TB Around the World and the new Canadian TB Standards 7th Ed.

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Objectives

- Epidemiology of TB around the world

- Highlights of the Canadian TB Standards

Available at: http://www.respiratoryguidelines.ca/tb-standards-2013
Challenging task...

*TB around the world*

In 2012:
~8.6 Mio developed Tb
~1.3 Mio died of Tb

3.6% of new and 20% of previously treated cases estimated to be MDR-TB
Challenging task...

*TB Standards 7th Edition*

16 Chapters
5 Appendices
467 pages in total

in 40 minutes... 5.1 seconds per page

Available at: http://www.respiratoryguidelines.ca/tb-standards-2013
Objectives

- Epidemiology of TB around the world, *in Canada, and Ontario*

- Highlights of the Canadian TB Standards

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Objectives

- Epidemiology of TB around the world, in Canada, and Ontario

- Highlights of the Canadian TB Standards relevant for infection prevention in the healthcare setting in Ontario
Canadian TB Standards 7th Edition

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Available at: http://www.respiratoryguidelines.ca/tb-standards-2013
TB around the world

Available at: http://wwwnc.cdc.gov/travel/content/yellowbook/2014/map_3-13.pdf
TB around the world

From: Public Health Agency of Canada, Tuberculosis in Canada: 2002-2012
TB around the world

Ontario: Lowest rates but 40% of Canadian cases

From: Public Health Agency of Canada, Tuberculosis in Canada: 2002-2012
TB around the world

From: Public Health Agency of Canada, Tuberculosis in Canada: 2002-2012
TB around the world

Highest rates in Canada/100,000 in 2012:

- Inuit: 262.2
- First nations: 23.7

- Africa, high HIV prevalence: 38.9
- South East Asia: 30.0
- Western Pacific: 22.7
- Africa, low HIV prevalence: 20.8

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Highest rates in Canada (per 100,000 in 2012):
- Inuit: 262.2
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- 38.9

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From: Canadian TB Standards 7th Edition
TB around the world

From: Canadian TB Standards 7th Edition
MDR-TB around the world

Available at: http://wwwnc.cdc.gov/travel/content/yellowbook/2014/map_3-14.pdf
MDR-TB around the world

Resistance rates in Canada 2012:

- INH resistance: 8%
- RMP resistance: 0.6%
- EMB resistance: 0.3%
- PZA resistance: 2.8%

→ Any resistance in 10% (90% mono-resistance)
→ MDR-TB 0.6% (Ontario: 1.8%)
→ XDR-TB 0.1%

Trends:

Available at: http://wwwnc.cdc.gov/travel/content/yellowbook/2014/map_3-14.pdf
TB in Canada 1924-2012

From: Public Health Agency of Canada, Tuberculosis in Canada: 2002-2012
TB in Canada 1924-2012

From: Public Health Agency of Canada, Tuberculosis in Canada: 2002-2012
TB in Canada 2012, by age group

From: Public Health Agency of Canada, Tuberculosis in Canada: 2002-2012
TB in Canada 2002-2012

- 75% pulmonary TB (5% primo-infection)
- 13% CNS TB
- 10% Lymph node TB

From: Public Health Agency of Canada, Tuberculosis in Canada: 2002-2012
Canadian TB Standards 7th Edition


- Collaboration lead by the Canadian Thoracic Society (with Canadian Lung Association, Public Health Agency of Canada, Association of Medical Microbiology and Infectious Diseases)

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Pathogenesis and transmission

- Reservoir: humans
- Fomites: insignificant (not airborne, die quickly)
- Inhalation of bacilli-containing droplets
- Cell-mediated immunity is key
  - Once established (18 months), primary infection due to re-exposure 5x less likely
Pathogenesis and transmission

- Transmission risk is associated with:
  - **Bacterial burden** (smear positivity, cavitary lesions, adult>>children)
  - **Location** (upper lung zones, laryngeal>pulmonary disease)
  - Amount and severity of cough
  - Duration of exposure
  - Proximity to source case
  - Crowding and room ventilation
  - Delays in diagnosis and effective treatment
Pathogenesis and transmission

Exposure to an Infectious Case of TB

Initial Infection

~5%

Primary Disease

~95%

Hypersensitivity Reactions

Latent TB Infection

~5%

Reactivation TB

~90%

No Disease

~90%

Pulmonary

Extra-pulmonary

New Infections

Available at: http://www.respiratoryguidelines.ca/tb-standards-2013
Typically 2-6 months post exposure. At risk: infants, young children, immunocompromised
>18-24 months post exposure
Majority of cases in Canada

Available at: http://www.respiratoryguidelines.ca/tb-standards-2013
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Diagnosis of active TB

- Indication for testing: signs and symptoms consistent with TB and at high risk of TB disease
  - >2-3 weeks of cough
  - Initially non-productive, later-on productive
  - Fever, night sweats, hemoptysis, anorexia, weight loss, chest pain...
  - Sensitivity and specificity insufficient
Diagnosis of active TB

- Indication for testing: signs and symptoms consistent with TB and at high risk of TB disease

- Microbiological testing:
  - Smear microscopy and culture+DST
    - 3 sputum samples, >1 hour apart (sensitivity similar to three morning sputum, approximately 70%)
    - Induced sputum with sensitivity of 75%
    - Bronchoscopy similar yield as sputum samples (sensitivity 77%)
    - Alternative: Gastric acid aspirate (sensitivity approx. 50%)
    - Culture: 2-8 weeks, >90% sensitivity with 3 samples (vs. 6 samples)
Diagnosis of active TB

- Indication for testing: signs and symptoms consistent with TB and at high risk of TB disease

- Microbiological testing:
  - Smear microscopy and culture+DST
  - NAAT for *M. tuberculosis* complex
    - Sensitivity >95% in smear positive and 50-70% in smear negative TB
    - Increases yield of smears by 25%
    - E.g. GeneXpert → detects MTB and RMP resistance within 2 hours
    - Test 1 smear positive sample, smear negative on request
    - Need confirmation by smear and culture+DST
Diagnosis of active TB

- Indication for testing: signs and symptoms consistent with TB and at high risk of TB disease
- Microbiological testing:
  - Smear microscopy and culture+DST
  - NAAT for *M. tuberculosis* complex
- Supported by: Chest x-ray
  - upper lobe, volume loss, cavitation
  - sensitivity 70-80%, specificity 60-70%
Diagnosis of active TB

- Indication for testing: signs and symptoms consistent with TB and at high risk of TB disease
- Microbiological testing:
  - Smear microscopy and culture+DST
  - NAAT for *M. tuberculosis* complex
- Supported by: Chest x-ray
- NOT recommended: TST and IGRA
  - Cannot discriminate between latent and active TB
  - Insufficient sensitivity, in particular with HIV co-infection
  - Recommended as an adjunct for diagnosis in children
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Drug resistant TB

- Risk factors in Canada:
  - previous TB treatment
  - born in a country where drug-resistant TB is prevalent
  - exposed to drug-resistant TB
- All cultures to undergo DST
  - INH, RMP, PZA, EMB
  - second-line DST for RMP-resistant strains
- Treatment of latent TB based on DST in source patient
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Paediatric TB

- Canadian-born Aboriginal and foreign-born children
- Source case identification if <5 y/o
- Gastric aspirates and induced sputum
- High risk of progression
- Low culture yield:
  - TB diagnosed on positive TST/IGRA, chest x-ray, history of contact, signs and symptoms
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Contact Follow-Up

- Goal is to minimize the risk of transmission. Priorities:
  1) Early identification and treatment of active TB cases
  2) Identify secondary cases (& source case), and those recently acquired latent TB (on average 4-6 close contacts, of these typically 1-2% have active TB and 5% will develop active TB <2 years)
  3) Offer treatment to source case and preventive treatment for latent TB in TST positive contacts
Contact Follow-Up

- How long back to consider someone infectious? Expert opinions:
  - Smear positive ~3 months before onset of respiratory symptoms/diagnosis
  - Asymptomatic cases with no cavities: 1 month
Contact Follow-Up

Interviews to identify contacts should include the following information:

- Any contact with children and their ages
- Any contact with immunosuppressed people (HIV positive, cancer patients, etc.)
- Description of the household/congregate setting; household contacts and their ages (includes anyone who regularly sleeps in the home)
- Close friends and relatives who are seen at least once per week – how often, for how long?
- Work or school location and description of setting (type of work, size of room, ventilation, etc.)
- Transportation to work/school – bus, car-pool, etc.
- Place of worship, clubs, sports teams, recreation programs or hobbies
- Any other places or groups the case has regularly been in or with while infectious
- Any contacts who are ill with potential TB symptoms or who have known TB
- Any major events (e.g. weddings, funerals, parties) the case attended while infectious
- Any recent travel or visitors staying at the home within the previous 2 years – if so obtain details

Available at: http://www.respiratoryguidelines.ca/tb-standards-2013
Contact Follow-Up

- For smear positive and negative cases
- Priority on contacts at high risk of being infected or at risk of developing active TB: (no longer classic concentric approach)
  - **High**: household contacts + immunologically vulnerable non-household contacts (e.g. children <5 y/o)
  - **Medium**: close non-household contacts with +/- daily exposure
  - **Low**: casual contacts
For smear positive and negative cases

- Priority on contacts at high risk of being infected or at risk of developing active TB:
  - **High**: household contacts + immunologically vulnerable non-household contacts (e.g. children <5 y/o)
  - **Medium**: close non-household contacts with +/− daily exposure
  - **Low**: casual contacts

Household contacts: sleeping regularly in the same household, including "couch-mates", boarders...

- Contacts with only few group members
- Classroom contacts: co-workers, close friends (no longer classic concentric approach)
For smear positive and negative cases:

- Priority on contacts at high risk of being infected or at risk of developing active TB:
  - (no longer classic concentric approach)
  - High: household contacts + immunologically vulnerable non-household contacts (e.g. children <5 y/o)
  - Medium: close non-household contacts with +/− daily exposure
  - Low: casual contacts

More shared airspace
(risk increases by approx. 1% per hour)

Household contacts:
- Sleeping regularly in the same household, including "couch-surfers".

Non-household contacts:
- Classroom contacts, co-workers, close friends

Casual contacts:
- Classmates with only few shared courses, school bus group members
Contact Follow-Up

- For smear positive and negative cases
- Priority on contacts of smear positive case being infected
  (no longer classic concentric approach)
  - **High**: household contacts + immunologically vulnerable non-household contacts (e.g. children <5 y/o)
  - **Medium**: close non-household contacts with +/- daily exposure
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Problem:
The amount of exposure constituting significant risk is unknown and there is no 0% risk exposure
Contact Follow-Up

- For smear positive and negative cases
- Priority on contacts at high risk of being infected or at risk of developing active TB:
  (no longer classic concentric approach)
  - **High**: household contacts, immunologically vulnerable non-household contacts (e.g. children <5 y/o)
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  - **Low**: casual contacts

Smear-negative, non-cavitary pulmonary TB

Smear-positive/cavitary/laryngeal TB
Contact Follow-Up

- Expand to next group if transmission considered:
  - TST converters
  - Rate of TST >10mm higher than expected for a certain group (e.g. unvaccinated HCW 5-18%)
  - <5 y/o infected without obvious source
# Contact Follow-Up

<table>
<thead>
<tr>
<th>TST result</th>
<th>Situation in which reaction is considered positive*</th>
</tr>
</thead>
</table>
| 0-4 mm     | In general this is considered negative, and no treatment is indicated.  
Child under 5 years of age and high risk of TB infection |
| ≥5 mm      | HIV infection  
Contact with infectious TB case within the past 2 years  
Presence of fibronodular disease on chest x-ray (healed TB, and not previously treated)  
Organ transplantation (related to immune suppressant therapy)  
TNF alpha inhibitors  
Other immunosuppressive drugs, e.g. corticosteroids (equivalent of ≥15 mg/day of prednisone for 1 month or more; risk of TB disease increases with higher dose and longer duration)  
End-stage renal disease |
| ≥10 mm     | All others, including the following specific situations:  
- TST conversion (within 2 years)  
- Diabetes, malnutrition (<90% ideal body weight), cigarette smoking, daily alcohol consumption (>3 drinks/day)  
- Silicosis  
- Hematologic malignancies (leukemia, lymphoma) and certain carcinomas (e.g. head and neck) |

Available at: http://www.respiratoryguidelines.ca/tb-standards-2013
## Canadian TB Standards 7th Edition

<table>
<thead>
<tr>
<th>Chapter</th>
<th>Title</th>
<th>Available?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chapter 1</td>
<td>Epidemiology of Tuberculosis in Canada</td>
<td>✓</td>
</tr>
<tr>
<td>Chapter 2</td>
<td>Pathogenesis and Transmission of Tuberculosis</td>
<td>✓</td>
</tr>
<tr>
<td>Chapter 3</td>
<td>Diagnosis of Active Tuberculosis and Drug Resistance</td>
<td></td>
</tr>
<tr>
<td>Chapter 4</td>
<td>Diagnosis of Latent Tuberculosis Infection</td>
<td>X</td>
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<tr>
<td>Chapter 5</td>
<td>Treatment of Tuberculosis Disease</td>
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</tr>
<tr>
<td>Chapter 6</td>
<td>Treatment of Latent Tuberculosis Infection</td>
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<tr>
<td>Chapter 7</td>
<td>Nonrespiratory Tuberculosis</td>
<td>X</td>
</tr>
<tr>
<td>Chapter 8</td>
<td>Drug-resistant Tuberculosis</td>
<td>✓</td>
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<tr>
<td>Chapter 9</td>
<td>Pediatric Tuberculosis</td>
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<td>Chapter 10</td>
<td>Tuberculosis and Human Immunodeficiency Virus</td>
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<td>Chapter 11</td>
<td>Nontuberculous Mycobacteria</td>
<td>X</td>
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<tr>
<td>Chapter 12</td>
<td>Contact Follow-up and Outbreak Management in Tuberculosis Control</td>
<td>✓</td>
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<tr>
<td>Chapter 13</td>
<td>Tuberculosis Surveillance and Screening in Selected High-risk Populations</td>
<td></td>
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<tr>
<td>Chapter 14</td>
<td>Tuberculosis Prevention and Care in First Nations, Inuit and Métis Peoples</td>
<td>X</td>
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<tr>
<td>Chapter 15</td>
<td>Prevention and Control of Tuberculosis Transmission in Health Care and Other Settings</td>
<td></td>
</tr>
<tr>
<td>Chapter 16</td>
<td>Bacille Calmette-Guérin (BCG) Vaccination in Canada</td>
<td>X</td>
</tr>
</tbody>
</table>

TB in the Health Care setting

- Latent TB rates in HCW increase with:
  - Number of years working in a health care setting where TB patients are cared for, ED or medical wards, and HIV infected patients
  - Number of annual TB cases in a specific setting
  - High-risk activities like cough-producing procedures, bronchoscopy, intubation, autopsy, microbiology lab procedures
  - Effective IPAC program can reduce risk of TB transmissions
Risk factors in Health Care setting

<table>
<thead>
<tr>
<th>Patient factors</th>
<th>Diagnostic/laboratory risk factors</th>
<th>Treatment factors</th>
<th>Environmental factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory (pulmonary or laryngeal) disease*</td>
<td>Cough-inducing procedures, e.g. sputum induction, bronchoscopy or administration of aerosolized therapies</td>
<td>Incorrect, ineffective or no therapy*</td>
<td>Inadequate ventilation to remove airborne infectious M. tuberculosis*</td>
</tr>
<tr>
<td>Number of patients with respiratory TB disease*</td>
<td>Delayed diagnosis*</td>
<td>Delayed treatment</td>
<td>Inadequate TB infection prevention and control measures for containment of M. tuberculosis</td>
</tr>
<tr>
<td>Respiratory secretions that are acid-fast bacteria (AFB) smear positive</td>
<td>Autopsy and preparation of pathology specimens</td>
<td></td>
<td>Duration of exposure and proximity to infectious patient*</td>
</tr>
<tr>
<td>Presence of cough</td>
<td>Improper handling of laboratory specimens containing M. tuberculosis</td>
<td></td>
<td>Overcrowding*</td>
</tr>
<tr>
<td>HIV infection*</td>
<td></td>
<td></td>
<td>Absence of sunlight</td>
</tr>
<tr>
<td>Atypical manifestations of disease</td>
<td></td>
<td></td>
<td>High humidity</td>
</tr>
</tbody>
</table>

Available at: http://www.respiratoryguidelines.ca/tb-standards-2013
The bad and the ugly...

- Delayed diagnosis in 50% of respiratory TB cases
- 24 HCW on average exposed per case

→ Early detection, airborne precautions, and treatment is key to prevent transmission
→ Note: <5 y/o consider source in family

Suggested case definition

RECOMMENDATIONS
(Conditional recommendations, based on strong evidence)

- A cough of 2-3 weeks’ duration with or without weight loss and fever in a person belonging to one of the at-risk groups below should prompt a thorough investigation to determine whether active respiratory TB is the cause:7,10
  - People with a history of active TB;
  - Staff and residents of homeless shelters;
  - The urban poor;
  - Staff and inmates of correctional facilities and previously incarcerated people
  - Injection drug users;
  - Aboriginal Canadians residing in communities with high TB rates;
  - People infected with HIV;
  - People born in Canada and other low TB incidence countries prior to 1966;
  - People born or previously residing in countries with a high TB incidence in Asia, Eastern Europe, Africa and Latin America;
  - People with high risk factors listed in Chapter 6, Table 1;
  - HCWs serving at-risk groups.

Available at: http://www.respiratoryguidelines.ca/tb-standards-2013
Steps for Isolation

Available at: http://www.respiratoryguidelines.ca/tb-standards-2013
Steps for Isolation

Available at: http://www.respiratoryguidelines.ca/tb-standards-2013
Discontinuation of AIIR

RECOMMENDATIONS
(Strong recommendations, based on moderate evidence)

Suspect TB cases
- Airborne precautions may be discontinued if three successive samples of sputum (spontaneous or induced) are negative on smear unless TB is still strongly suspected and no other diagnosis has been made.²⁴,³²,³³

RECOMMENDATIONS
(Strong recommendations, based on moderate evidence)

Confirmed TB cases
- Patients with **smear-negative, culture-positive drug-susceptible respiratory TB:**
  These patients should be kept under airborne precautions until there is clinical evidence of improvement and a minimum of 2 weeks of effective therapy has been completed. Patients may be discharged to home isolation for the period requiring airborne precautions providing there is clinical improvement, drug-resistant TB is not suspected and there is no contraindication for home isolation (see Figure 2).
- Patients with **smear-positive, culture-positive drug-susceptible respiratory TB:**
  These patients should be kept under airborne precautions until there is clinical evidence of improvement, evidence of adherence to at least 2 weeks of effective multidrug therapy based on the known antibiotic sensitivity of the patient's organism, and three consecutive negative AFB sputum smears.³⁴ Patients may be discharged to home isolation for the period requiring airborne precautions provided there is clinical improvement, drug-resistant TB is not suspected and there is no contraindication for home isolation (Figure 2).

Available at: http://www.respiratoryguidelines.ca/tb-standards-2013
No recommendation on whether or not NAAT should be considered in ruling out TB → 3 smears theoretically less sensitive than 1-2 negative smears PLUS negative NAAT

(Strong recommendations, based on moderate evidence)

Suspect TB cases

- Airborne precautions may be discontinued if three successive samples of sputum (spontaneous or induced) are negative on smear unless TB is still strongly suspected and no other diagnosis has been made.24,32,33

RECOMMENDATIONS
(Strong recommendations, based on moderate evidence)

Confirmed TB cases

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Available at: http://www.respiratoryguidelines.ca/tb-standards-2013
Conditions for home isolation

- Supervised therapy, if indicated, has been arranged;
- The person does not share a common airspace with non-household members (e.g., rooming house) and the household air is not being recirculated to other housing units (e.g., apartment complex);
- All household members have been previously exposed to the person. If any household members are TST negative, they should be informed and understand the potential risks;
- No children under the age of 5 or persons with immunocompromising conditions are present in the home (an exception would be if they are receiving prophylaxis or treatment for active TB disease or latent TB infection);
- No visitors should be allowed in the home except for HCWs;
- The person is counselled on and is willing and able to comply with limitations to their movement outside of the home (e.g., does not go to work, school or any other public indoor environment);
- The person should not be allowed to use any form of public transportation (if absolutely necessary, a taxi can be used to attend essential healthcare appointments provided the person is wearing a mask);
- The person should be allowed to ambulate outdoors since the risk of transmission is negligible provided they are not in very close contact with susceptible individuals for prolonged periods of time.

3Home isolation may be discontinued when the patient has clinical evidence of improvement, three consecutive negative sputum smears for acid-fast bacteria and there is evidence of adherence to at least 2 weeks of effective therapy. Multi-drug resistant TB cases and those with mono-resistance to RMP should have three consecutive negative sputum cultures after 6 weeks of incubation prior to discontinuing home isolation.

Available at: http://www.respiratoryguidelines.ca/tb-standards-2013
Conditions for home isolation

- Homeless shelters and drop-in centers:
  - Patients cannot be isolated
  - For primary prevention of TB shelters should improve ventilation (open windows), UVGI

Available at: http://www.respiratoryguidelines.ca/tb-standards-2013
Environmental Controls

- Airborne infection isolation rooms (AIIR):
  - Negative pressure, exhausted outdoors or through HEPA filter
  - Doors and windows closed at all times
  - Increase from 1 to 6 air changes per hour (ACH) improves clearance 5-6x, but little (from 7-12x) to minimal (>12x) additional benefit with higher rates
  → at least 6 for existing and 9 for new AIIRs
    (recommendations vary, CSA + CDC suggest 12)

Beggs et al. BMC Infect Dis 2012; 1-0:247
Environmental Controls

- When to re-enter the room without PPE?

<table>
<thead>
<tr>
<th>Air changes per hour</th>
<th>Minutes required for removal of airborne microorganisms</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>99% removal</td>
</tr>
<tr>
<td>2</td>
<td>138</td>
</tr>
<tr>
<td>4</td>
<td>69</td>
</tr>
<tr>
<td>6</td>
<td>46</td>
</tr>
<tr>
<td>12</td>
<td>23</td>
</tr>
<tr>
<td>15</td>
<td>18</td>
</tr>
<tr>
<td>20</td>
<td>14</td>
</tr>
<tr>
<td>50</td>
<td>6</td>
</tr>
</tbody>
</table>
Environmental Controls

- What if AIIRs are not available?
- Acceptable alternatives include:
  - Ultra-violet Germicidal Irradiation (UVGI), equivalent to 20 ACH
  - Portable High-efficiency Particulate Air (HEPA) Filtration units can replace higher ACH rates by cleaning circulating air
Personal Protection Controls

- N95 respirators
  - must be available for all staff for all contacts with suspected TB cases
  - Minimal effect in AIIR environment
  - fit-testing endorsed (jurisdictional requirement), but not supported by evidence

- Masks
  - For patients when leaving AIIR/transfer

Fennelly et al. ICHE 2009; 19: 754-9
Post-exposure follow-up

- TST negative HCW at baseline:
  - One single TST 8 weeks post exposure
- TST positive HCW at baseline:
  - TST of limited value; IGRA can be considered but is not recommended
  - Early assessment for signs/symptoms of active TB is key
Long-term care facility

- Same recommendation for N95 and masks, respectively, as in acute care setting
- TST not generally recommended >65y/o (neither baseline nor post exposure)
  - Low sensitivity
  - Harm may outweigh benefit for treatment of latent TB
- Screening to focus on active TB (posterior-anterior and lateral chest x-ray upon admission)
TB Prevention: specific situations

- **Intubation**: bacterial filter on endotracheal tube to prevent contamination of the ventilator

- **Surgery**:
  - Postponed when possible
  - Exhaust to the outside
  - Postoperative recovery in OR or AIIR

- **Ambulatory care**:
  - Postponed when possible
  - Schedule at the end of the day
  - Mask at arrival for patient until in AIIR or closed single room
Major Changes in 7th Edition

- Active TB: Three specimens on same day and incorporation of NAAT

- Contact f/u: Change from classic concentric circle model to prioritization based on infectiousness of source and susceptibility of exposed contacts
Take home messages

- Approximately 1800 TB cases/year in Canada
- High risk groups include immigrants and Aboriginal Canadians
- Control of TB in health care setting is based on a strong IPAC/TB control program, environmental control, and PPE

Main challenge remains unspecific signs and symptoms with delay in diagnoses...
Thank you!