TB-HIV International Community Partnership

Community Partners & Community Research Advisors Group
September 11, 2015
Introductions

Russell Campbell, Office of HIV/AIDS Network Coordination

Cynthia Lee, Tuberculosis Trials Consortium Community Research Advisors Group

Rona Siskind, Division of AIDS
Overview

• TB-HIV – Russell Campbell

• Integration of TB and HIV in Research and Practice – Cynthia Lee

• TB-HIV International Community Partnership – Rona Siskind

• Q & A
Acknowledgements

- TBTC CRAG
- Community Partners
- Mike Frick
- Jeff Schouten
### USCA 2015 TB/HIV Workshop Assessment

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Integration of TB and HIV in Research and Practice

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September 11, 2015

Cynthia C Lee, EdD, MS, MA, CHES
CRAG Member
About the CRAG

- an international, community-based advisory body
- ensures the meaningful engagement of TB-affected communities in research conducted by the TBTC
- supports a TBTC research agenda that is responsive to community needs and scientific priorities

8 members from TBTC sites in 6 countries:
- United States
- South Africa
- Uganda
- Vietnam
- Spain
- Peru
Tuberculosis Trials Consortium

• Research network at US Centers for Disease Control Department of TB Elimination
• Conducts drug research for TB infection and TB disease
• Mission to conduct programmatically-relevant research

8 U.S. sites (Texas, New York, Tennessee, California, Washington, D.C.)

8 International sites (Spain, Peru, South Africa, Vietnam, Uganda, Kenya, Hong Kong)
Priorities issues in TB research

• **Long duration**
  
  (6 months for DS-TB; 2 years for MDR-TB;)

• **High pill burden**
  
  (up to 12 pills/day for DS-TB; up 15,000 pills for full course of MDR-TB treatment)

• **Toxic side-effects**
  
  (irreversible deafness; neuropathy; skin discoloration; psychosis; vomiting)

• **Painful injectables**
  
  (for early stage of MDR-TB treatment)
Why integrate TB and HIV in research and practice?

2013 WHO Report:

- 9 million people developed TB, 1.5 million TB deaths
- 1.1 million PLHIV developed TB (4/5 of these in Africa)
- 360,000 people with HIV died of TB
- 510,000 women died from TB; 1/3 of these were women with HIV
- 70% of PLHIV with TB are on ARVs
- 40% of TB patients know their HIV status
“The reality is that in sub-Saharan Africa, TB and HIV are one disease. We must treat them together.”
—Mark Dybul, Global Fund

“We need to integrate TB and HIV and treat these as one disease.”
—Jarbas Barbosa, Brazil

“Life is forcing us to put TB and HIV together.”
—Aaron Moatsaledi, South Africa
...with two research agendas?

1. Money spent on research:
   - **HIV**: US 2.6 billion, (drug R&D, 2011)
   - **TB**: US 676.6 million, (all R&D, 2013)

2. Number of new drugs approved by FDA since 1987:
   - **HIV**: 36 drugs
   - **TB**: 2* drugs

3. Number of clinical trials behind the newest drugs:
   - **HIV**: Dolutegravir, 61 trials
   - **TB**: Delamanid, 6 trials
Key Populations—some shared, some different

Global Fund definition of “key population”
1. Epidemiologically, group faces increased risk
2. Access to relevant services is lower for the group
3. The group faces frequent human rights violations or marginalization

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<td>People with HIV</td>
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<td>Migrants and refugees</td>
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<tr>
<td>Miners</td>
</tr>
<tr>
<td>Healthcare workers</td>
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<tr>
<td>People who use drugs and alcohol</td>
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<tr>
<td>Children and adolescents</td>
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“All people living with HIV, and who currently have, or have survived, TB, fall within this definition of key populations”

Are these key populations equitably represented in TB and TB/HIV R&D?
Where are people with HIV in TB R&D?

- PLHIV often in phase IIb and III studies, but at higher CD4 counts ($\geq 250$)
- PLHIV on ARVs less frequently included in phase IIb and III trials
- People with extra-pulmonary TB, including many PLHIV, are almost always excluded from trials
- Children with HIV often not included in trials
What needs to change?

• Having HIV shouldn’t be an exclusion criteria for TB drug research
• Taking ARVs shouldn’t be an exclusion criteria, either
• DDI studies between TB and HIV drugs need to happen sooner—preferably by time TB drug enters phase IIa trials
• TB investigators need to become more comfortable enrolling PLHIV
• HIV investigators need to become better acquainted with TB research
CAN TB AND HIV DRUGS BE USED TOGETHER? It’s complicated.

Rifampin is one of the primary drivers of TB-killing activity in the standard six-month, four-drug regimen for treatment of DS-TB. Rifampin interacts with many other medications, notably protease inhibitors, making rifabutin a more suitable candidate for people on HIV medicines. Although numerous, generic sources of quality-assured rifampin exist globally, supply-chain issues continue to disrupt regular access to the drug, leading to dangerous programmatic stock-outs. Several studies are currently examining the efficacy and safety of higher doses of rifampin, and its potential for shortening TB treatment.

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<th>Adverse Effects of Note</th>
<th>Potential TB and HIV Drug Interactions</th>
<th>Maternal/Pediatric Concerns</th>
<th>EML/GDF Inclusion</th>
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<td>Body fluid discoloration, skin allergies; flu-like symptoms; gastrointestinal upset and distress; jaundice; elevated liver enzymes; kidney failure; hemolytic anemia; thrombocytopenia; neutropenia</td>
<td>TB: bedaquiline: decreased concentration of bedaquiline; clarithromycin: decreased concentration of clarithromycin; isoniazid and pyrazinamide: increased risk of elevated liver enzymes</td>
<td>Pediatric formulations available</td>
<td>EML: Yes, for adults and children</td>
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<td>HIV: protease inhibitors (PIs): decreased concentrations of PIs; non-nucleoside reverse transcriptase inhibitors (NNRTIs), except efavirenz: decreased concentrations of NNRTIs; integrase inhibitors: decreased concentrations of integrase inhibitors; ketoconazole: decreased concentrations of both ketoconazole and rifampin</td>
<td></td>
<td>Limited data on risk during pregnancy (damage to fetus was seen in animal studies; bleeding in infant and mother post delivery reported when given with isoniazid in last weeks of pregnancy); secreted in human milk (breastfeed with caution)</td>
<td>GDF: Yes, as part of fixed-dose combination for adults and children</td>
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</table>
Not yet studied in people with TB/HIV who are using ARVs. Not been studied in people who use drugs or may be on opioid substitution therapies.

Small studies giving people HIV medicines and a single dose of bedaquiline at a time suggest:

- **Efavirenz**: appears to reduce amount of bedaquiline in the body by about half
- **Lopinavir/ritonavir**: slightly raises the amount of bedaquiline in the body
- **Ketoconazole**: increases the amount of bedaquiline in the body; patients taking ketoconazole and bedaquiline have an increased risk of QT prolongation
Where are children in TB R&D?

The “missing cohort” of TB research

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<th>Trial</th>
<th>Phase</th>
<th>TB Type</th>
<th>Adolescent Inclusion</th>
<th>Regimen</th>
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<tr>
<td>C213</td>
<td>III</td>
<td>MDR</td>
<td>✗</td>
<td>DLM + OBR (18–24 months)</td>
</tr>
<tr>
<td>STREAM</td>
<td>III</td>
<td>MDR</td>
<td>✗</td>
<td>Stage 1: 9 month w/ injectable</td>
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<td></td>
<td></td>
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<td></td>
<td>Stage 2: 9 month all oral w/ BDQ</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>6 month w/ injectable + BDQ</td>
</tr>
<tr>
<td>STAND</td>
<td>III</td>
<td>DS/MDR</td>
<td>?</td>
<td>6 month all oral (PaMZ)</td>
</tr>
<tr>
<td>Nix-TB</td>
<td>IIb</td>
<td>XDR</td>
<td>✔️</td>
<td>6–9 month all oral (Pa,LZD,BDQ,Z?)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(14+ yrs.)</td>
<td></td>
</tr>
<tr>
<td>MARVEL</td>
<td>IIb</td>
<td>MDR</td>
<td>?</td>
<td>Shortened regimen (novel drugs–TBD)</td>
</tr>
<tr>
<td>NC005</td>
<td>IIb</td>
<td>DS/MDR</td>
<td>✗</td>
<td>Shortened regimen (BDQ,Pa,Z)</td>
</tr>
<tr>
<td>TBTC S31</td>
<td>III</td>
<td>DS</td>
<td>✔️</td>
<td>4 month HPZE/HP</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(12+ yrs.)</td>
<td>4 month HPZM/HPM</td>
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Where do we go from here?

• Greater collaboration between TB and HIV research networks

• Progressive inclusion of people with HIV (including those taking ARVs) in TB clinical trials

• Earlier inclusion of adolescents and children (including those with HIV) in TB clinical trials

• Earlier and more comprehensive drug-drug interaction studies: between TB/TB drugs; and TB/HIV drugs

• More research designed to address key challenges facing TB/HIV treatment and prevention (pill burden; drug-drug interactions; long treatment duration; patient-friendly delivery systems; extra-pulmonary TB)

• Increased joint TB/HIV research activities and funding commitments for these activities
THANK YOU

mike.frick@treatmentactiongroup.org
http://crag-tb.tumblr.com/
TB-HIV International Community Partnership

Community Partners &
Community Research Advisors Group

September 11, 2015

Rona Siskind, MHS
Division of AIDS
National Institute of Allergy & Infectious Diseases

National Institutes of Health
NIAID/DAIDS Strategic Goals

- **NIAID**: Provide the scientific basis for achieving an “AIDS-free generation” by developing a safe and effective HIV vaccine as well as improved combination prevention strategies, optimization of treatment modalities, and novel therapeutic approaches towards a cure for HIV infection.

- **DAIDS**: Develop and support the infrastructure and biomedical research needed to:
  1. Halt the spread of HIV through the development of an effective vaccine and biomedical prevention strategies that are safe and desirable.
  2. Develop novel approaches for the treatment and cure of HIV infection.
  3. Treat and/or prevent co-infections and co-morbidities of greatest significance.
  4. Foster partnerships with scientific and community stakeholders to develop and implement effective interventions.
Network Clinical Research Sites
What Is Community Partners (CP)?

Community Partners organized through the HIV/AIDS Network Coordination Office and works with the NIH funded HIV/AIDS networks.
The Mission of Community Partners is to maximize the scope, effectiveness, and benefits of community engagement in clinical research within and across the National Institutes of Health funded HIV Clinical Trials Networks.
CP Cross-Network Activities & Mission

- Community engagement
- Scientific agendas
- Ethical conduct of clinical trials
- Community education
- Communication/information dissemination
- Community participation
- CAB support
CP & CRAG Collaboration

- Joint participation in CP and CRAG activities
- Webinar: TB/HIV International Research & Community Engagement
- Address stigma
- Increase HIV and TB literacy & understanding of co-infection
- Foster mentorship & collaboration
- Jointly develop TB/HIV materials and resources
CP & CRAG Collaboration

- **CRAG presented at CP 2014 F2F**
  - Overview of TB research issues and co-infection
- **CP presented at CRAG 2015 F2F**
  - Presentation of Recommendations for Community Engagement
  - Overview of ongoing & planned NIAID TB/HIV trials
- **Ongoing communication**
TB/HIV International Research & Community Engagement Engagement

- Address the impact of TB/HIV co-infection – (S. Nachman)
- Discuss CRAG/CP global efforts focused on TB/HIV research literacy and community engagement – (L. McKenna)
- Discuss new TB research agendas and potential community impact – (A. Gupta & A. Hesseling)
TB Disease Continuum

TB exposure

TB infection

TB disease

Disease severity

• HIV affects each step

Death

Risk factors for disease are young age, malnutrition and HIV

Courtesy S. Nachman, University of New York at Stony Brook
The Challenge of HIV and TB Co-infection

- Greater difficulty with diagnosis
- Perhaps poorer response to therapy
- Drug-drug interactions

Percentage of notified TB patients with known HIV status by country, 2013

Courtesy S. Nachman, University of New York at Stony Brook
Resources

- Activist Guide to Clinical Trials Protocols
- Article and letter regarding stigmatizing language
- TB-HIV Infection Control Parameters
- TB-HIV Fact Sheet
- TB Resources for Communities (www.HANC.info)
- CRAG Website
End stigmatizing language in tuberculosis research and practice

BMJ 2015; 350 doi: http://dx.doi.org/10.1136/bmj.h1479 (Published 23 March 2015) Cite this as: BMJ 2015;350:h1479

- Article
- Related content
- Metrics
- Responses

1. Mike Frick, project officer, Treatment Action Group, New York, NY, USA,
2. Dalene von Delft, cofounder, TB Proof, Cape Town, South Africa,
3. Blessina Kumar, chair, Global Coalition of TB Activists, New Delhi, India

1. Correspondence to: M Frick mike.frick@treatmentactiongroup.org

Terms that invoke metaphors of transgression and punishment cause harm, say Mike Frick, Dalene von Delft, and Blessina Kumar
TB-HIV Infection Control Parameters

**TB is spread air-borne**

**TB Patient**

**Non-TB patient**

**Goals:**
- Minimize releasing TB mycobacterium to air
- Minimize exposure to airborne TB mycobacterium

**Potentially TB Infectious Patients**

- Educate individuals about TB transmission
- Prompt identification and separation
- Time is crucial for potentially infectious TB patients, hurry
- Control spread by using tissues and No-Touch waste bins

**Sputum collection**

- Wash hands
- Separate from general waiting area
- Written procedures for special protection for individuals that may be potentially TB infectious

**Waiting Area**

- **FACILITY**
  - **Evaluation and Set-up**
    - Air Flow Assessment
    - Vent System
    - Air Cleaning methods: HEPA, UV Light
    - Sufficient Space in Waiting Area
    - Planned renovation or new construction
  - Use of PPE (Personal Protective Equipment)
  - Use of explantorics
  - Written procedures for high-risk TB situations (drug-resistant, multi-drug-resistant)
  - Handwashing Policy
  - No-Touch waste bins for tissues

**TB Surveillance of (HCW) Health Care Workers**

- TB Screening
- Isosclav therapy availability
- Member TB control measures

**TB Education for HCWs**

- Continuous staff training
- Documentation (Posters and pamphlets) for HCW, individuals, and study participants

**HIV Prevention and Care for HCWs**

- In-Country guidelines for HIV Testing
- Written documentation of forms and test results
- Training, written description, and availability of -HIV preventative methods
- Available ART

**FACILITY**

- Infection Control Officer
- Written Policies
- Written Procedure for Rapid TB Identification

Infection Control measures are guidelines, used with written procedures, tracked by in-house staff, preferably with an Infection Control officer.

Surveys conducted under guidance of HANC TB LD WHO (TB Lab Diagnostics Working group) start 2013. Infection Control measures are for guidance and neither mandated nor punitive.
CRAG – CP Mentorship

• Mentorship – linking CRAG & CP members in common locations (South Africa, Uganda and Peru)
  – Attend network/site meetings and workshops
  – Provide updates on current activities and research
  – Assist in the development of advisory groups
  – Facilitate co-infection information exchange

“The cross networking has been extremely educational and beneficial. I got to learn about the more practical side of adherence counselling from field workers point of view and not just from clinical research angle” CP member
http://www.treatmentactiongroup.org/tb/community-engagement/crag

The Community Research Advisors Group (CRAG) is an international, community-based advisory body that works to ensure the meaningful participation and engagement of affected communities in research conducted by the U.S. Centers for Disease Control and Prevention’s (CDC’s) Tuberculosis Trials Consortium (TBTC). This group of research-literate advocates supports a robust and innovative TBTC research agenda that reflects both community needs and scientific priorities. TAG coordinates the CRAG and supports CRAG members as they engage in advocacy at a number of levels—among TB-affected communities, individual TBTC trial sites, the TBTC consortium, and national and international policy makers—and work to raise awareness of TB and TB research in their communities. CRAG members actively participate in TBTC working groups and advise TBTC researchers on protocol development, informed consent administration, community research priorities, and dissemination of study findings back to communities.

Recent accomplishments of CRAG members include:

- The CRAG, together with the U.S. CDC Department of TB Elimination, has developed a monitoring and evaluation (M&E) framework to measure the impact of CRAG member activities. This is one of the first M&E systems designed to capture the social and scientific value of community engagement in TB clinical research. These simple M&E tools will be available online to other interested research consortia soon.
TB Resources for Communities

As part of the mandate from DAIDS to work with other disease groups, Community Partners (CP) and the TB Community Research Advisors Group (CRAG) are collaborating and working together on a joint TB/HIV project. The Community Research Advisors Group is an international, community-driven advisory body that works to ensure the meaningful representation and engagement of affected communities in research conducted by the U.S. Centers for Disease Control and Prevention's Tuberculosis Trials Consortium. This group of research-literate activists supports a robust, comprehensive and innovative TBTC research agenda that is responsive to community needs as well as scientific priorities.

One goal of the CP/CRAG partnership is to help educate TB community members and researchers about HIV and to help educate HIV community members and researchers about TB and how the two diseases are connected.

Useful Documents

- TB-HIV Infection Control Parameters
- TB-HIV Webinar Presentation with audio 27May2015
- TB/HIV Webinar Slides 27May2015
- Open Letters: Retiring stigmatizing and criminalizing language from the global TB discourse
- Activist Guide to Clinical Trial Protocols

TB Links

- TB Quick Facts
- TB/HIV Activist Toolkit slide set
- Good Participatory Practices for TB Drug Trials
- TB Online
- Critical Path to New TB Drug Regimens
- Tuberculosis Trends - United States, 2014
- TB Community Research Advisory Group (CRAG)
- WHO: Treatment of tuberculosis: guidelines for national programmes
- WHO: Guidelines on the management of latent tuberculosis infection
- UK: National Institute for Health and Care Excellence: TB Research Recommendations
- CDC: Slide Set — Guidelines for Preventing the Transmission of M. tuberculosis in Health Care Settings, 2005
- NIAID Role in Addressing TB, Drug-Resistant TB, and TB in People with HIV/AIDS
- The Tuberculosis Clinical Diagnostics Research Consortium (TDCRC)
- Stop TB Partnership
- PATH - HIV/AIDS and TB Global Health Program

Links to videos about TB

- TB Unmasked
- Exposed: The Race Against TB
Future Plans

- Cross CAB and CRAG protocol review
- Additional conference presence
- Webinar: How to Review a Protocol
Questions and Contacts?

- Cynthia Lee, CRAG
ccl2117@gmail.com
- Russell Campbell, HANC Community Partners
rcampbell@fredhutch.org
- Rona Siskind, DAIDS, NIAID
rsiskind@niaid.nih.gov
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