LTBI complete chemoprophylaxis if they are found to be TST positive.
- This is due to losses and drop-outs at the many different steps in the process including; failure to present for or complete screening, failure to report for medical evaluation if screening test positive, MD failure to prescribe chemoprophylaxis for those eligible, patient refusal to start treatment, and finally poor chemoprophylaxis completion rate.
- Only 74% (range 34% to 93%) of individuals on average present and complete screening,
- 71% of MD comply with LTBI screening and INH prescribing guidelines
- 47% (range 11% to 72%) of individuals complete LTBI treatment.

## What is the Impact of Present LTBI Screening Programs?

- Active TB cases in the FB 2002-2003 in San Francisco, N=223
- Only 38% (N=85) were preventable – ie **missed opportunities**
  - Medical conditions: 24 (28%); Recent Immigrants :43 (51%);
  - Evidence of prior TB: 16 (19%); Epi Risk: 9 (11%)
- 19% (N=43) were NOT preventable through finding and treating LTBI
- 43% (N=95) had no indication for testing ie had been in the US for >5years, 30% of whom had been in the US >20 years.
- All cases of TB in the US 2004, N=14, 517
- 24% in US < 1yr, 26% 1-5 years, 50% had been living in the US >5 years

Walter CID 2008;46:103-6 , Cain AMRCCM 2007;175:75-79

## Barriers present programs and to expanding to large scale screening for LTBI

### Sub-Optimal tests

- Chest X-Ray poorly sensitive and specific
- TST poorly specific test, cross reacts with BCG and NTM, IGRAs more specific but neither can predict the 1 of 10 that will develop active TB

### Lengthy Treatments with poor compliance

- Poor physician compliance to prescribe (70-80%)
- Poor patient compliance to take treatment (~50-70%)
- TST treatment not cost-effective due to poor compliance

### Lack of targeting all populations at risk



Table 4a: Numbers needed to Treat for LTBI to prevent one case of active TB by Age, Time since Arrival and Compliance

Age (years)	Years since arrival	Cumulative Lifetime Risk of Active TB	Number needed to Treat (NNT) with LTBI			
			Compliance			
			100%	70%	50%	30%
10	1-2 yrs	8.2%	14	20	27	45
	3-5 yrs	7.6%	15	21	29	49
	>5 yrs	7.2%	16	22	31	51
20	1-2 yrs	7.2%	16	22	31	51
	3-5 yrs	6.6%	17	24	34	56
	>5 yrs	6.2%	18	26	36	60
35	1-2 yrs	5.7%	20	28	39	65
	3-5 yrs	5.1%	22	31	44	72
	>5 yrs	4.7%	24	34	47	79
50	1-2 yrs	4.1%	27	39	54	90
	3-5 yrs	3.5%	32	45	63	106
	>5 yrs	3.1%	36	51	72	119
65	1-2 yrs	2.6%	43	61	85	142
	3-5 yrs	1.96%	57	81	113	189
	>5 yrs	1.6%	69	99	139	231

1. Assume 0.1% annual risk of infection with a RR of developing active TB for each year since arrival of: <1yr: 5.08, 1.1-2 yrs: 2.96, 2.1-3 yrs: 2.35, 3.1-4 yrs: 2.06, 4.1-5 yrs: 1.87, 5.1-6 yrs: 1.89, 6.1-7 yrs: 1.36 all vs >7 yrs.<sup>21, 32, 166</sup>
2. Assume live to age 80 years
3. Assume 90% efficacy of INH if high compliance<sup>24, 49</sup>

Age (years)	Years Since Arrival	Lifetime Risk of Active TB	Lifetime Risk of Active TB with Risk Factor	Number Needed to Treat with LTBI			
				Compliance			
				100%	70%	50%	30%
<b>35 years</b>							
High RR>15	1-2 yrs	5.7%	86%	2	2	3	5
	3-5 yrs	5.1%	77%	2	3	3	5
	>5 yrs	4.7%	71%	2	3	4	6
Intermed RR=5	1-2 yrs	5.7%	29%	4	6	8	13
	3-5 yrs	5.1%	26%	5	7	9	15
	>5 yrs	4.7%	24%	5	7	10	16
Low/Int RR=2	1-2 yrs	5.7%	11%	10	14	20	34
	3-5 yrs	5.1%	10%	11	16	22	37
	>5 yrs	4.7%	9%	12	18	25	41
<b>50 years</b>							
High RR>15	1-2 yrs	4.1%	62%	2	3	4	6
	3-5 yrs	3.5%	53%	2	3	4	7
	>5 yrs	3.1%	47%	2	3	5	8
Intermed RR=5	1-2 yrs	4.1%	21%	5	8	11	18
	3-5 yrs	3.5%	18%	6	9	13	21
	>5 yrs	3.1%	16%	7	10	14	23
Low/Int RR=2	1-2 yrs	4.1%	8%	14	20	28	46
	3-5 yrs	3.5%	7%	16	23	32	53
	>5 yrs	3.1%	6%	19	26	37	62
<b>65 years</b>							
High RR>15	1-2 yrs	2.6%	39%	3	4	6	9
	3-5 yrs	1.96%	29%	4	5	8	13
	>5 yrs	1.6%	24%	5	7	9	15
Intermed RR=5	1-2 yrs	2.6%	13%	9	12	17	28
	3-5 yrs	1.96%	10%	11	16	20	37
	>5 yrs	1.6%	8%	14	20	28	40
Low/Int RR=2	1-2 yrs	2.6%	5%	22	32	44	74
	3-5 yrs	1.96%	4%	28	40	56	93
	>5 yrs	1.6%	3%	35	50	71	123

## Barriers to Large Scale LTBI Screening

- Cultural/linguistic barriers to screening, uptake and completion of LTBI and understanding of toxicity of treatment
- Large population with lifelong increased risk of TB reactivation without easy access to population
- Ongoing risk of exposure to TB endemic countries

## Cultural and Socioeconomic Considerations Barriers to uptake of screening and LTBI

- Patient: Linguistic barriers, cultural taboos and stigmatization, low education level, low risk perception of progressing from LTBI to active disease, belief that a positive TST is due to BCG, not wanting to have venipunctures, and economic factors (costs of travel, lack of insurance, delays in obtaining insurance, and missed days at
- Provider: Inadequate knowledge of which migrants should be screened or how they should be followed.



## Cultural and Socioeconomic Considerations

### Interventions to improve uptake and adherence to LTBI treatment

- Patient reminders and adherence coaches that speak the same language have increased uptake of screening and LTBI
- In an RCT, educating primary care providers on how and who to screen increased screening (0.4% to 57%) , identification of LTBI from (9% vs 19%)
- In study in Seattle cultural case managers (of the same ethnic background as the patient) increased adherence to LTBI (82% vs 37%) as compared to standard clinic based management

Griffiths et al Lancet 2007;369(9572):1528-1534  
Goldberg et al IJTL 2004;8(1):76-82

## Large Untargeted Population at Risk

- Only ~250,000 immigrants, selected visitors, foreign workers, and students are screened (with CXR) of ~ 1 million at risk
- The proportion of TB cases due to unscreened groups (ie most visitors, foreign workers, students etc) may be substantial (24% in one study in Ontario).
- 4 million at risk living for LTBI unscreened in Canada



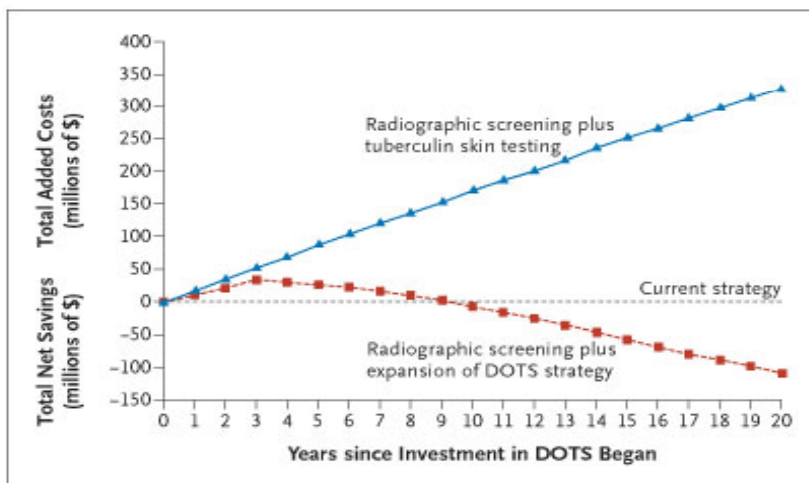
## Effect of Re-exposure during Travel to TB Endemic Countries

- The impact due to VFR travel both into (~560,000/year) and out of Canada (~ 1.2 million trips per year) may be substantial
- 20% of all cases of FBTB in Britain occurred due to recent travel to a TB endemic country.
- Receipt of visitors from high TB incidence countries has been associated with a risk (2.0 odds) of being TST positive



Wobeser CMAJ 2000;163(7):823-828, Enarson ARD1979;119(1):11-18  
 McCarthy Br J Dis Chest 1984;78(3)248-253, Lobato 1998;15(6):1871-1875

### Net Savings from DOTS Expansion or Added Costs for TST screening (relative to the status quo) over 20 years - Migrants to the US from MEXICO



Schwartzman, Menzies et al. NEJM 2005;353:1008-1020

## Conclusions

- New diagnostic tools and treatments
- Ensure that those at highest risk for developing TB are targeted
- New creative strategies will need to be adopted to engage the immigrant community.
- To be successful, target population for screening will need to be broadened BUT with resources to address cultural differences and concerns and with adequate translators.
- This may be most successfully implemented at the level of the primary care provider using an integrated preventive health care strategy.

## Conclusions

- Given the degree of migration and travel, the control of TB in low TB incidence countries will ultimately depend on controlling TB in high TB incidence countries

