Objectives

- List three recommended treatment options for latent tuberculosis infection (LTBI)
- Compare the advantages and disadvantages of the recommended LTBI treatment regimens
- Identify adverse side effects of LTBI treatment regimens and discuss monitoring and treatment of these side effects
Disclosures

- I will be presenting on investigational or off-label use of rifabutin for LTBI treatment.
- No financial disclosures

LTBI Treatment Options

- Isoniazid
- Isoniazid + Rifapentine (3HP)
- Rifampin
- Isoniazid + Rifampin
- Fluoroquinolones +/- ethambutol (MDR)
Isoniazid (INH)

- Duration of treatment:
  - Adults
  - Children
  - HIV-infected
  - TB-4 (abnormal CXR)

  ![9 mo.]

- *Non-HIV-infected adults: 6 mo acceptable*
Isoniazid

Why is 6 mo recommended by some programs?

- Efficacy of INH based on duration of treatment and compliance

<table>
<thead>
<tr>
<th>Duration of INH</th>
<th>Risk Reduction</th>
<th>Compliance</th>
<th>Risk Reduction if Compliant</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 mo</td>
<td>21%</td>
<td>87%</td>
<td>31%</td>
</tr>
<tr>
<td>6 mo</td>
<td>65%</td>
<td>78%</td>
<td>69%</td>
</tr>
<tr>
<td>12 mo</td>
<td>75%</td>
<td>68%</td>
<td>93%</td>
</tr>
</tbody>
</table>

N = 28,000, IUAT (fibrotic disease)  
Bull WHO 1982; 60:555

Isoniazid

Why is 6 mo recommended by some programs?

- Cost-effectiveness of INH for LTBI treatment

<table>
<thead>
<tr>
<th>Treatment Duration Months</th>
<th>3</th>
<th>6</th>
<th>12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Net costs, $</td>
<td>47,500</td>
<td>75,000</td>
<td>192,000</td>
</tr>
<tr>
<td>Cases prevented</td>
<td>3.28</td>
<td>10.54</td>
<td>11.99</td>
</tr>
<tr>
<td>Cost per case prevented</td>
<td>$14,488</td>
<td>$7,112</td>
<td>$16,024</td>
</tr>
</tbody>
</table>

Snider JAMA 1986; 255:1579
Isoniazid- Why 9 months?

- 9 months appears optimal
- 6 months less efficacious
- No significant gains if rx extended to 12 months

Isoniazid- Completion

ATS/CDC LTBI guidelines, 2000

- 9 months preferred for maximal benefit
- 6 months less effective, but may be more cost effective and result in greater adherence
  - Acceptable in non-HIV adults, program-based decision
- Completion based on total number of doses
- INH can be given either daily or twice weekly
  (Must be directly observed (DOPT) if intermittent)
Isoniazid- Adverse Reactions

- Clinical hepatitis
- Asymptomatic hepatic enzyme elevation
- Peripheral neuropathy
- Rash
- Mild neurologic symptoms
- Drug interaction – increases dilantin, carbamazepine and antabuse levels

INH-induced liver injury

- Incidence of hepatitis in persons taking INH is lower than previously thought (0.1 to 0.15%)
- Hepatitis risk increases with age
  - Uncommon in persons <20 years old
  - Nearly 2% in persons 50 to 64 years old
- Risk increased with underlying liver disease or heavy alcohol consumption
INH-induced liver injury

- Past data suggested much higher rates of hepatotoxicity, but that included asymptomatic rise in transaminases. Newer data, used signs and sx to trigger lab diagnosis (AST/ALT >5x nl)
- Good clinical monitoring, rather than routine lab testing can produce reasonably low rates of adverse events.

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>Cases/1000</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 20</td>
<td>0.0</td>
</tr>
<tr>
<td>20-34</td>
<td>3.0</td>
</tr>
<tr>
<td>35-49</td>
<td>12.0</td>
</tr>
<tr>
<td>50-64</td>
<td>23.0</td>
</tr>
<tr>
<td>&gt; 64</td>
<td>8.0</td>
</tr>
</tbody>
</table>

Nolan CL, JAMA 1999, Seattle Public Health TB clinic


Isoniazid- Adverse Reactions

- Asymptomatic elevation of hepatic enzymes are more common - seen in 10%-20% of people taking INH
- Levels usually return to normal even when treatment is continued (and after completion of treatment)
Peripheral neuropathy
- Occurs in <0.2 % using conventional INH doses
- Consider pyridoxine supplement (B6) 25 – 50 mg daily:
  - Diabetes, HIV, renal failure, alcoholism, malnutrition
  - Pregnant or breastfeeding mothers (and infant)
3HP (INH+RFP)

- INH + Rifapentine, once weekly x 12 weeks
- Recommended as an equal alternative to INH x 9 mo in healthy patients ≥12 yo and HIV-infected patients not on ART.
- Not recommended in the following:
  - Children <2yo
  - HIV-infected patients on ART*
  - Pregnant or planning to become pregnant
  - Contact to INH/RIF resistant cases
  - Prior adverse events / hypersensitivity to INH/RIF

Recommendations for Use of an Isoniazid–Rifapentine Regimen with Direct Observation to Treat Latent Mycobacterium tuberculosis Infection. MMWR 2011;60:1650–1653

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### Table: Three Months of Rifapentine and Isoniazid for Latent Tuberculosis Infection

<table>
<thead>
<tr>
<th></th>
<th>INH-RPT</th>
<th>INH</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>3,986</td>
<td>3,745</td>
</tr>
<tr>
<td>Administration</td>
<td>Directly-observed therapy</td>
<td>Self-administered therapy</td>
</tr>
<tr>
<td>Frequency</td>
<td>Weekly</td>
<td>Daily</td>
</tr>
<tr>
<td>Duration</td>
<td>12 weeks</td>
<td>9 months</td>
</tr>
</tbody>
</table>

Prevent TB Study Results

<table>
<thead>
<tr>
<th></th>
<th>INH-RPT</th>
<th>INH</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Effectiveness</strong></td>
<td>1.9 per</td>
<td>4.3 per</td>
<td>Non-inferior</td>
</tr>
<tr>
<td></td>
<td>1,000</td>
<td>1,000</td>
<td></td>
</tr>
<tr>
<td><strong>Completion rate</strong></td>
<td>82.1%</td>
<td>69.0%</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td><strong>Hepatotoxicity</strong></td>
<td>0.4%</td>
<td>2.7%</td>
<td>P&lt;0.001</td>
</tr>
</tbody>
</table>


3HP- Adverse Reactions

- Possible hypersensitivity (3.8%)
- Rash (0.8%)
- Hepatotoxicity (0.4%)
- Thrombocytopenia (rare)
- Other toxicities (3.2%)

- Monitoring- similar to INH or RIF
- RFP drug-drug interactions similar to RIF

Recommendations for Use of an Isoniazid–Rifapentine Regimen with Direct Observation to Treat Latent Mycobacterium tuberculosis Infection. MMWR 2011;60:1650–1653
Rifampin

Rifampin - Current recommendations

- Consider 4 month regimen of RIF (CDC/MMWR, 2000) in:
  - Patients with INH intolerance
  - Contacts to INH-resistant TB
- Included as 1 of 4 treatment options (WHO, 2015) for TB infection
- New Change: Rifampin daily for 4 months in children (previously 6 month AAP recommendation)
- Better completion rates, Lower rates of hepatotoxicity
- Cost effective
- Optimal duration is not known

- Targeted Tuberculin Testing and Treatment of Latent Tuberculosis Infection. MMWR 2000; 49 (No. RR-6)
- Guidelines on the management of latent tuberculosis infection, WHO, 2015
- American Academy of Pediatrics, Red Book 2015
### Efficacy of 3R in silicosis

- **RCT, n= 679**
- **Silicosis, PPD+**
  - PI- placebo
  - HR3- INH/RIF x 3 mo
  - H6- INH x 6 mo
  - R3- RIF x 3 mo
- Active pulmonary TB more frequent in placebo vs chemoprophylaxis groups (p<0.01)
- No significant difference between 3 chemoprophylaxis regimens


### Rifampin- Efficacy

- Meta-analysis of 62 studies. Compared to placebo, rifampin was shown to be effective
- **Multi-center Phase 3 RCT: 4R vs 9H**
  - Results expected in 2018
  - Study sites: Canada, Australia, Benin, Brazil, Ghana, Guinea, Indonesia, Korea, Saudi Arabia
  - Objectives:
    - Effectiveness- incidence of confirmed active TB within 28 months post-randomization
    - Efficacy- incidence of confirmed active TB in those who took at least 80% of doses within allowed time
    - Serious adverse events

Menzies, D. 4 Months of Rifampin for the Treatment of LTBI. As presented at National TB Controller’s Association Conference, Atlanta, GA, June 11, 2014
### Hepatotoxicity: Favors RIF > INH

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Rifampicin Events</th>
<th>INH Events</th>
<th>Total Events</th>
<th>Total Weight</th>
<th>Risk Ratio M.H. Fixed</th>
<th>95% CI</th>
<th>Risk Ratio M.H. Fixed</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chan 2012 (1)</td>
<td>0</td>
<td>190</td>
<td>0</td>
<td>190</td>
<td>0.03 [0.00, 0.52]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIKCS 1992 (2)</td>
<td>1</td>
<td>172</td>
<td>2</td>
<td>174</td>
<td>0.14 [0.02, 1.16]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mendis 2004</td>
<td>0</td>
<td>58</td>
<td>3</td>
<td>61</td>
<td>0.14 [0.01, 2.71]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mendis 2008</td>
<td>3</td>
<td>418</td>
<td>16</td>
<td>434</td>
<td>0.19 [0.06, 0.64]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>4</td>
<td>838</td>
<td>836</td>
<td>98.8%</td>
<td>0.12 [0.05, 0.30]</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 888

Heterogeneity: Chi^2 = 1.48, df = 3 (P = 0.69), I^2 = 0%

Test for overall effect: Z = 4.54 (P = 0.00001)

Favours Rifampicin


### Adherence: Favors RIF > INH

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Rifampicin Events</th>
<th>INH Events</th>
<th>Total Events</th>
<th>Total Weight</th>
<th>Risk Ratio M.H. Random</th>
<th>95% CI</th>
<th>Risk Ratio M.H. Random</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chan 2012 (1)</td>
<td>163</td>
<td>190</td>
<td>353</td>
<td>423</td>
<td>1.15 [0.99, 1.32]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIKCS 1992</td>
<td>142</td>
<td>165</td>
<td>307</td>
<td>352</td>
<td>1.17 [1.05, 1.33]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mendis 2004</td>
<td>52</td>
<td>59</td>
<td>111</td>
<td>122</td>
<td>1.20 [1.04, 1.44]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mendis 2008</td>
<td>328</td>
<td>420</td>
<td>748</td>
<td>868</td>
<td>1.31 [1.19, 1.44]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>833</td>
<td>835</td>
<td>98.6%</td>
<td>1.19 [1.16, 1.36]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 886

Heterogeneity: Tau^2 = 0.00, Chi^2 = 6.63, df = 3 (P = 0.08), I^2 = 55%

Test for overall effect: Z = 4.30 (P = 0.00001)

Favours INH

Rifampin- Adverse reactions

- Hepatotoxicity
  - Rare severe hepatitis, more common when combined with other medications
- Asymptomatic hyperbilirubinemia (0.6%)
- Dermatologic: Pruritis, rash (up to 6%)
- Hypersensitivity reaction (0.07-0.3%)
- GI: nausea, anorexia, abdominal pain
- Immune-mediated: thrombocytopenia, TTP, hemolytic anemia (<0.1%)
- Orange discoloration of body fluids

Lessons Learned: RIF + PZA

HIV/LTBI studies: Good news: 2 mo. RIF/PZA works

<table>
<thead>
<tr>
<th>Location, Year</th>
<th>Treatment</th>
<th>Rate of TB per 100 person/ys</th>
<th>Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haiti, 1994</td>
<td>6 mo INH</td>
<td>1.7</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>2 mo RIF/PZA</td>
<td>1.8</td>
<td>1.1</td>
</tr>
<tr>
<td>Zambia, 1999</td>
<td>6 mo placebo</td>
<td>8.1</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>6 mo INH</td>
<td>4.9</td>
<td>0.62</td>
</tr>
<tr>
<td></td>
<td>3 mo RIF/PZA</td>
<td>4.6</td>
<td>0.58</td>
</tr>
<tr>
<td>US, Haiti, Brazil, Mexico, 1999</td>
<td>12 mo INH</td>
<td>1.1</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>2 mo RIF/PZA</td>
<td>0.8</td>
<td>0.73</td>
</tr>
</tbody>
</table>
### Lessons Learned: RIF + PZA

**Non-HIV/LTBI studies:** **Bad news:** Severe hepatotoxicity/deaths

<table>
<thead>
<tr>
<th>Study, Site</th>
<th>N</th>
<th>% Liver Injury, Grade 1-2</th>
<th>% Liver Injury, Grade 3-4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bock, ATL</td>
<td>168</td>
<td>4.8</td>
<td>1.2</td>
</tr>
<tr>
<td>Jasmer, SF/Bos/ATL</td>
<td>207</td>
<td>18.3</td>
<td>7.8</td>
</tr>
<tr>
<td>Lobato, Jails</td>
<td>715</td>
<td>4.9</td>
<td>6.0</td>
</tr>
<tr>
<td>McNeil, NC</td>
<td>110</td>
<td>5.5</td>
<td>7.3</td>
</tr>
<tr>
<td>Stout, NC</td>
<td>114</td>
<td>12.2</td>
<td>7.9</td>
</tr>
<tr>
<td>Leung, Hong Kong</td>
<td>40</td>
<td>12.5</td>
<td>35</td>
</tr>
<tr>
<td>Lee, Chicago</td>
<td>157</td>
<td>ND</td>
<td>8.9</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>1511</td>
<td>7.7</td>
<td>7</td>
</tr>
</tbody>
</table>

### Summary: Treatment Regimens for Latent TB Infection

<table>
<thead>
<tr>
<th>Drug(s)</th>
<th>Duration</th>
<th>Interval</th>
<th>Minimum Doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoniazid</td>
<td>9 months</td>
<td>Daily</td>
<td>270</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Twice weekly</td>
<td>76</td>
</tr>
<tr>
<td></td>
<td>6 months</td>
<td>Daily</td>
<td>180</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Twice weekly</td>
<td>52</td>
</tr>
<tr>
<td>Isoniazid &amp; Rifapentine</td>
<td>3 months</td>
<td>Once weekly</td>
<td>12</td>
</tr>
<tr>
<td>Rifampin</td>
<td>4 months</td>
<td>Daily</td>
<td>120</td>
</tr>
</tbody>
</table>
TB Infection Treatment Completion, Seattle

<table>
<thead>
<tr>
<th></th>
<th>3HP</th>
<th>RIF x 4 mo</th>
<th>INH x 9 mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Started Treatment</td>
<td>87</td>
<td>82</td>
<td>222</td>
</tr>
<tr>
<td>Completed Treatment</td>
<td>74 (85.1%)</td>
<td>70 (85.4%)</td>
<td>115 (51.8%)</td>
</tr>
</tbody>
</table>

Cost effectiveness

- Analysis of 4R, 9H (SAT vs DOT), 3HP, and no treatment
- 4R was least expensive; also more effective than 9H
- 3HP more expensive than 4R, but more effective
- 3HP became cost savings in high risk patients (progression or non-adherence)
Monitoring

ATS/CDC LTBI guidelines, 2000
- Routine baseline / follow-up laboratory testing → Not needed
- Except for:
  - HIV infection
  - Pregnancy / Early postpartum (<3mo)
  - History of liver disease / hepatitis
  - Regular EtOH use
Also consider for: Statin/other hepatotoxic meds, age >50
Monitoring

Evaluate monthly for:

- Adherence
- Symptoms of hepatitis or other side effects
  - Anorexia, nausea, vomiting, or abdominal pain in right upper quadrant
  - Fatigue or weakness
  - Dark urine
  - Rash
  - Persistent numbness in hands or feet

Management of side effects:

Drug-induced liver injury

- Review hepatotoxic meds (tylenol, statins, etc), ETOH use, prior hepatitis risk/screen
- HOLD Treatment if:
  - AST/ALT > 3 times the upper limit of normal + symptoms of hepatotoxicity
  - AST/ALT > 5 times the upper limit of normal + asymptomatic
- If less than parameters above, continue treatment with plan to repeat labs in 1-4 weeks.
- Depending on above, consider alternate therapy with close LFT monitoring.
Management of Side Effects: Derm

- Fixed drug eruption
- Rash, itching (1-5%, RIF)
- Pemphigoid reaction
- DRESS / DIHS
- Anaphylaxis, urticaria

- Mild: anti-histamine, topical steroids, f/u visit
- Mild-moderate: hold meds and above, consider re-challenge once resolves
- Mod-severe: hold meds and above, emergency care / derm consult as needed. Consider alternate therapy once resolves

Rifamycin: Drug-Drug Interactions

Requires re-dosing or alternate:

- Coumadin
- Opioids (e.g. Methadone)
- Antiretrovirals
- OCPs
- Proton-pump Inhibitor
- Chemotherapy
  - Cyclosporine
  - Tacrolimus
  - Tamoxifen

Monitor and titrate:

- Endo:
  - Levothyroxine
  - Corticosteroids
  - sulfonylureas
- CNS
  - Benzodiazepines
  - Phenytoin, lamotrigine
  - SSRI
- Cardiac
  - Statins
  - Anti-HTN: b-blocker, ACE-I, ARB, Ca-channel blockers
Rifamycin: Drug-drug Interaction

- Rifabutin is a less potent inducer of CYP3A4 than rifampin. Thus, can be considered in certain cases with close monitoring (methadone, anti-coagulation, anti-retrovirals)

Resources:
- Lexicomp / Micromedex Drug Interaction Look-up

Special situations

- Missed doses
- Pregnancy and Lactation
- LTBI re-treatment
- Window prophylaxis
- Drug-resistant contacts
Help!
I have a 45 yr. old physician with LTBI on INH who consistently arrives one week late for monthly refills. She has missed seven weeks in the past eight months.

When can I call her treatment completed?

<table>
<thead>
<tr>
<th>Regimen</th>
<th># doses</th>
<th>Timeframe to complete within</th>
</tr>
</thead>
<tbody>
<tr>
<td>INH daily x 9 months</td>
<td>270</td>
<td>12 months</td>
</tr>
<tr>
<td>INH BIW x 9 months</td>
<td>76</td>
<td>12 months</td>
</tr>
<tr>
<td>INH daily x 6 months</td>
<td>180</td>
<td>9 months</td>
</tr>
<tr>
<td>INH BIW x 6 months</td>
<td>52</td>
<td>9 months</td>
</tr>
<tr>
<td>RIF/RFB daily x 4 months</td>
<td>120</td>
<td>6 months</td>
</tr>
<tr>
<td>INH+RFP</td>
<td>12</td>
<td>16 weeks</td>
</tr>
</tbody>
</table>

CDC. Targeted tuberculin testing and treatment of latent TB infection. MMWR 2000.
Treatment completion / Missed Doses

- Extend or re-start treatment if interruptions were frequent or prolonged enough to preclude completion

- When treatment has been interrupted for more than 2 months, patient should be examined to rule out TB disease

- Recommend and arrange for DOT as needed

CDC. Targeted tuberculin testing and treatment of latent TB infection. MMWR 2000.

Treatment changes / Partial Credit

- No guidelines or data. Recommend consultation with TB expert.
- Options: start over vs partial credit for time taken

- SFDPH example:
  - Pt completes 4.5 months of INH (50% of planned regimen). Needs 50% left of RIF regimen (i.e. 2 mo if using 4 mo RIF regimen)
Pregnancy

- Treatment for LTBI controversial
  - Pregnancy does not increase risk for reactivation
  - Risk for increased hepatotoxicity during pregnancy and early post-partum
  - Proceed to LTBI tx if HIV infected, close contact, or converter. Otherwise, consider waiting until 3 mo post-partum.
- INH = preferred treatment
  - Crosses placental barrier, but no teratogenicity
  - Supplement with Vitamin B6
- RIF likely safe
  - lacks efficacy data, possibly higher rate of fetal abnormalities

CDC. Targeted tuberculin testing and treatment of latent TB infection. MMWR 2000.

Lactation

- Breastfeeding not contraindication:
  - Infant will get small amount of INH (sub-therapeutic)
  - In one study, no more than 20% of usual therapeutic levels of INH; <11% of other anti-TB meds
  - No toxic effects reported
- Give both mother and breastfeeding infant Vit B6
- Levels of INH in breast milk not adequate for treatment of infant

CDC. Targeted tuberculin testing and treatment of latent TB infection. MMWR 2000.
Contacts

Once active disease is ruled out:
- Contacts with PPD >5 mm (or IGRA positive) should be treated for LTBI regardless of age

Contacts: “Window-prophylaxis”

Definition: LTBI tx of high-risk contacts with initial negative TB testing and active disease ruled out

Purpose: Prevent progression to active TB in high-risk contacts that may have initial negative testing (early TB infection)
- Recommended in the following:
  - Children <5 y.o.
  - HIV/immunosuppressed contacts should be fully treated, even if repeat testing remains negative

Follow-up: Repeat TB testing 8-10 weeks after exposure ended or contact no longer contagious
Contacts: Re-treatment for LTBI

- What is the probability of acquiring new infection?
- Recommended in:
  - Those at risk for rapid progression: HIV infected or other immune-compromise, prior to severe immune suppression (e.g. transplant, anti-TNF), < 5 years old
  - Contact to MDR or drug-resistant case
- Consider transmission and infectiousness:
  - E.g. in <21 years old who have been in contact with a smear-positive case

MDR contacts

- No consensus – 1994 Delphi review with 31 experts
- Select drugs based on source case drug susceptibility test results
- ATS/CDC 2000 guidelines suggest:
  - Fluoroquinolone (levo, moxi) + ethambutol
  - Ethambutol + pyrazinamide
  - Pyrazinamide + fluoroquinolone*
- Micronesia study**: 104 patients started 12-month FQ based MDR LTBI treatment (+/- EMB)
  - None developed MDR TB over 36 month f/u
  - 3/15 that refused Rx + 15 unidentified contacts developed MDR disease

MDR contacts

- Immunocompetent:
  - Can be observed (closely) without treatment
  - Or treated for at least 6-12 months
- Immunocompromised:
  - Treat for 12 months
- If suspect MDR infection:
  - Follow for 2 years, irrespective of treatment

Resources:

- CDC/MMWR, Targeted Tuberculin Testing and Treatment of Latent Tuberculosis Infection, 2009
- Guidelines on the management of latent tuberculosis infection, WHO, 2015
- CDC. Updated guidelines for using interferon gamma release assays to detect Mycobacterium tuberculosis infection – United States - 2010. MMWR 2010;59(RR05).
- Treating LTBI in Special Situations.
  [link](http://sntc.medicine.ufl.edu/TrainingOnline.aspx#.VB9z7CtdVro)
Latest and Greatest (?)

- Phase III Non-inferiority study of Rifampin vs INH (Menzies, et al)
- 3HP DOT vs SAT
  - SAT non-inferior to DOT (in US)
  - Ann Intern Med, Nov 2017 (TBTC iAdhere Study Team)
  - MMWR this week on DOT vs SAT
- Studies of short course therapies:
  - INH + Rifapentine, daily x 1 month in HIV (ACTG, presented at CROI 2018)
  - Rifapentine daily x 6 weeks

THANK YOU!

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Direct: 415-206-3387
# Outcome of TB Infection Treatment

**San Francisco, 2012-13**

Cohort: All TB clinic patients starting LTBI treatment from 9/1/12 to present with known treatment end reason.

<table>
<thead>
<tr>
<th></th>
<th>3HP*</th>
<th>INH</th>
<th>INH + RIF</th>
<th>RIF</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Started Treatment</strong></td>
<td>71</td>
<td>295</td>
<td>50</td>
<td>180</td>
</tr>
<tr>
<td><strong>Completed</strong></td>
<td>60 (85%)</td>
<td>213 (72%)</td>
<td>44 (88%)</td>
<td>154 (86%)</td>
</tr>
<tr>
<td><strong>Adverse Reaction</strong></td>
<td>3 (4%)</td>
<td>2 (1%)</td>
<td>0</td>
<td>2 (1%)</td>
</tr>
<tr>
<td><strong>Chose to Stop/Lost/Refused</strong></td>
<td>8 (11%)</td>
<td>64 (22%)</td>
<td>5 (10%)</td>
<td>19 (11%)</td>
</tr>
<tr>
<td><strong>Moved</strong></td>
<td>0</td>
<td>6 (2%)</td>
<td>0</td>
<td>2 (1%)</td>
</tr>
<tr>
<td><strong>Provider Decision</strong></td>
<td>0</td>
<td>2 (1%)</td>
<td>0</td>
<td>1 (1%)</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td>0</td>
<td>8 (3%)</td>
<td>1 (2%)</td>
<td>2 (1%)</td>
</tr>
</tbody>
</table>

*Includes both TB Clinic and Study 33 patients