Drug-Resistant TB Update
Can we do better?
(p.s. thank goodness for Barbara :)

Lisa Chen MD
Professor of Medicine, UCSF
4 Corners/Moab, December 5, 2017
Overview

...trials and tribulations of being an optimist....

• New US CDC/ATS/IDSA/ERS DR-TB Guidelines
• Can we shorten treatment duration?
  – 9-12 mo “Bangladesh” MDR shorter treatment regimen
  – “Union” 9-country observational study
  – Preliminary results of STREAM trial (& NIX?)
• Are we using the best drugs?
  – Reflecting on use of second-line injectable agents
• Something practical – new tools to try
one person’s story
(we all have many)

30 yo F from Vietnam – recent arriver, ESL student

• May 2016: Resistant to INH, RIF, Strep, EMB
  – Initial Tx: MFX-LZD-AM-PZA-ETO-PAS (multiple changes)
  – Culture converted mo2, +/- good CXR response
  – Depression since dx, severe N/V, socially isolated, injection site pain (declined PICC), rash, peripheral neuropathy, early optic neuritis (LZD just stopped)

• Only 14mo post-culture conversion (total 16mo to date), need to change rx again…continue push…..
......so can we go shorter?
MDR-TB Treatment Duration

WHO 2011 DR-TB Guidelines (& 2016)

Based on individual patient data meta-analysis:

Recommendations:

• Intensive phase: at least 8 months
• Total duration: at least 20 months (if no prior rx for MDR; if prior MDR rx at least 24 months)

Standardized WHO regimen: 5 drugs (including PZA)

• Example: FQ-IA-ETO-CS-PZA
• [Access to resistance testing often limited/variable]
MDR-TB Treatment Duration: U.S.

• 2003 ATS/CDC/IDSA guidelines: 18-24 mo (new DR-TB guidelines pending)

2016 CITC Survival Guide v3 – Expert consensus:
Utilize culture conversion to help guide minimum duration within U.S. high-resource setting

• Intensive phase: at least 6 mo beyond culture conversion for use of injectable agent
• Total duration: at least 18 months beyond culture conversion

[U.S. highly individualized regimen – using 4-6 (optimally 5) likely effective drugs]
Short standardized regimens for MDR

Prospective observational study: 6 sequential regimens resulted in identifying highly effective 9mo regimen

N=206
Completion 5.3%
Cure 82.5%
Success 87.8%
Default 5.8%
Failure 0.5%
Death 5.3%
Relapse 0.5%

1+2: Oflo-based, Pth plus INH throughout
3: Oflo-based, Pth throughout, no INH
4: Oflo-based, Pth intensive phase, INH throughout
5: Oflo-based, Pth intensive phase, INH and Clo throughout
6: Gati-based, Pth and INH intensive phase, Clo throughout

Treatment Outcomes in Patients with MDR-TB, 2007-2012 Cohorts

WHO, Global Tuberculosis Report 2015
Shorter course “Bangladesh” regimen

*KJM Aung et al. Int J Tuberc Lung Dis 2014;18(10)*

Nine (to 12) month MDR regimen: n=515

- 4 mo: GFX\textsuperscript{HD}-CFZ-EMB-PZA + KM-PTO-INH\textsuperscript{HD}
- 5 mo: GFX\textsuperscript{HD}-CFZ-EMB-PZA
  (Extended intensive phase if delayed smear conversion)

- 2005-2011: **Treatment success 84.4%**
  - Strongest risk for unfavorable outcome was FQ resistance
    (particularly if also initial PZA resistance)

- Endorsed for use in **WHO 2016 guidelines**
- Encouraged further studies:
  - 9-country observational study (Union)
  - STREAM trial/RCT
2016 WHO Policy Recommendation
MDR-TB Shorter Treatment Regimen (STR)

Recommendation:
In patients with RR or MDR-TB
• who have not been treated with second-line drugs (> 1mo) and
• in whom resistance to FQs and SLI agents has been excluded or is considered to be highly unlikely

a shorter MDR-TB regimen of 9-12 mos may be used instead of a conventional regimen*

(conditional recommendation, very low certainty in the evidence)

*Additional: Not to be used if resistant/intolerant to medicines in the regimen (except INH), pregnant, or extrapulmonary
# Treatment Success*

Shorter vs. Conventional Regimens

IPD data (6 studies) evaluated for WHO 2016 guidelines

<table>
<thead>
<tr>
<th>Resistance pattern</th>
<th>Shorter MDR-TB Regimen (N=1116)</th>
<th>Conventional MDR-TB Regimen (N = 5850)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All cases</td>
<td>90.3%</td>
<td>78.3%</td>
</tr>
<tr>
<td>PZA susceptible; FQN susceptible</td>
<td>96.8%</td>
<td>83.5%</td>
</tr>
<tr>
<td>PZA resistant; FQN susceptible</td>
<td>88.8%</td>
<td>81.4%</td>
</tr>
<tr>
<td>PZA susceptible; FQN resistant</td>
<td>80.0%</td>
<td>64.4%</td>
</tr>
<tr>
<td>PZA resistant; FQN resistant</td>
<td>67.9%</td>
<td>59.1%</td>
</tr>
</tbody>
</table>

*Treatment success – cure or completed

WHO 2016 Update

Decreasing success
Treatment outcomes with a short multidrug-resistant TB regimen in nine African countries

Trebuchet al. IJTID ePub: Nov 17, 2017

- Union sponsored study - West/Central Africa: Benin, Burkina Faso, Burundi, Cameroon, Central African Republic, Cote d’Ivoire, Democratic Republic of the Congo, Niger, and Rwanda
- Prospective observational study design
- 9mo “Bangladesh” regimen: 7-drug intensive (4mo) + 4-drug continuation (5mo)
  - MODIFIED: Substituted GFX\textsuperscript{HD} with \textit{standard dose} MFX
- 1006 adult MDR patients (20% HIV+)
- Inclusion: Rif-resistant (Xpert/LPA or in-country phenotypic DST)
- Exclusion: Prior second-line rx, known pre-/XDR, pregnant, known drug intolerance, baseline QT>500ms
Treatment outcomes with a short multidrug-resistant TB regimen in nine African countries (2) Trebuchet et al. IJTID ePub Nov 17, 2017

Results*:

- 72% Cure + 9% Treatment complete = 82% Tx Success
- 6% Failure
- 8% Death
- 5% LTFU
- (relapse data pending – future publication)

• HIV > death overall; among survivors – no difference tx success
• Supra-national DST/sequencing analysis (58% cases)
  - FQ resistance associated with failure
  - No bacteriologic influence by PZA, PTO, EMB resistance**
• Notable adverse effect: 11% hearing loss (4 mo injectable)

*[Note: 56% low BMI, 65% extensive CXR (>1/2 lung fields)]
**Multivariate analysis of individual effect (remove influence of FQ-resistance)
STREAM Trial stage 1: Design (1)

• Multi-country, randomized-controlled trial, non-inferiority design (began July 2012)

• Evaluate safety and efficacy of “modified” Bangladesh 9mo regimen ($MFX^{HD}$ replaced $GFX^{HD}$)
  – ↑ safety/monitoring evaluation for higher dosing MFX

• Study: 7-drug (7d/wk) intensive + 4-drug continuation
  – $9mo(MFX^{HD*}-CFZ-EMB-PZA) + initial 4mo(INH^{HD*}-PTO-KM)$
    (extended intensive 1-2mo if delayed smear conversion)

• Control: 5-drug (20-24mo)
  – Locally-used WHO 2011 standardized regimen
    (ex. FQ-IA-CS-ETO-PZA)

*High Dose weight-based (may not be consistent with common US practice)
STREAM Trial stage 1: Design

- Inclusion: adult, Sm+ Mtb, RIF-resistant (Xpert/LPA or phenotypic DST)
  - 2nd line LPA done for all +RIF resistant
  - On ART if found HIV+
- Exclusion: pre-/XDR, pregnant/breastfeeding, QTc >500, AST or ALT >5xULN, extrapulmonary, critical condition (clinician opinion unsafe)

Nunn et al. Trials 2014, 15:353
STREAM Trial stage 1: Design (3)

• Enrollment 2:1 study vs. control arm
  – Higher study arm for more safety & efficacy data

• Power calculation:
  – Assumed under research conditions that control will do better (70% success rather than 65% assumed efficacy); study arm might not perform as well outside of Bangladesh (75% compared with published 85%); non-inferiority margin 10%
STREAM Trial stage 1: **Preliminary Results** (1)

**Preliminary** results shared at IUATLD/Guadalajara, October 2017 (final early 2018)

- Sites: Ethiopia, Mongolia, South Africa, Vietnam
- \( N = 424 \) MDR-TB patients (33% HIV+)
- Primary efficacy outcome:
  - Favorable outcome at 132 wks
  - Unfavorable outcome: +culture at 132 wks, restarting treatment, death (any cause), LTFU before 15 mo

Lancet online: 48th Union World Conference on Lung Disease; October 23, 2017
[http://dx.doi.org/10.1016/S221302699(17)30423-X](http://dx.doi.org/10.1016/S221302699(17)30423-X); & conference notes
STREAM Trial stage 1: *Preliminary Results* (2)

Favorable outcome:
- 78.1% in 9 mo regimen
- 80.6% in 20-24 mo standard regimen

9 mo regimen did not have statistically significant non-inferiority

Deaths: More deaths (all cause) in study arm, but not statistically significant
- 8.5% in 9 mo regimen
- 6.4% in 20-24 mo standard regimen

Lancet online: 48th Union World Conference on Lung Disease; October 23, 2017
http://dx.doi.org/10.1016/S2213-0269(17)30423-X; & conference notes
STREAM trial stage 1: Discussion (1)

Study leads (www.tbonline.info/posts/2017/10/13):

• 9 mo regimen did as well or even better than expected
• BUT … “20 mo regimen did much better than routinely reported outcomes from program settings…..more patients completed than we know is often the case in most real-life settings”
STREAM trial stage 1: Other results

*Preliminary:*

- **Adverse events:** incidence of grade 3-5 adverse events similar between two regimens
  - 46% in 9mo regimen
  - 45% in 20-14mo regimen
- **Health economic analysis:** reduction in direct costs to patients (fewer visits, reduced supplementary food costs, quicker return to work)
- **Reduced pill burden** by 1/3 in 9mo regimen
STREAM trial stage 1: Discussion (2)

Overall, in terms of global MDR context: Conference discussion - still a successful regimen

- Patient/advocate point of view: Only 9mo of therapy highly desirable, results great compared to real program performance......in regards to 2% difference in favorable results.... “when I brought home a test score of 78%, my family would still slaughter a goat”

- Await final report in 2018........
What are implications for US practice? (1)

Success rates using US standard of care (using highly individualized regimen strategies) are higher: (Marks et al, Emerging Infectious Diseases May 2014)

- Program performance CA/NYC/TX (2005-2007); n=130
  - Treatment completion 78%
  - Death 9%
  - LTFU 2%
  - Failure/relapse 0% (but 1% stopped due to AE)
  - Transfer out 9%
- Case-management/DOT approx. 90%
- Expert consultation 81%
- **Median duration:** Resistance pattern - INH/RIF 20mo, INH/RIF +more 24mo, Pre-XDR 25mo, XDR 32mo
What are implications for US practice? (1)

Access to extensive (rapid) genotypic & phenotypic DST
- Includes molecular tests for EMB & PZA (known issues with growth-based DST reliability/confidence)

⇒ Using strict WHO recommendations, low numbers would qualify for short MDR regimen
  - CA data 2009-2015: n=171 (with full DST and including \( inhA \) mutation inferring ETO-R) only 14% eligible for STR (Barry et al, AJRCCM Dec 2017)
  - European data suggest only 8% eligible for STR (Lange et al, AJRCCM Oct 2016)
Population model: Projected Incidence of MDR-TB with Different Regimens

Population-level implications of scale-up:
Assumptions: Short-course regimen would double treatment access and achieve long-term efficacy seen in cohort studies

Population model: Projected Incidence of MDR-TB with Different Regimens

BUT – if assumptions: 30% of MDR-TB case ineligible

Many questions in need of answers...

• Why does this combination work (despite documented resistance to some drugs)?
  – Synergy? Mixed populations?

• Would it work better if we could substitute based on *known sensitivity with better drugs*?

• [List could go on…….]


STREAM Trial stage 2

Comparisons (expected completion 2019?)
Regimen A: Locally-used WHO 2011 regimen
Regimen B: Modified Bangladesh (9mo)
Regimen C: 7-drug all oral regimen (9mo)
   9mo: BDQ-CFZ-EMB-LFX-PZA (+ 4mo intensive phase adds INH$^{HD}$-PTO)
Regimen D: Shorter 6-drug (6mo)
   6mo: BDQ-CFZ-LFX-PZA (+ 2mo intensive phase adds INH$^{HD}$-KM)
Nix-TB Trial: Pretomanid-BDQ-LZD for XDR

Participants are required to have documented XDR-TB, or MDR TB treatment intolerance or failure (TI or Fr)

Pretomanid 200 mg
Bedaquiline 200 mg tiw after 2 week load
Linezolid 1200 mg qd*

6 months of treatment
Additional 3 months if sputum culture positive at 4 months
Follow up for relapse-free cure over 24 months

*Amended from 600 mg bid strategy

(Preliminary data announced Oct 2017, IUATLD)

From TB Alliance: Conradie et al, CROI presentation/Seattle Feb 2017
Time to reconsider favored status of injectables?

(Reuter et al, IJTLD Nov 2017)

• Review of efficacy, safety and tolerability of IA
  – One small RCT (1940’s) of streptomycin monotherapy
  – Observational cohort data support IA use – but variable
  – Large >9000 pt. IPD (Ahuju 2012) – no association between use of any IA and probability of treatment success
  – Significant evidence for disability due to hearing loss (lack of audiometry, underappreciated, progression post-rx)

• Growing confidence/data on efficacy and AE management for new (BDQ, DLM) and repurposed (LZD, CFZ) drugs
  – Stronger RCT + observational study data
…one woman’s take (for what its worth)…..

• 9-12 month regimen could be considered in select cases that meet current WHO criteria (don’t use if resistance to drug in regimen)……and wait for more data

• Shorter MDR duration is feasible - we probably treat longer than we need in many (not all) cases

• We should employ strategies to use our better new & repurposed drugs more often (advocate for better access)

• Wishlist: Clinical study designs that captures key components of US-based care strategies:
  – ie. duration dependent on parameters of response to treatment, # of drugs reflect relative efficacy of drugs available to use, consideration of co-morbidities and extent of disease?
…..now for some practical tools

Fruita, Utah
what’s the catch with our new BFF(?)

drugs for DR-TB?

- Bedaquiline
- Moxifloxacin
- Clofazamine
- (Delaminid)
Brush up on QTc calculation

- Recommended to do manual read if QTc abnormal (or borderline)
- **Fredericia** method is preferred (used in phase II BDQ & DLM trials)

Guidance on requirements for QTc measurement in ECG monitoring when introducing new drugs and shorter regimens for the treatment of Drug-resistant Tuberculosis

...helpful hints for manual read...

Defining end of T-wave using maximum slope intercept; Use leads II, v5 or v6 (choose best view T wave)
Calculators/nomogram for QTc

- Many phone or online apps to do calculations
- Or use nomogram

\[
\text{QTcF} = \frac{QT}{3 \sqrt{RR}}
\]

**Example calculation using the nomogram**

- Heart rate: 75 bpm
- R-R interval: 320 msec

**Results**

- Corrected QT interval: 345 msec
Nursing Job Aid: DR-TB Adverse effects

Made by nurses for nurses:

• Reviewed key reference documents which summarized common side effects of second-line anti-TB drugs
  – WHO Companion Handbook (WHO 2011 guidelines)
  – Partners In Health Guide to the Medical Management of MDR-TB
  – CITC Drug-Resistant TB Survival Guide v3
• Reviewed nursing literature for each of the symptoms
• Input from nurses experienced in caring for MDR-TB
### Job Aid Structure: Presenting Symptoms

<table>
<thead>
<tr>
<th>SYMPTOM(s)/POTENTIAL TOXICITY</th>
<th>POSSIBLE OFFENDING DRUG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Some combination of the following symptoms:</td>
<td>Anti-TB: Cs, FQs (Lfx, Mfx), Inh, Eto/Pto</td>
</tr>
<tr>
<td>Mood changes, agitation, irritability, difficulty concentrating, and/or sleep disturbances</td>
<td>ARVs: EFV</td>
</tr>
<tr>
<td>CENTRAL NERVOUS SYSTEM (CNS) TOXICITY:</td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td></td>
</tr>
</tbody>
</table>

- Presents symptoms that a patient may express during treatment
- Indicates the potential toxicity: diagnosis associated with these presenting symptoms
- Lists possible TB and/or anti-retroviral (ARV) drugs associated with the symptom(s)/toxicity
Job Aid Structure: Nursing Assessment

NURSING ASSESSMENT

Observe for and refer immediately if the patient shows signs of acute depression or reports thinking of hurting him/herself.

Ask the patient:
- When did you first notice these symptoms?
- Have you had thoughts of hurting yourself or that you would be better off dead?
- Other psychosocial stressors?

Check for signs of depression:
- Where available, use a depression screening tool (baseline and monthly if patient is taking Cs)

Check:
- Recent TSH result

• What to observe for?
• What questions to ask the patient?
• What tests or evaluations should the nurse check for?
Job Aid Structure: Nursing Interventions

- Urgent action to take when indicated (criteria provided)
- Information to cover in counseling the patient
- When to bring to the doctor’s attention and what questions to raise with the doctor regarding potential medical interventions

<table>
<thead>
<tr>
<th>NURSING INTERVENTIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seek urgent medical evaluation when signs of acute depression or suicidal ideation.</td>
</tr>
<tr>
<td>Counsel the patient (and family):</td>
</tr>
<tr>
<td>• To watch for and report any changes in the patient’s mood or behavior</td>
</tr>
<tr>
<td>• Importance of avoiding alcohol use while on MDR-TB treatment (detox/rehab if indicated)</td>
</tr>
<tr>
<td>When a patient shows signs of depression, discuss with the doctor and/or social worker:</td>
</tr>
<tr>
<td>• How to address other psychosocial stressors if present</td>
</tr>
<tr>
<td>• Whether antidepressant therapy is needed</td>
</tr>
<tr>
<td>• Whether dose of Cs can be decreased</td>
</tr>
<tr>
<td>• Psychiatric evaluation</td>
</tr>
</tbody>
</table>
Job Aid Structure: Comments

- Provides additional information on potential causes of the symptom(s)
- May provide location for additional resources
- May provide information on related considerations for management

**COMMENTS**

Severe depression can be seen in 2.4% of patients receiving EFV. Consider substitution of EFV if severe depression develops.

Some situational depression can be expected for patients who have been dealing with the challenges accompanying DR-TB and treatment.

Some patients taking Cfx with resulting skin color changes have experienced reactive depression.

PHQ-9 depression screening tool translated in multiple languages:
Nursing Job Aid: Pilot Test

Development/support:

**International Council of Nurses**
- Carrie Tudor (ICN)
- Ann Raftery (CITC)
- Lisa True (CADPH)
- Catalina Navarro (HNTC)

[Multiple country support contributors for local adaptation, translation, and pilot process]

Pilot Test Locations:
- China
- Russia
- Mexico
- USA
- Uganda
- Tanzania
- Zambia - underway
- Indonesia - underway
- Thailand - underway
Heartland MDR-TB Care Plan

### MDR TB CARE PLAN

<table>
<thead>
<tr>
<th>Baseline</th>
<th>Initiation of Treatments</th>
<th>Month 1</th>
<th>Month 2</th>
<th>Month 3</th>
<th>Month 4</th>
<th>Month 6</th>
<th>Month 9</th>
<th>Month 12</th>
<th>Month 18</th>
<th>Month 24</th>
</tr>
</thead>
<tbody>
<tr>
<td>CXR-PA/Lat. Compare to old film</td>
<td>Consider CT &amp; alternate views</td>
<td>Consider CXR</td>
<td>CXR</td>
<td>CXR</td>
<td>Consider CT</td>
<td>CXR</td>
<td>Consider CT</td>
<td>CXR</td>
<td>Consider CT</td>
<td></td>
</tr>
<tr>
<td>TST/Report case</td>
<td>Physician assessment q 1-2 wks</td>
<td>Physician assessment</td>
<td>Physician assessment q 1-2 wks</td>
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<td>Physician assessment q 1-2 wks</td>
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<td>Physician assessment q 1-2 wks</td>
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<tr>
<td>Baseline</td>
<td>Update drug o-gram</td>
<td>Update drug o-gram</td>
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<tr>
<td>Baseline TSH</td>
<td>CBC, BUN, Cr, LFT's, Ca, Mg, HB, HCV, glucose</td>
<td>CBC, BUN, Creat, LFT's, K, Ca, Mg at least q 3 months</td>
<td>CBC, BUN, Creat, LFT's, K, Ca, Mg at least q 3 months</td>
<td>CBC, BUN, Creat, LFT's, K, Ca, Mg at least q 3 months</td>
<td>CBC, BUN, Creat, LFT's, K, Ca, Mg at least q 3 months</td>
<td>CBC, BUN, Creat, LFT's, K, Ca, Mg at least q 3 months</td>
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<td>CBC, BUN, Creat, LFT's, K, Ca, Mg at least q 3 months</td>
<td>CBC, BUN, Creat, LFT's, K, Ca, Mg at least q 3 months</td>
</tr>
<tr>
<td>Review prior lab: CBC, BUN, Cr, LFT’s, 24 hr Cr, Ca, Mg, HB, HCV, glucose</td>
<td>If positive CD4, viral load</td>
<td>If positive evaluate for treatment</td>
<td>If positive evaluate for treatment</td>
<td>If positive evaluate for treatment</td>
<td>If positive evaluate for treatment</td>
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<td>If positive evaluate for treatment</td>
<td>If positive evaluate for treatment</td>
<td>If positive evaluate for treatment</td>
</tr>
<tr>
<td>Review prior sputum results. Repeat sputum smear &amp; culture</td>
<td>Sputum q a.m. x 3 days</td>
<td>Sputum q a.m. x 3 days</td>
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<td>Sputum q a.m. x 3 days</td>
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<tr>
<td>Review susceptibility, request extended susceptibility test</td>
<td>Repeat susceptibility if sputum positive</td>
<td>Repeat susceptibility if sputum positive</td>
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<td>Repeat susceptibility if sputum positive</td>
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<tr>
<td>Infection control isolation</td>
<td>Continue until culture negative x3</td>
<td>Continue until culture negative x3</td>
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<td>Continue until culture negative x3</td>
<td>Continue until culture negative x3</td>
</tr>
<tr>
<td>Aminoglycoside and/or Capreomycin IV (IM) 5 day/wk</td>
<td>Peak/trough drug level</td>
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<tr>
<td>4-6 oral drugs</td>
<td>Peak drug levels 2 hrs post dose (PAS 6 hr)</td>
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<td>Peak drug levels 2 hrs post dose (PAS 6 hr)</td>
<td>Peak drug levels 2 hrs post dose (PAS 6 hr)</td>
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<tr>
<td>DOT initiated/patient educated</td>
<td>Educate as needed</td>
<td>Educate as needed</td>
<td>Educate as needed</td>
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<td>Educate as needed</td>
</tr>
<tr>
<td>Pyridoxine 100mg</td>
<td>As long as ethionamide, linezolid, or cycloserine given</td>
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<tr>
<td>Baseline weight &amp; height</td>
<td>Calculate BMI</td>
<td>Weigh weekly</td>
<td>Weigh monthly</td>
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<tr>
<td>Nutritional assessment</td>
<td>Nutritional supplement as needed (no milk products, aluminum, Ca, Mg containing antacids, iron or OVI's within 2 hours of Furazolidone)</td>
<td>Nutritional supplement as needed (no milk products, aluminum, Ca, Mg containing antacids, iron or OVI's within 2 hours of Furazolidone)</td>
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<tr>
<td>Audiogram/VESTIBULAR screen</td>
<td>Continue monthly as long as aminoglycoside/caprormycin given</td>
<td>Continue monthly as long as aminoglycoside/caprormycin given</td>
<td>Continue monthly as long as aminoglycoside/caprormycin given</td>
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<td>Continue monthly as long as aminoglycoside/caprormycin given</td>
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<tr>
<td>Vision screen</td>
<td>Continue as long as ethambutol, rifabutin, linezolid, clofazamine given</td>
<td>Continue as long as ethambutol, rifabutin, linezolid, clofazamine given</td>
<td>Continue as long as ethambutol, rifabutin, linezolid, clofazamine given</td>
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<td>Substance abuse/psychosocial factors influencing compliance</td>
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<td>Education needs/Completion of Assess &amp; Address contact evaluation with health department</td>
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*Repeat clearance if decreased & adjust medications (aminoglycosides, capreomycin, ethambutol, FIA, levofloxacin, cycloserine)
† For patients at high risk for MDR-TB request rapid molecular assay for drug resistance (consultation required)

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...thankfully it can all work
Let’s just do it better

January 2012: 33 kg

July 2012: 59 kg
thank you

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