Seminar for Global TB/HIV Research:

Research Topics for TB/HIV

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3 August, 2018
Recent History

• 2005: TB/HIV research priorities in resource-limited settings
  – Preventive therapy for TB for PLWHIV
  – Cotrimoxazole prophylaxis delivery for HIV/TB
  – Timing/safety of ART in people with TB
  – Intensified case-finding for TB in PLWHIV
  – Tools & algorithms for smear-negative TB in adults and children
2006 XDR-TB outbreak, South Africa
485 cases
75% HIV+ co-infection
85% mortality
• 2010: Priority Research Questions for TB/HIV in HIV-prevalent and resource-limited settings
  – TB prevention
  – Intensified case-finding
  – TB treatment for PLWHIV (*timing of ART)
  – M/XDR-TB and HIV
  – Maternal/childhood TB & HIV
  – TB & HIV integration
2018 Caveat

• Focus on immediate, patient-proximal questions
• Not basic science → THOUGH IMPORTANT
• Clinical, therapeutic, and operational/implementation questions
  – Slight focus on optimizing current tools
  – Recognize need for new & better prognostics, diagnostics, drugs, and biomarkers.
Key advances

• **2005 Priority Question**: What is the optimal timing of ART initiation in people with TB/HIV?
  – Need for viral control vs. IRIS risk

• **2010 Priority Question**: What is the optimal timing of ART initiation in people with TB/HIV?
  – SapIT (2011)
  – CAMELIA (2011)
  – STRIDE (2011)

→ WHO guideline: CD4<50: Start ART within 2 weeks of TB treatment; CD4>50: Start ART within 8 weeks of TB treatment.
Progress!

• Deaths from TB in PLWHIV decreased 37% between 2005-2016
• But...
• 2018: TB is the leading cause of mortality among people with HIV
• TB responsible for ~33% deaths in PLWHIV

UNAIDS, 2018; WHO, 2018
Landscape evolution since 2010...

HIV
- Diagnostics: rapid tests, self-test
- Treatment: better ART, FDC, DTG?
- Treat All (universal test & treat, any CD4)
- Rapid ART initiation
- Prevention: PrEP
- Targets: 90-90-90
- Differentiated service delivery: out of clinic

TB
- Diagnostics: GeneXpert, LPAs, LAM
- Treatment: New MDR-TB drugs, shorter regimens
  - Can’t shorten DS-TB treatment
- Prevention: new preventive tx regimens
- Targets: Missing 1/3rd
- Community-based MDR-TB treatment
What questions remain?

• Prevention
• Screening/Detection
• Treatment optimization
• Treatment delivery, treatment integration
• Reduce mortality
• Reduce transmission
Prevention

FIG. 5.3
Gaps in TB preventive treatment for people who were newly enrolled in HIV care in 2016, selected countries

- Indonesia
- Myanmar
- India
- Liberia
- Swaziland
- Sierra Leone
- Nigeria
- Philippines
- Malawi
- Ethiopia
- Zimbabwe

- Scanned on preventive treatment
- Detected and notified with active TB disease
- Gap in TB detection and TB prevention

TRTC
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What is the best strategy to improve uptake of TB preventive therapy for people with HIV?

- **IPT**
  - Demonstrated effectiveness (TEMPRANO)
  - Low uptake, missed opportunity for TB prevention, mortality prevention, transmission interruption

- **New regimens:**
  - 3HP: WHIP-TB study ongoing (3HP + ART)
  - 1HP: Good efficacy with TDF/FTC/EFV (FDC), but what about other ART? DTG?
  - Efficacy AND Effectiveness
• How should TB preventive therapy be provided to HIV+ persons at risk of MDR-TB?
  – High mortality for HIV/MDR, HIV/XDR
  – PHOEInx study: enrollment/results pending
    • Delamanid vs. INH to prevent TB in high-risk HH contacts (including HIV+) of MDR
Screening/Detection

• What is the optimal TB screening algorithm for outpatients with HIV?
  – Symptom screen
  – Introduce new biomarkers, new triage/diagnostic tests, imaging? Is there a better combination?
  – Right test, Right place, Right patient
    • Which tool?
    • Where is tool located? Who uses tool? Pt, nurse, doctor?
    • Risk-stratify patients?
  – Optimal screening algorithm & frequency after HIV treated?
• How can we improve case detection of TB (Missing 1/3), especially among people with HIV?
  – To screen HIV+ for TB, must identify HIV+
  – Bi-directional screening in households, communities, risk settings
What approach for TB screening & treatment should be used in hospitalized persons with HIV to reduce early mortality?

- Empiric TB treatment doesn’t reduce mortality in advanced HIV:
  - REMEMBER (CD4<50, outpatients) (2016)
  - TB-FAST Track (CD4<150, outpatients with high risk of TB) (2016)
  - STATIS (CD4<100, outpatients) (2018)
• Urine LAM to screen all HIV+ inpatients?
  – Peter et al (2016): LAM + SOC dx vs. SOC dx for HIV+ with TB sx
    • small mortality benefit
  – STAMP (2018): LAM+ Xpert+SOC vs. Xpert + SOC dx for all HIV+
    • LAM associated with mortality benefit
    • Significant increase in number of TB cases started on tx
Questions of Service Delivery Integration

• In the clinic, what are the best models for integrated TB/HIV care?

• What are the best ways to integrate TB/HIV testing?
  – How to improve HIV testing (1st 90) among people with TB? People being tested for TB?
• DSD: As HIV diagnosis and treatment moves out of the clinic, how can TB diagnosis and treatment/prevention safely and effectively move with it?
  – Frequency of screening for TB while on treatment?
  – Initiate treatment outside of clinic?
  – Coordinate fast-track or community treatment (prevention) delivery?
  – Monitoring adherence, success: mHealth tools?
Way forward

• Many possible screening, diagnostic, treatment, prevention, and delivery models to try!
  – Mathematical models can inform & help narrow down options

• Ongoing creativity necessary

• Ongoing questioning of “answered questions” necessary:
  – TB screening algorithm?
  – Timing of treatment?
Acknowledgments

**Project Mentors:** Connie Celum, Ruanne Barnabas, Paul Drain

**AHF/IPHC Clinic Team:** Sabina Govere, Hilary Thulare, research team

**CRP Collaborators:** Ting Hong (UW), Afton Dorasamy, Jacques Grosset (KRITH/AHRI, SA), Carole Wallis (BARC-Lancet Labs, SA)

**SA DO ART team:** Heidi van Rooyen, Alastair van Heerden, Mbongeni Mbangwa (HSRC); Olivier Koole, Nsika Sithole (AHRI), field teams; **UW DO ART team:** Meighan Krows, Torin Schaafsma, Susan Morrison

**Clinical mentorship, SA:** M. Yunus Moosa, UKZN

**Funding**
- AES: T32 AI07140
- DO ART: BMGF
- CRP-TB: Harvard Global Health Institute (PKD); the Vanderbilt Fogarty International Clinical Research Program [R24 TW007988] (PKD); IDSA Education & Research Foundation and National Foundation for Infectious Diseases (PKD); MGH Executive Committee on Research (PKD); the Harvard Center for AIDS Research [P30 AI060354] (PKD); and the NIAID [T32 AI007433], [K23 AI108293] (PKD)