Epidemiology of Tuberculosis: Global and Local

McGill Tuberculosis Course
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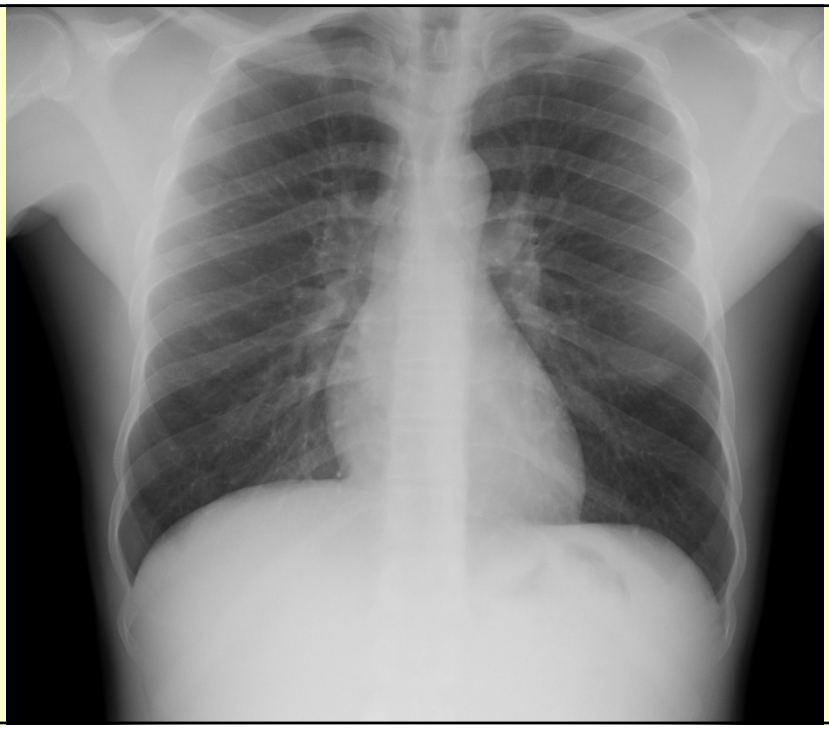
Objectives

Participants will be able to:

- Describe key features of current TB epidemiology, at the global and local level
- Identify major determinants of trends in TB incidence globally, and in Canada
- Identify key elements of global and Canadian TB control strategies

Case 1

- 32 y.o. male refugee claimant from DR Congo presented to RVH ER with herpes zoster involving left V1 distribution, with probable bacterial superinfection
- Wife known to be HIV-infected
- Hospitalized, confirmed HIV+ with CD4 ~70
- Minor hemoptysis; sputum induction performed

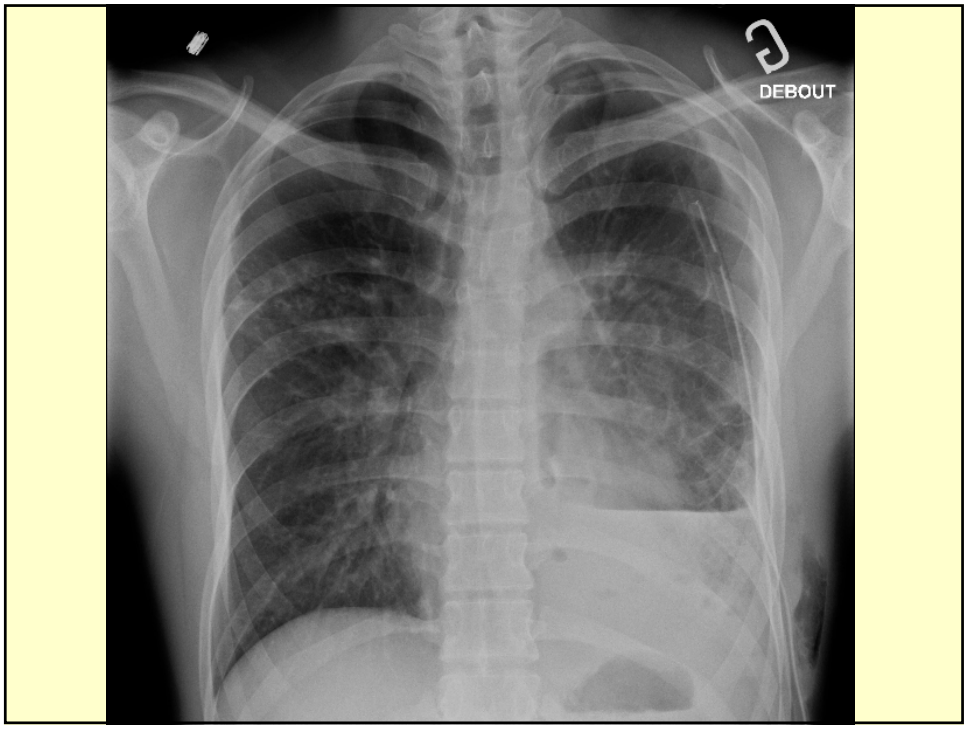


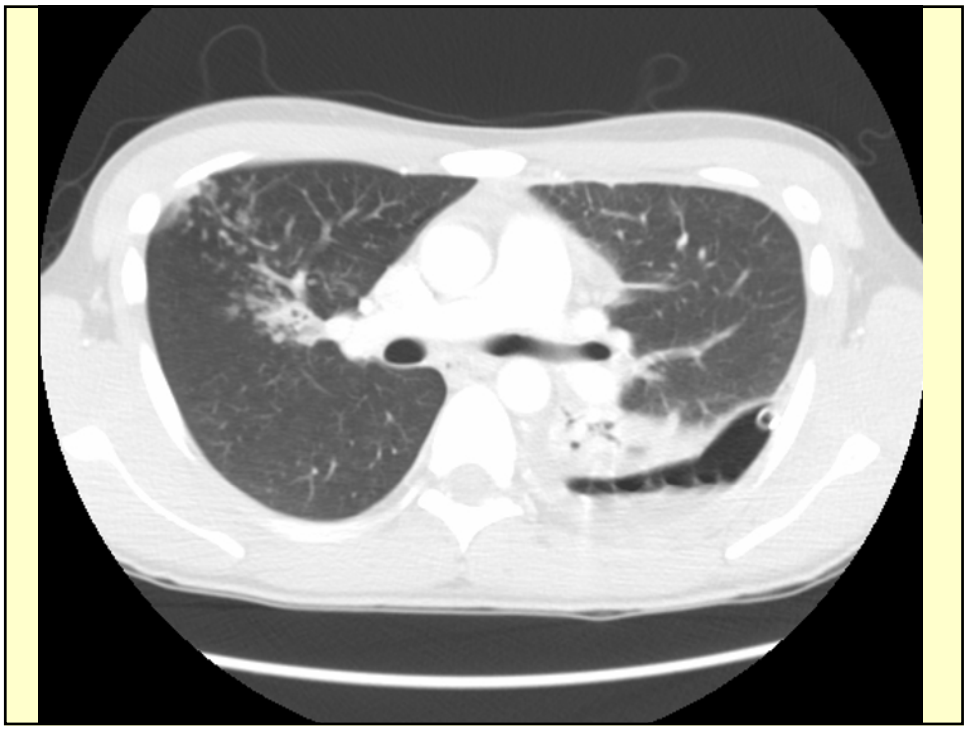
Case 1

- Found to have smear-negative, culture-positive pulmonary TB
- Sensitive to all first line anti-TB drugs
- Treated successfully with microbiologic cure
- HAART instituted with excellent response

Case 2

- 20 y.o. Peruvian-born male, in Canada for several years
- No past medical history of any kind
- Presented with sudden onset severe chest pain and dyspnea ~one week after returning from visit to Peru by airplane


DEBOUT

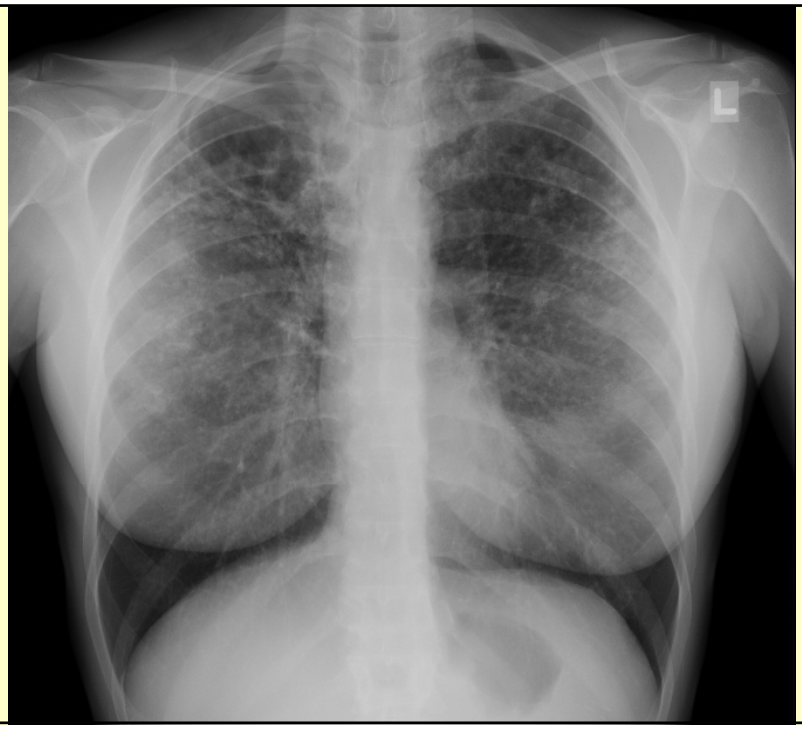


Case 2

- Culture-positive on pleural fluid, BAL
- Found to have MDR-TB i.e. probable primary MDR
- Hospitalized for over 3 months with bronchopleural fistula
- Still on complex treatment regimen

Case 3

- 43 y.o. Quebec-born female
- No past medical history of any sort
- Referred to MCI clinic for persistent cough of several months duration
- Minor fatigue, weight loss



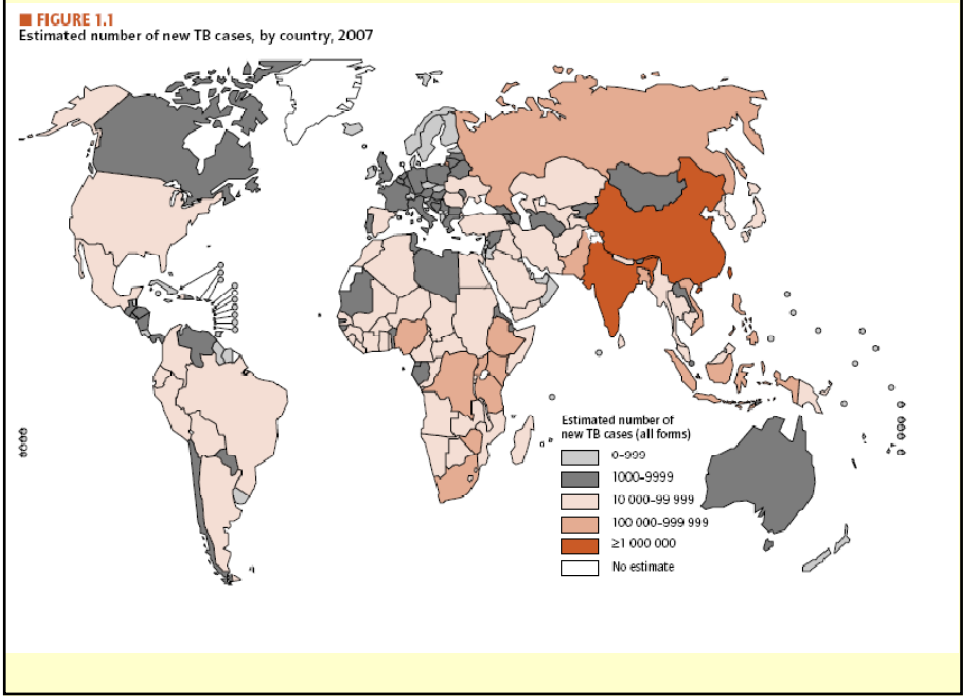
Case 3

- Immediately admitted to hospital
- 3+ smear positive on spontaneous sputum
- TB sensitive to all
- No clear exposure history; HIV-negative
- Prolonged hospitalization (> 3 months) as slow to clear sputum
- Ultimately cured

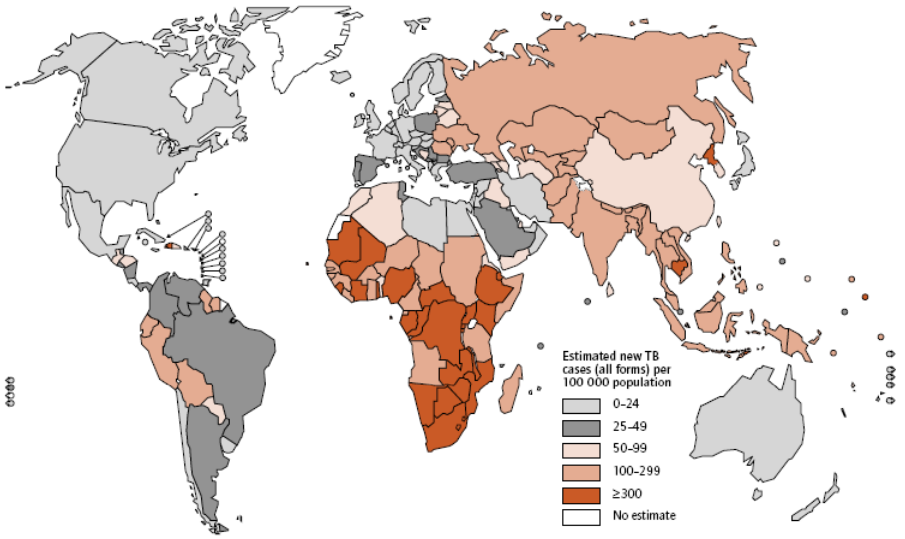
"I thought TB had disappeared"

- 2007: WHO estimated 9.3 million new cases, vs. 8.3 million cases in 2000 and 6 million cases in 1990
- 55% in Asia, 31% in Africa
- Overall global incidence 137 per 100,000 annually, down from peak 142 in 2004
- 1.3 million deaths in HIV-negative individuals, 450,000 deaths in HIV-positive individuals (~25% of all deaths in HIV-infected persons)

http://www.who.int/tb/publications/global_report/2009/en/index.html



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



■ **TABLE 1.2**
Estimated epidemiological burden of TB, 2007

		INCIDENCE[a]				PREVALENCE[a]		MORTALITY				
		ALL FORMS		SMEAR-POSITIVE		ALL FORMS		HIV-NEGATIVE		HIV-POSITIVE		HIV PREV. IN INCIDENT TB CASES[b]
	POPULATION 1000s	NUMBER 1000s	PER 100 000 POP PER YEAR	NUMBER 1000s	PER 100 000 POP PER YEAR	NUMBER 1000s	PER 100 000 POP PER YEAR	NUMBER 1000s	PER 100 000 POP PER YEAR	NUMBER 1000s	PER 100 000 POP PER YEAR	%
1 India	1 169 016	1 962	168	873	75	3 305	283	302	26	30	2.5	5.3
2 China	1 328 630	1 306	98	585	44	2 582	194	194	15	6.8	0.5	1.9
3 Indonesia	231 627	528	228	236	102	566	244	86	37	5.4	2.4	3.0
4 Nigeria	148 093	460	311	195	131	772	521	79	53	59	40	27
5 South Africa	48 577	461	948	174	358	336	692	18	38	94	193	73
6 Bangladesh	158 665	353	223	159	100	614	387	70	44	0.4	0.3	0.3
7 Ethiopia	83 099	314	378	135	163	481	579	53	64	23	28	19
8 Pakistan	163 902	297	181	133	81	365	223	46	28	1.4	0.9	2.1
9 Philippines	87 960	255	290	115	130	440	500	36	41	0.3	0.3	0.3
10 DR Congo	62 636	245	392	109	174	417	666	45	72	6.0	10	5.9
11 Russian Federation	142 499	157	110	68	48	164	115	20	14	5.1	3.6	16
12 Viet Nam	87 375	150	171	66	76	192	220	18	20	3.1	3.5	8.1
13 Kenya	37 538	132	353	53	142	120	319	10	26	15	39	48
14 Brazil	191 791	92	48	49	26	114	60	5.9	3.1	2.5	1.3	14
15 UR Tanzania	40 454	120	297	49	120	136	337	12	29	20	49	47
16 Uganda	30 884	102	330	42	136	132	426	13	41	16	52	39
17 Zimbabwe	13 349	104	782	40	298	95	714	6.9	52	28	213	69
18 Thailand	63 884	91	142	39	62	123	192	10	15	3.9	6.0	17
19 Mozambique	21 397	92	431	37	174	108	504	10	45	17	82	47
20 Myanmar	48 798	83	171	37	75	79	162	5.4	11	0.9	1.9	11
21 Cambodia	14 444	72	495	32	219	96	664	11	77	1.8	13	7.8
22 Afghanistan	27 145	46	168	21	76	65	238	8.2	30	0.0	0	0
High-burden countries	4 201 761	7 423	177	3 245	77	11 301	269	1 058	25	339	8.1	14

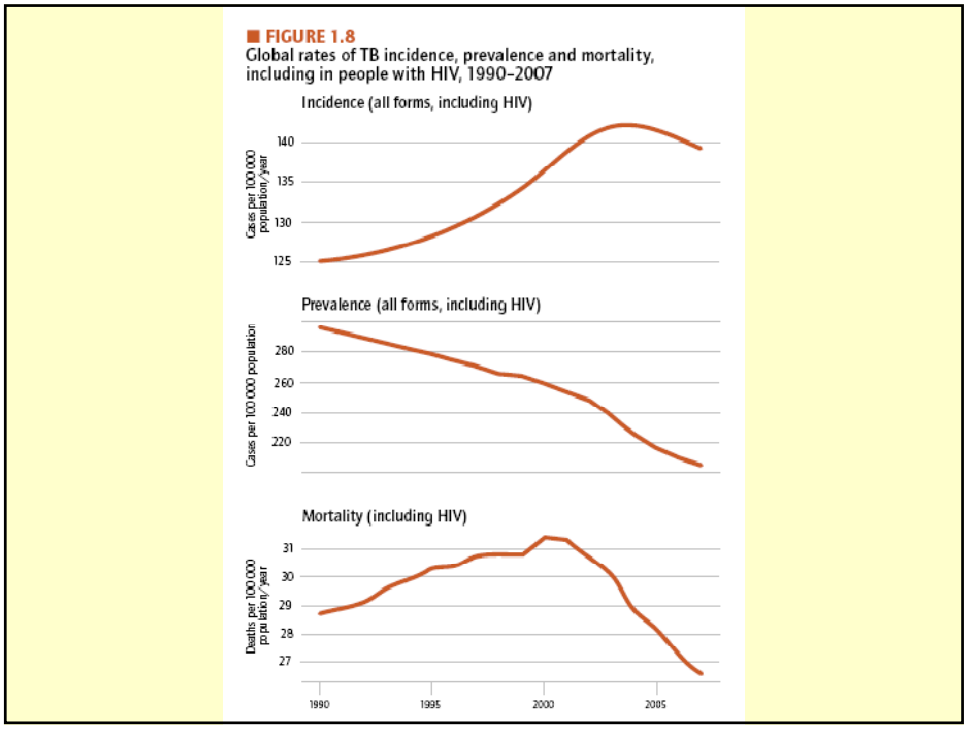


FIGURE 1.8
Global rates of TB incidence, prevalence and mortality, including in people with HIV, 1990–2007
Incidence (all forms, including HIV)
Cases per 100 000 population/year
140
135
130
125
Prevalence (all forms, including HIV)
Cases per 100 000 population
280
260
240
220
Mortality (including HIV)
Deaths per 100 000 population/year
31
30
29
28
27
1990
1995
2000
2005

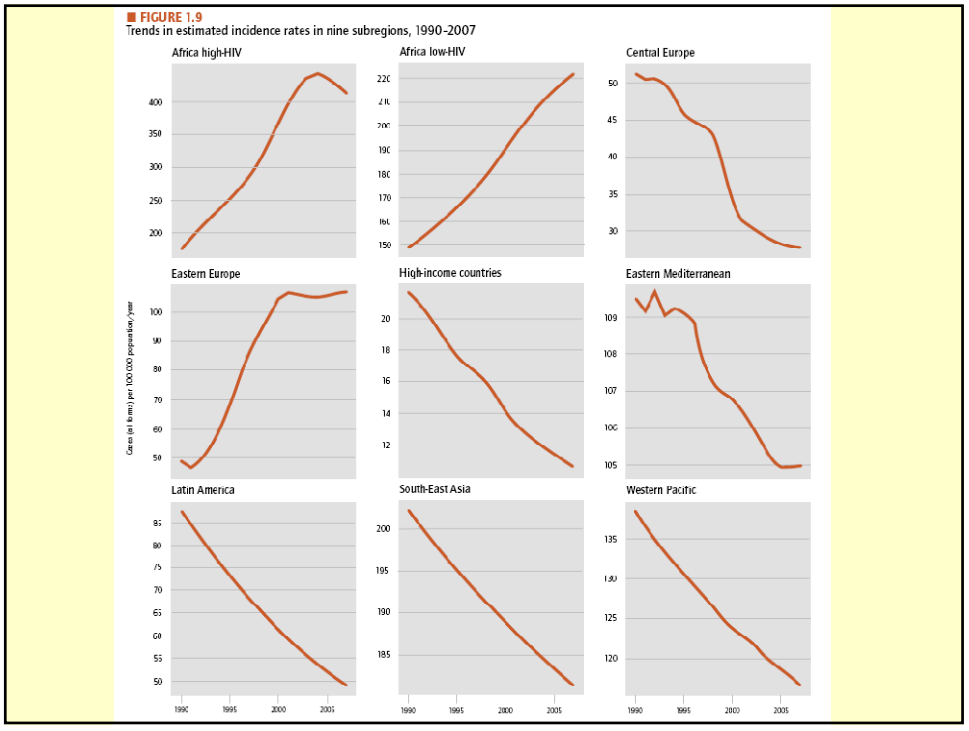
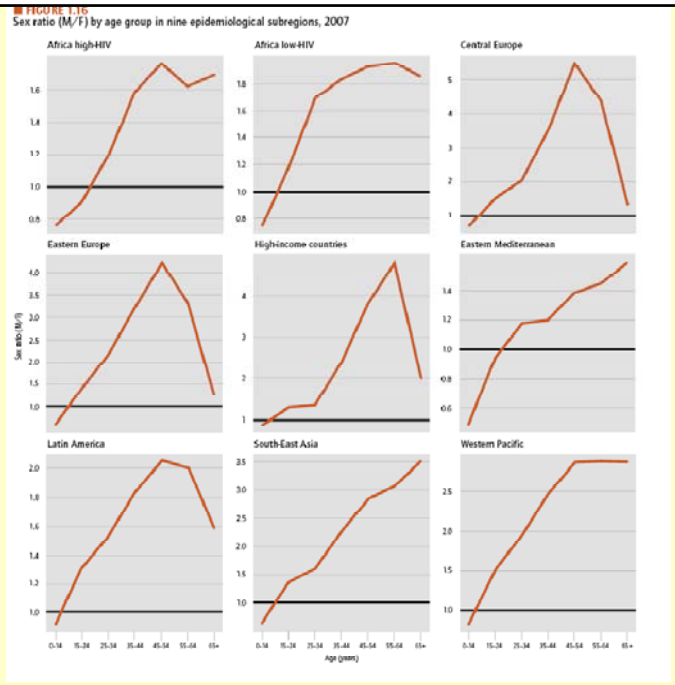


FIGURE 1.9
Trends in estimated incidence rates in nine subregions, 1990–2007
Africa high-HIV
Africa low-HIV
Central Europe
Eastern Europe
High-income countries
Eastern Mediterranean
Latin America
South-East Asia
Western Pacific
Cases (all forms) per 100 000 population/year
1990
1995
2000
2005



Overall 1.8 male:1 female

Limitations

- Reported TB cases (notifications) account for a variable proportion of all TB cases depending on the country
- Notifications will increase with improvements in diagnosis and reporting, regardless of underlying true incidence
- Notifications will decrease when national TB control programs worsen
- Total TB cases (reported + unreported) must therefore be estimated indirectly from other data e.g. prevalence surveys, annual risk of infection surveys, mortality data, extrapolation from “DOTS areas” etc.
- Substantial implications for program quality indicators

Major Determinants

- Basic elements of TB control e.g. diagnosis, consistent and appropriate treatment
- Health system infrastructure e.g. national control programs, public vs. private providers etc.
- General socioeconomic and health status, tobacco, alcohol
- HIV
- Drug resistance
- Obviously all these are interrelated

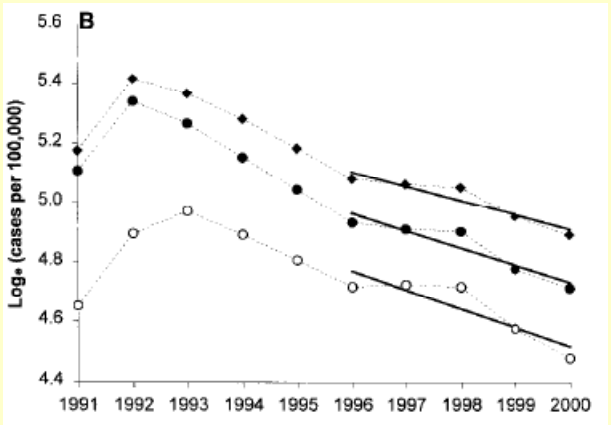


Figure 3. *A,* Case report rates of new sputum smear (ss)–positive tuberculosis (TB) cases per 100,000 population in 25 departments of Peru, plotted on a log$_e$ scale. *B,* National case report rates of all new TB cases (♦), new pulmonary cases (●), and new smear-positive cases (○). Lines were fitted by regressions for the years 1996–2000.

Suarez et al, *JID* 2001

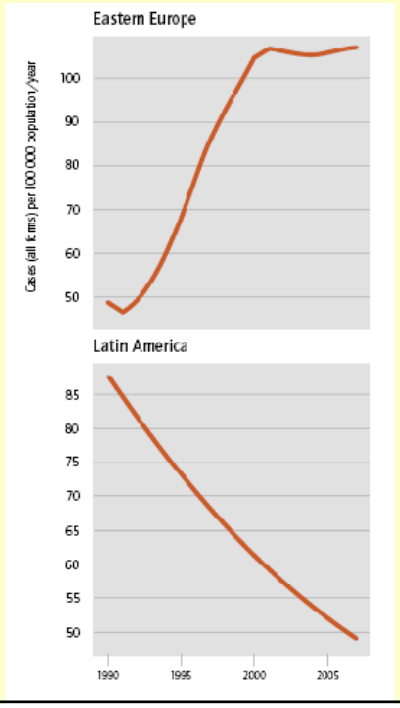


Table 3 Results of multivariate linear regression analysis of Models 1–3: adjusted estimated effect (95%CI) of the specific parameter in the specific model on the change in TB incidence rate/100 000, between 1990 and 2005

	Change in TB incidence rate/100 000		
Parameter	Model 1* (adjusted R^2 = 0.78)	Model 2* (adjusted R^2 = 0.78)	Model 3* (adjusted R^2 = 0.79)
Change in life expectancy (per 1 year increase in life expectancy between 1990 and 2005)	−7.8 (−11.3–−4.3)†		
Change in mortality in children aged <5 years (per 1/1000 increase in mortality among children aged <5 years between 1990 and 2005)		+1.0 (+0.5–+1.4)†	
Change in measles vaccination coverage (per 1% increase in measles immunization coverage over period 1990–2005)			−1.3 (−2.4–−0.8)†
Change in GDP per capita (per 1% increase in GDP between 1990 and 2005)	+0.003 (−0.1–+0.1)	−0.05 (−0.2–+0.09)	−0.06 (−0.2–+0.08)
HIV prevalence in 2005‡ (per 1% higher HIV prevalence)	+16.7 (+13.1–+20.3)†	+20.9 (+18.4–+23.4)†	+22.8 (+20.3–+25.4)†
Change in treatment success for smear-positive cases on DOTS (per 1% increase in success between 1990 and 2005)	−0.9 (−1.8–+0.02)	−0.9 (−1.8–+0.07)	−0.9 (−2.0–+0.1)

Oxlade et al, *IJTLD* 2009

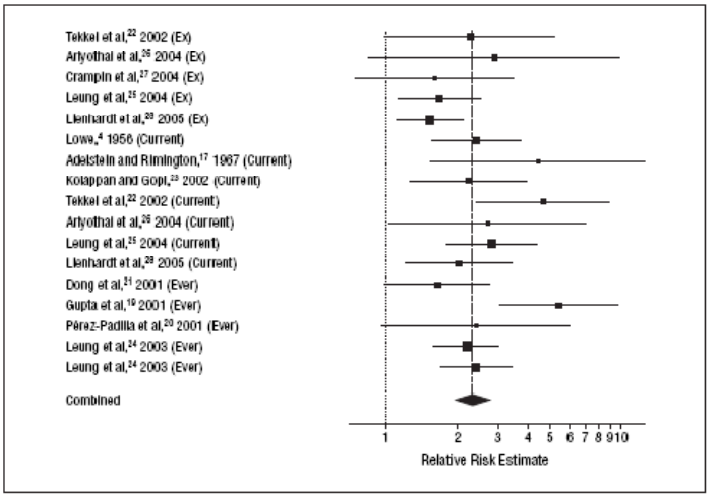
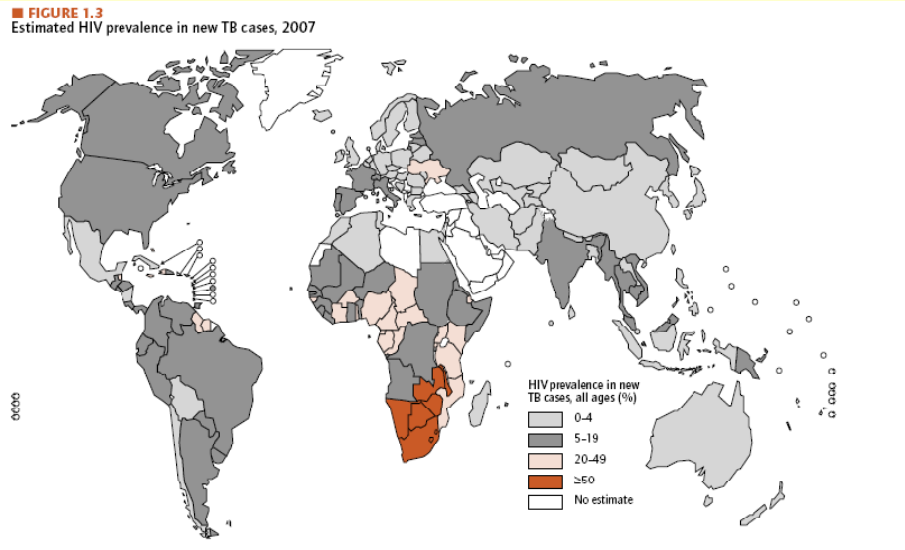


Figure 3. Forest plot of results for men only and for men and women combined in studies[4,17,19-28] that examined smoking and tuberculosis disease. The smoking type (ex-smokers [Ex], current smokers [Current], and ever smokers [Ever]) of the study population is shown on the y-axis.

Bates et al, *Arch Int Med* 2007

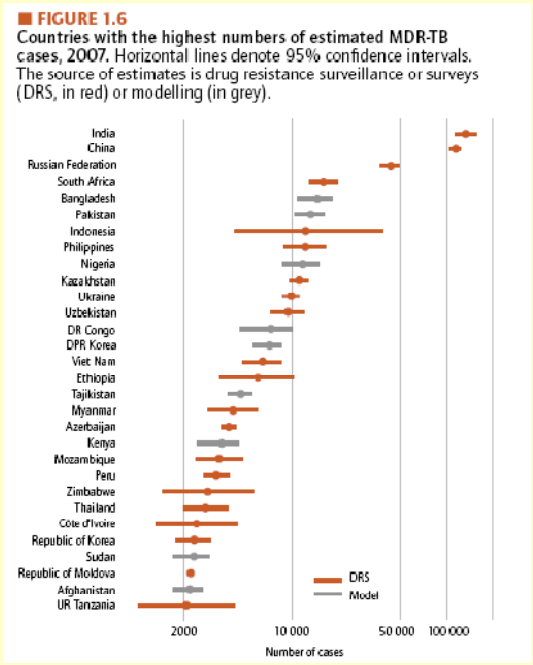
HIV

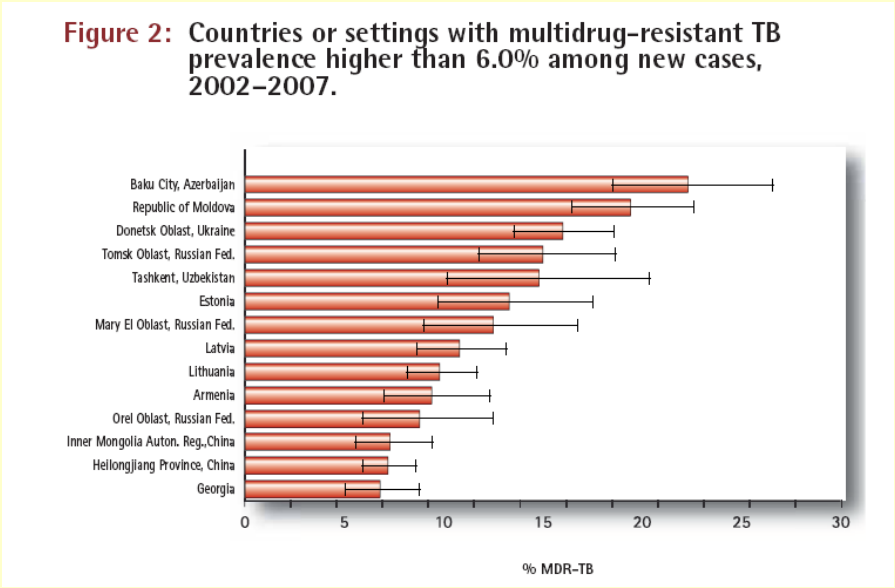
- Strongest known risk factor for TB disease
- Increases risk of progression/reactivation of latent TB infection by 100-fold or more
- To date, impact on global epidemiology most evident in sub-Saharan Africa, but concern re unknown magnitude of HIV-TB coinfection notably in India



Drug Resistance

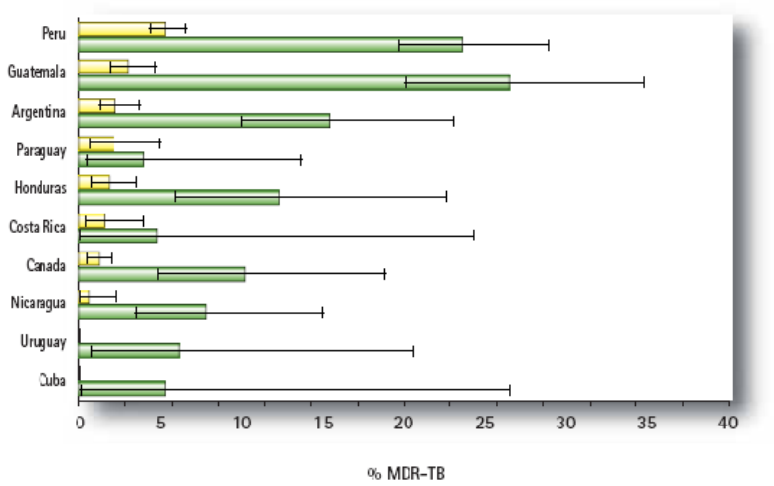
- In 2007, the estimated number of cases of multi-drug resistant TB was 511,000
- 3.1% of all new TB cases and 19% of retreatment cases were multi-drug resistant
  - Defined as resistance to isoniazid AND rifampin, with or without resistance to other antibiotics
- A marker of treatment program quality
- Poor prognosis, treatment complexity and expense





WHO, Anti-Tuberculosis Drug Resistance in the World, 2008

Figure 8: Prevalence of multidrug-resistant TB among new and previously treated cases in the WHO Region of the Americas, 2002–2007.



WHO, Anti-Tuberculosis Drug Resistance in the World, 2008

TB Control: DOTS

TABLE 2.2
Technical elements of the DOTS strategy

Case detection through quality-assured bacteriology Case detection among symptomatic patients self-reporting to health services, using sputum smear microscopy. Sputum culture is also used for diagnosis in some countries, but direct sputum smear microscopy should still be performed for all suspected cases.
Standardized treatment with supervision and patient support Standardized short course chemotherapy using regimens of 6–8 months for at least all confirmed smear-positive cases. Good case management includes directly observed treatment (DOT) during the intensive phase for all new smear-positive cases, during the continuation phase of regimens containing rifampicin and during the entirety of a re-treatment regimen. In countries that have consistently documented high rates of treatment success, DOT may be reserved for a subset of patients, as long as cohort analysis of treatment results is provided to document the outcome of all cases.
An effective drug supply and management system Establishment and maintenance of a system to supply all essential anti-TB drugs and to ensure no interruption in their availability.
Monitoring and evaluation system, and impact measurement Establishment and maintenance of a standardized recording and reporting system, allowing assessment of treatment results (see TABLE 2.7).

TABLE 2.1
Components of the Stop TB Strategy

1. Pursue high-quality DOTS expansion and enhancement
   a. Secure political commitment, with adequate and sustained financing
   b. Ensure early case detection, and diagnosis through quality-assured bacteriology
   c. Provide standardized treatment with supervision, and patient support
   d. Ensure effective drug supply and management
   e. Monitor and evaluate performance and impact
2. Address TB-HIV, MDR-TB, and the needs of poor and vulnerable populations
   a. Scale up collaborative TB/HIV activities
   b. Scale up prevention and management of multidrug-resistant TB (MDR-TB)
   c. Address the needs of TB contacts, and of poor and vulnerable populations, including women, children, prisoners, refugees, migrants and ethnic minorities
3. Contribute to health system strengthening based on primary health care
   a. Help improve health policies, human resource development, financing, supplies, service delivery and information
   b. Strengthen infection control in health services, other congregate settings and households
   c. Upgrade laboratory networks and implement the Practical Approach to Lung Health (PAL)
   d. Adapt successful approaches from other fields and sectors, and foster action on the social determinants of health
4. Engage all care providers
   a. Involve all public, voluntary, corporate and private providers through Public–Private Mix (PPM) approaches
   b. Promote use of the International Standards for TB Care (ISTC)
5. Empower people with TB, and communities through partnership
   a. Pursue advocacy, communication and social mobilization
   b. Foster community participation in TB care
   c. Promote use of the Patients' Charter for TB Care
6. Enable and promote research
   a. Conduct programme-based operational research, and introduce new tools into practice
   b. Advocate for and participate in research to develop new diagnostics, drugs and vaccines

TB Control

- Continued implementation and expansion of the basic DOTS strategy
  - Target 70% case detection, 85% treatment success
- Strengthen basic TB control programs

■ FIGURE 2.2
DOTS coverage by WHO region, 2007. The red portion of each bar shows DOTS coverage as a percent of the population. The numbers in each bar show the population (in millions) within (red portion) or outside (grey portion) DOTS areas.

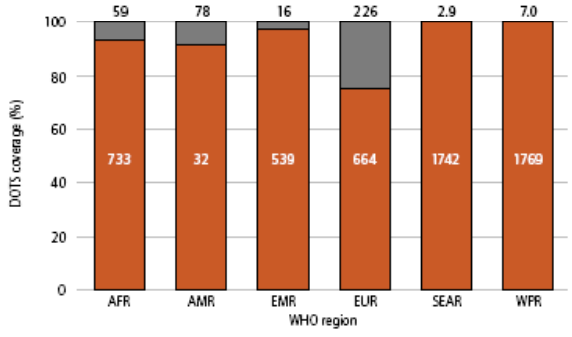


FIGURE 1.21
Smear-positive case detection rate under DOTS, by WHO region, 1995–2007. Heavy line shows global DOTS case detection rate.

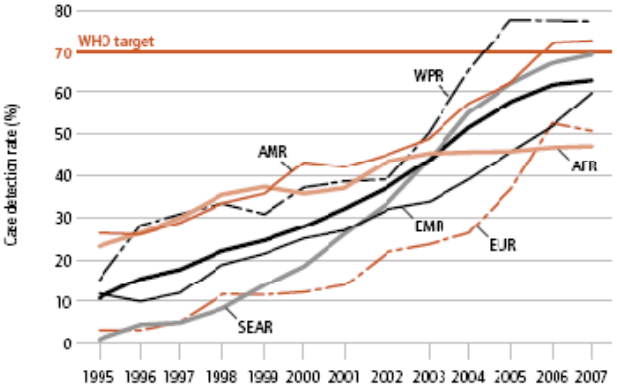


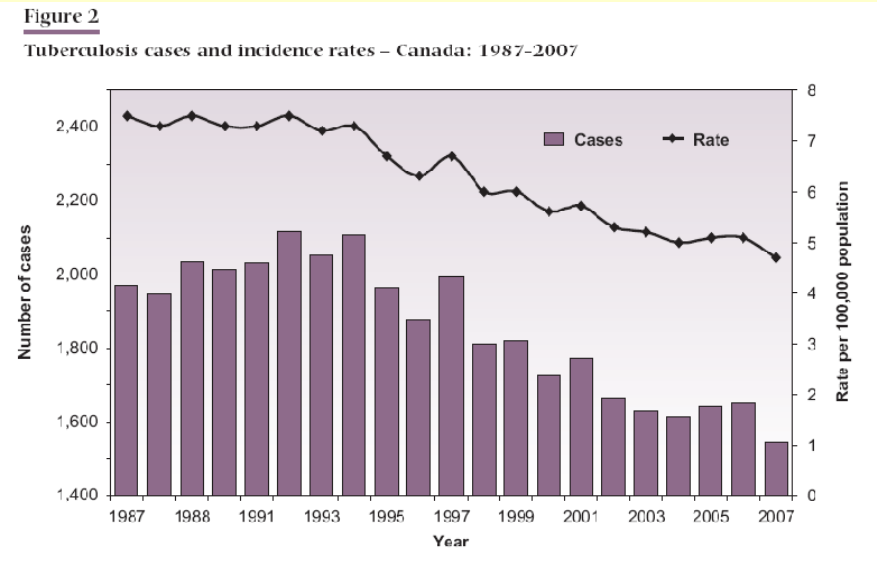
TABLE 1.7
Treatment outcomes for new smear-positive cases treated under DOTS, 2006 cohort

				TREATMENT OUTCOMES (%)[a]								
	NOTIFIED	REGISTERED[a]	REGST'D (%)	CURED	COMPLETED TREATMENT	DIED	FAILED	DEFAULTED	TRANS-FERRED	NOT EVAL'D	TREATMENT SUCCESS (%)	% EST[b] CASES SUCCESSFULLY TREATED UNDER DOTS
1 India	553 797	553 302	100	84	2.1	4.6	2.3	6.4	0.8	0.03	86†	55
2 China	468 291	470 436	100	92	1.7	1.5	0.8	0.6	2.9	0	94†	75
3 Indonesia	175 320	175 320	100	83	8.5	2.1	0.6	4.6	1.7	0	91†	67
4 Nigeria	39 903	39 903	100	65	11	5.8	1.9	10	2.2	3.6	76	16
5 South Africa	131 099	139 516	106	63	11	7.3	1.7	9.1	5.2	2.9	74	60
6 Bangladesh	101 967	101 761	100	91	0.8	3.2	0.5	2.0	1.5	0.6	92†	59
7 Ethiopia	36 674	36 674	100	69	15	4.8	0.5	4.5	5.1	1.0	84	23
8 Pakistan	65 253	65 589	101	75	13	2.8	0.6	6.2	2.4	0	88†	44
9 Philippines	85 740	85 797	100	80	7.9	2.3	1.0	3.9	2.4	2.0	88†	66
10 DR Congo	63 488	63 488	100	82	4.6	5.4	1.3	4.9	2.2	0	86†	51
11 Russian Federation	29 989	30 745	103	56	2.7	12	15	9.6	4.8	0	58	27
12 Viet Nam	56 437	56 470	100	90	2.3	2.6	1.0	1.6	2.1	0.7	92†	79
13 Kenya	39 154	39 154	100	73	12	4.5	0.3	7.3	2.7	0	85†	61
14 Brazil	32 463	34 818	107	33	39	4.2	0.1	8.3	3.3	12	72	50
15 UR Tanzania	24 724	24 724	100	80	4.5	7.9	0.2	3.2	4.0	0	85	42
16 Uganda	20 364	20 364	100	29	41	5.7	0.6	13	4.7	6.9	70	33
17 Zimbabwe	12 718	16 205	127	54	6.0	7.6	0.1	5.3	8.4	19	60	24
18 Thailand	29 081	28 856	99	71	6.3	8.2	1.8	5.8	2.9	4.0	77	57
19 Mozambique	18 275	18 275	100	82	1.1	10	0.9	4.5	1.9	0	83	40
20 Myanmar	40 241	40 350	100	77	7.3	5.5	3.2	5.0	1.9	0	84	94
21 Cambodia	19 294	19 349	100	90	3.1	3.0	0.3	1.6	1.6	0	93†	58
22 Afghanistan	12 468	12 468	100	80	4.9	2.1	1.1	2.1	5.6	4.6	84	53
High-burden countries	2 056 740	2 073 564	101	81	5.6	3.9	1.5	4.6	2.4	0.9	87†	56
AFR	555 361	562 884	101	65	10	6.2	1.2	7.7	4.1	5.3	75	36
AMR	114 680	116 925	102	55	20	4.4	0.9	6.3	3.2	10	75	55
EMR	131 820	132 001	100	75	11	2.8	1.0	6.1	2.7	1.2	86	45
EUR	100 102	94 266	94	61	9.3	8.4	8.9	7.2	3.2	2.3	70	35
SEAR	938 572	937 764	100	84	3.6	4.1	1.8	5.4	1.2	0.2	87†	59
WPR	662 273	663 261	100	89	3.1	2.1	0.9	1.4	2.8	1.1	92†	71
Global	2 502 808	2 507 101	100	78	6.3	4.2	1.6	5.0	2.5	2.2	85	52

Other Aspects of TB Control

- Improved diagnostics
- Better selection of drug treatment regimens
- Treatment of MDR-TB: Green Light Committee
- New drugs, vaccines

TB in Canada



Ellis et al, Public Health Agency of Canada

Ranked tuberculosis incidence in Canada – provinces/territories: 2007

Reporting province or territory	Abbreviation	Incidence rate per 100,000
Nunavut	Nvt.	99.2
Northwest Territories	N.W.T.	34.5
Saskatchewan	Sask.	10.6
Yukon	Y.T.	9.2
Manitoba	Man.	8.6
British Columbia	B.C.	6.4
Ontario	Ont.	5.1
Alberta	Alta.	3.2
Quebec	Que.	3.0
Newfoundland and Labrador	N.L.	1.4
Nova Scotia	N.S.	0.7
New Brunswick	N.B.	0.7
Prince Edward Island	P.E.I.	0.0
CANADA		**4.7**

Figure 6

Tuberculosis incidence rate by age group and sex – Canada: 2007

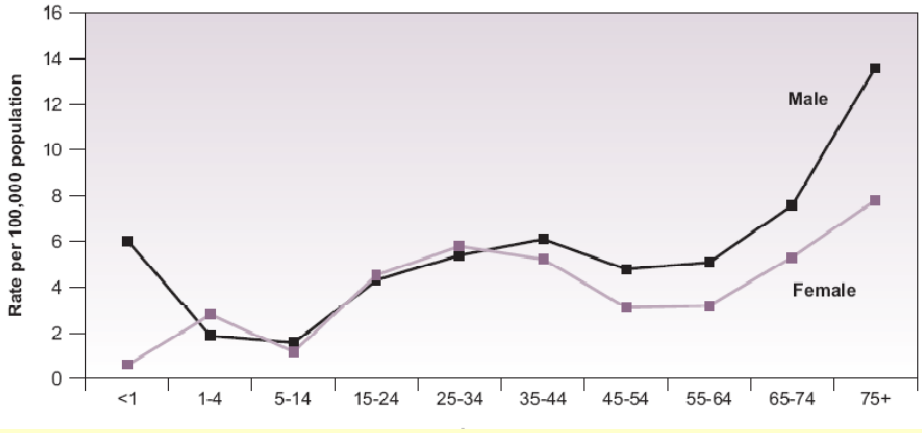


Figure 7

Percentage of tuberculosis cases by origin – Canada: 1987-2007

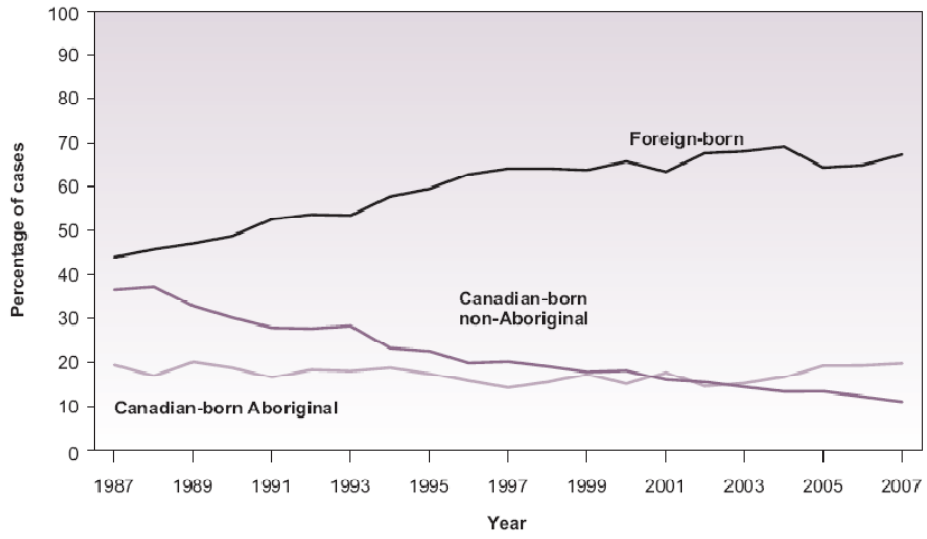


Figure 9

Tuberculosis incidence rate by origin – Canada: 1997-2007

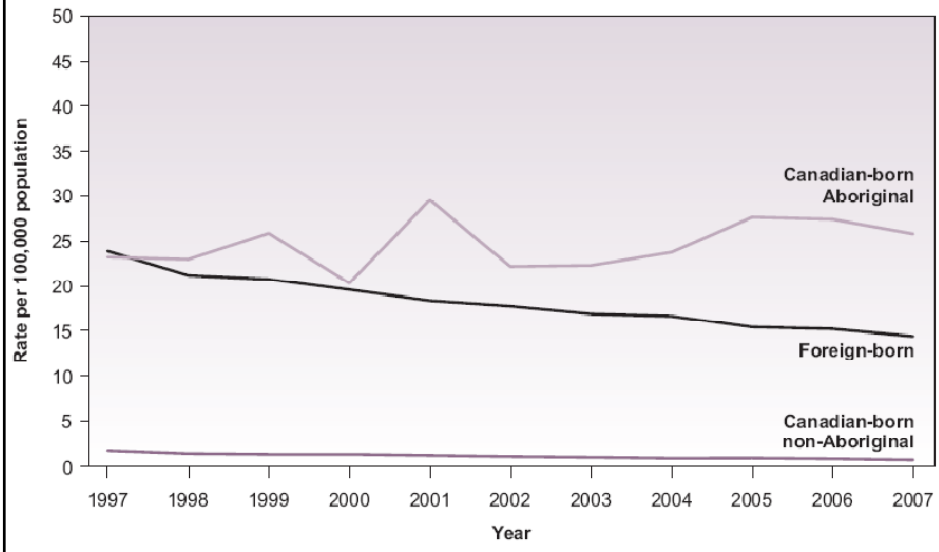


Table C

Comparison of the reported foreign-born tuberculosis incidence rate in Canada by STOP-TB Partnership/WHO TB epidemiological regions of birth (per 100,000 population) with WHO estimated tuberculosis incidence rate in the respective region

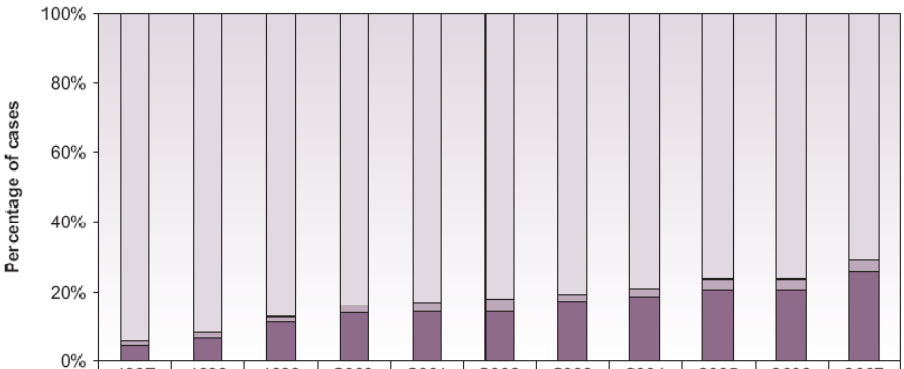
WHO regions*	Reported rate in Canada, 2007	WHO estimated TB incidence rate in regions, 2007**
Africa, High HIV Prevalence, (AFR High)	43.9	414
Africa, Low HIV Prevalence, (AFR Low)	29.7	217
American Region (AMR) - Latin American Countries (LAC)	9.4	56
Eastern Europe (EEUR)	7.2	91
Eastern Mediterranean (EMR)	15.7	104
Established Market Economies (EME) and Central Europe (CEUR)	2.3	12
South-East Asia (SEAR)	31.7	180
Western Pacific (WPR)	24.1	117
Overall	**14.4**	**139**

TB in the Foreign-Born

- Data consistently demonstrate parallel between incidence rates in countries of origin and incidence rates following arrival in destination country
- Incidence highest during the first years after arrival
  - Recently acquired infection
  - "Stressors" associated with migration?
- Disproportionately affects young adults

Figure 15

Percentage of tuberculosis cases by HIV status – Canada: 1997-2007



	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007
Unknown	94.4	91.7	87.1	84.2	83.4	82.2	80.8	79.2	76.5	76.3	71.1
Positive	1.6	1.5	1.4	2.1	2.5	4.0	2.3	2.4	3.4	3.5	3.6
Negative	4.0	6.8	11.5	13.6	14.1	13.8	16.9	18.4	20.2	20.2	25.3

Year

Drug Resistance in 2007

Of 1,188 Canadian cases with drug resistance data:

- 94 (8%) mono-resistance to first line drugs (82 INH), plus 6 INH/ethambutol
- 10 (0.8%) MDR-TB
- 1 (0.08%) XDR-TB

Montreal

- 123 reported active TB cases in 2007; maximum was 209 in 1994
- Corresponding decrease in incidence from 11.6 to 6.4 per 100,000
- Consistently ~80% of cases involve foreign-born persons

DSP Montréal-Centre, Bureau de surveillance épidémiologique

http://www.santepub-mtl.qc.ca/Mi/surveillance/mado/archives/90-2005/incidence90-2007.pdf

Elements of Canadian TB Control

- Successful completion of appropriate treatment for active TB
- Contact investigation, with suitable treatment of latent TB infection
- Screening of new immigrants and refugees for 1) active TB; 2) “high-risk” latent TB i.e. “inactive TB”
- Improved diagnosis and contact investigation among Aboriginals and other high-risk subgroups

Key Messages

- TB remains a global epidemic and public health emergency
- There are a number of reasons for this:
  - Basic TB control infrastructure
  - Limitations of current diagnostic tools and treatment
  - HIV
  - Drug resistance
  - General health and socioeconomic conditions
- Successful control will clearly require more than “basic DOTS”

Key Messages

- Relative to global incidence, TB in Canada is extremely rare
  - Incidence in Canada is clearly decreasing
  - TB is concentrated in several population subgroups including foreign-born, Aboriginals, those with “inner city risks”
  - We see the impact of global phenomena locally