USCA 2015

TB-HIV International Community Partnership

Community Partners &
Community Research Advisors Group

September 11, 2015

community partners

CRAG
TB Community Research Advisors Group

Introductions

Russell Campbell, Office of HIV/AIDS Network Coordination

Cynthia Lee, Tuberculosis Trials Consortium Community Research Advisors Group

Rona Siskind, Division of AIDS

Presenters

Cynthia Lee

Rona Siskind

Russell Campbell

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**

TB-HIV Assessment

ID

USCA 2015 TB/HIV Workshop Assessment

Please indicate whether you believe the following statements to be true or false about TB/HIV. If you are unsure, feel free to select "don't know."

		True	False	Don't know
1.	Globally, TB is the leading cause of death in people with HIV.	T	F	DK
2.	12 million persons are TB/HIV co-infected.	T	F	DK
3.	All TB drugs can be taken along with HIV medications.	T	F	DK
4.	People living with HIV are less likely to have TB outside of the lungs.	T	F	DK
5.	TB is easier to diagnose in people living with HIV; their sputum samples may often show infection.	T	F	DK
6.	People with HIV and latent TB infection are urged to take medicine to prevent progression to active TB disease.	T	F	DK
7.	In the United States, more money is spent on TB research than on HIV research.	T	F	DK
8.	Once someone has been treated for TB, they can never be re-infected.	T	F	DK
9.	Starting ART therapy early does not prevent progression to active TB disease in people with HIV and latent TB infection.	T	F	DK
10.	TB accounts for approximately one in four HIV-related deaths.	T	F	DK

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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

community partners

CRAG TB Community Research Advisors Group

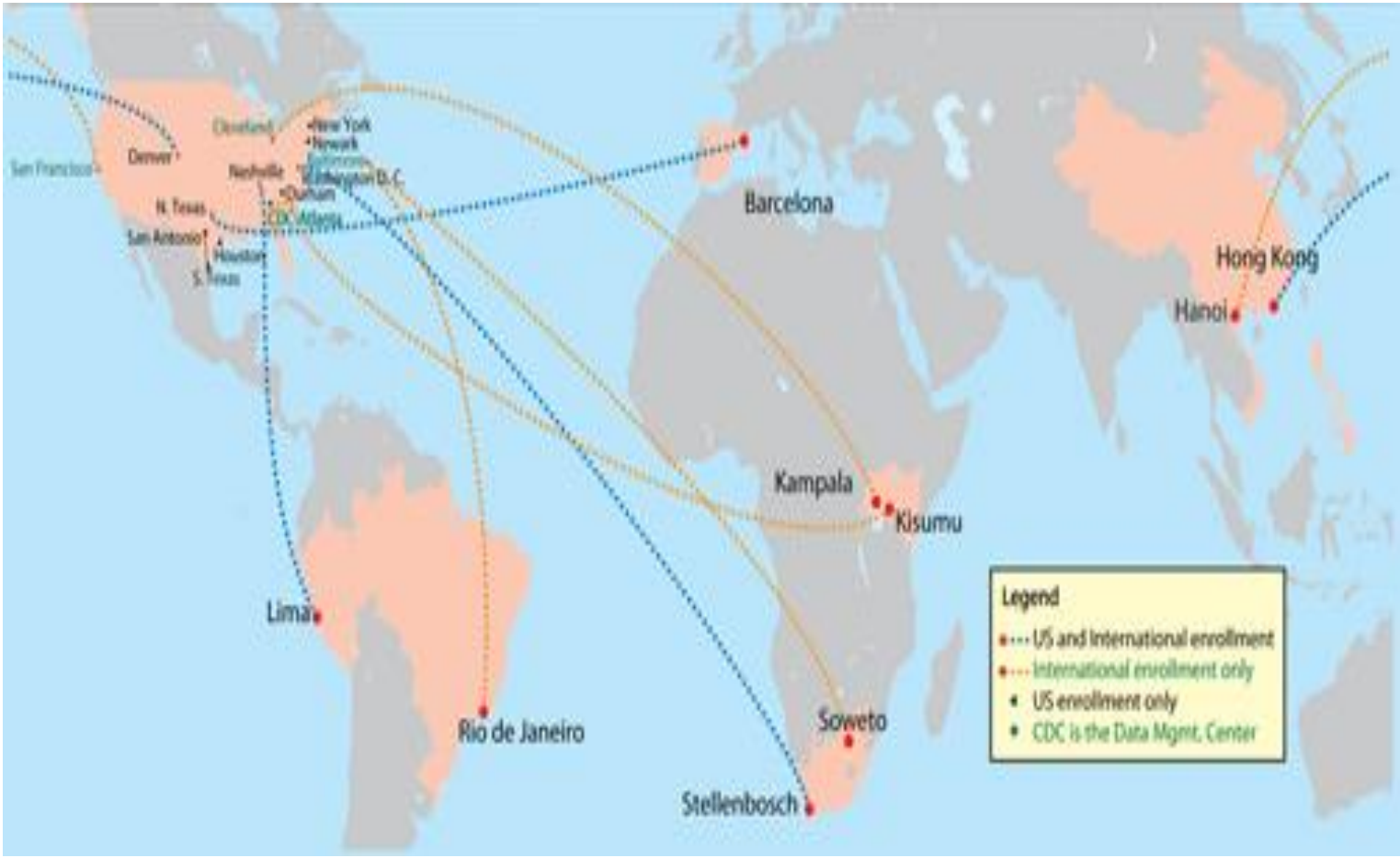
About the CRAG

- 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

TBTC Sites


Barcelona
Hong Kong
Hanoi
Kampala
Kisumu
Lima
Rio de Janeiro
Soweto
Stellenbosch
Legend
US and International enrollment
International enrollment only
US enrollment only
CDC is the Data Mgmt. Center

About the TBTC

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**

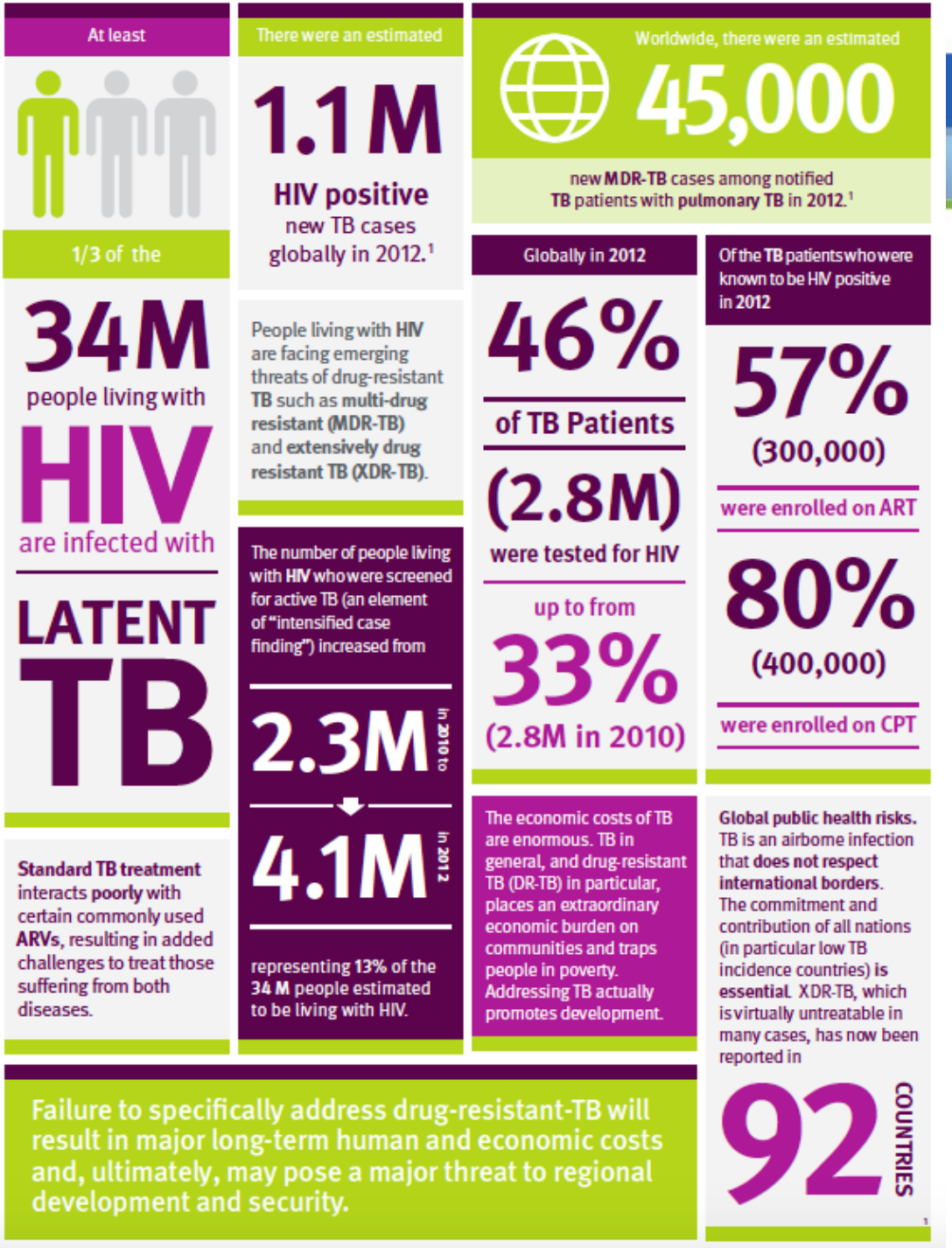
  (up to 12 pills/day for DS-TB; up 15,000 pills for full course of MDR-TB treatment)

- **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

TB/HIV: One disease…

“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

TB Key Populations

- Prisoners
- People with HIV
- Migrants and refugees
- **Miners**
- **Healthcare workers**
- **People who use drugs and alcohol**
- **Children and adolescents**

"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?

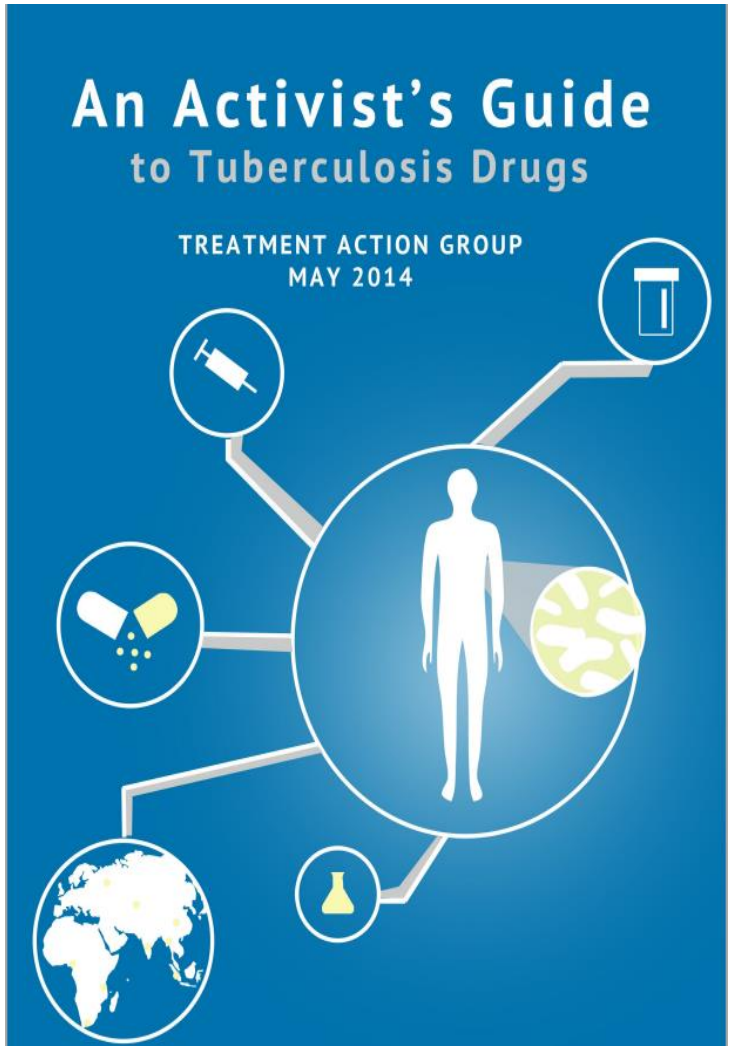
Where are people with HIV in TB R&D?

- PLHIV often in phase IIb and III studies, but at higher CD4 counts (≥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.

Adverse Effects of Note	Potential TB and HIV Drug Interactions	Maternal/Pediatric Concerns	EML/GDF Inclusion
Body fluid discoloration; skin allergies; flu-like symptoms; gastrointestinal upset and distress; jaundice; elevated liver enzymes; kidney failure; hemolytic anemia; thrombocytopenia; neutropenia	**TB**: bedaquiline: decreased concentration of bedaquiline; clarithromycin: decreased concentration of clarithromycin; isoniazid and pyrazinamide: increased risk of elevated liver enzymes **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	Pediatric formulations available 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)	**EML**: Yes, for adults and children **GDF**: Yes, as part of fixed-dose combination for adults and children

Activist Guide to Clinical Trials Protocols

A Protocol Review Companion for Activists

Written by Cynthia C Lee

Edited by Lindsay McKenna, Mike Frick, and the CRAG

January 2015

Example: MDR-TB drug bedaquiline

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

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

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/

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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

NIH HIV/AIDS Clinical Trials Networks

National Institute of Allergy and Infectious Diseases

National Institute of Allergy and Infectious Diseases

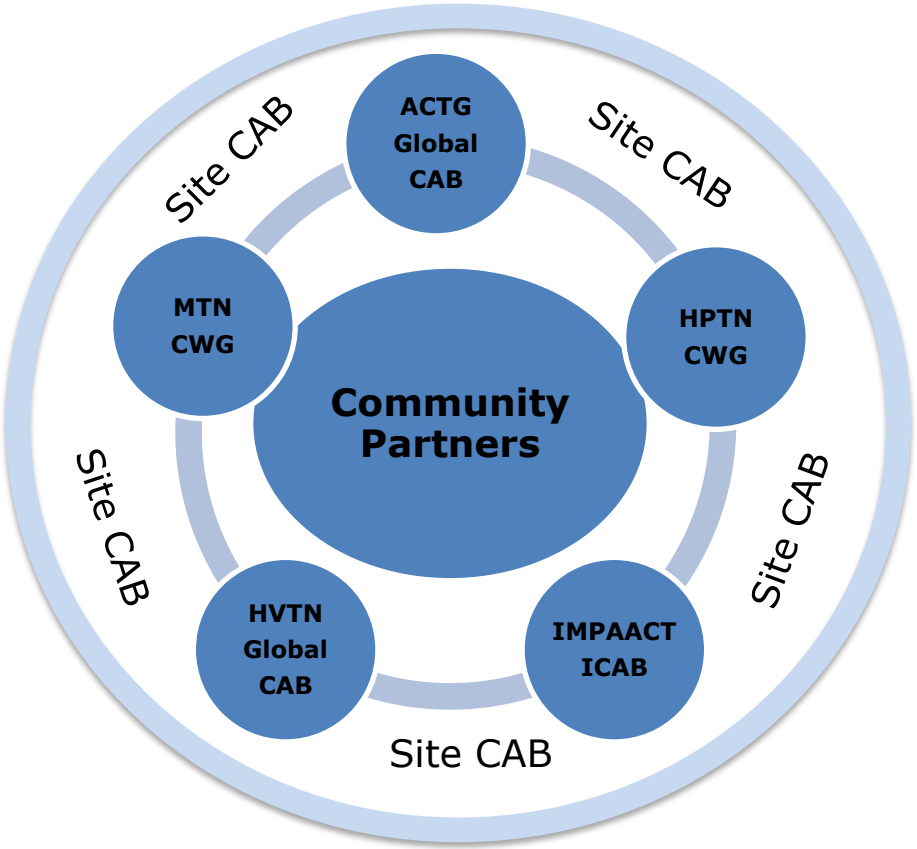
NIH Networks & Community Engagement

National Institutes of Health (NIH)

National Institute of Allergy and Infectious Diseases (NIAID)

Division of AIDS (DAIDS)

Clinical Trials Networks

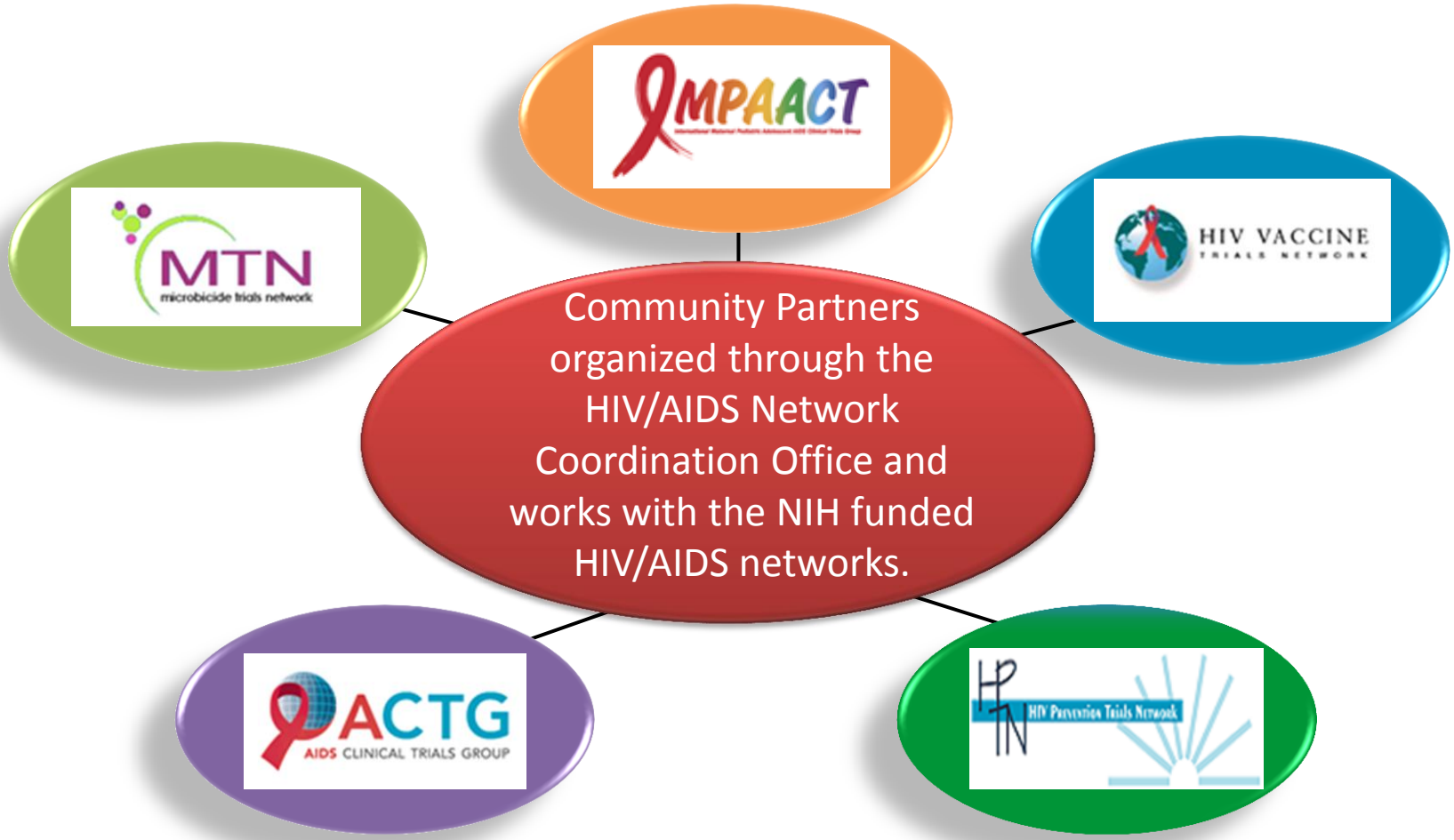


National Institute of Allergy and Infectious Diseases

Network Clinical Research Sites

National Institute of Allergy and Infectious Diseases

What Is Community Partners (CP)?



Community Partners

hanc
HIV/AIDS Network Coordination

community partners

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

NIH National Institute of Allergy and Infectious Diseases

CP Cross-Network Activities & Mission

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

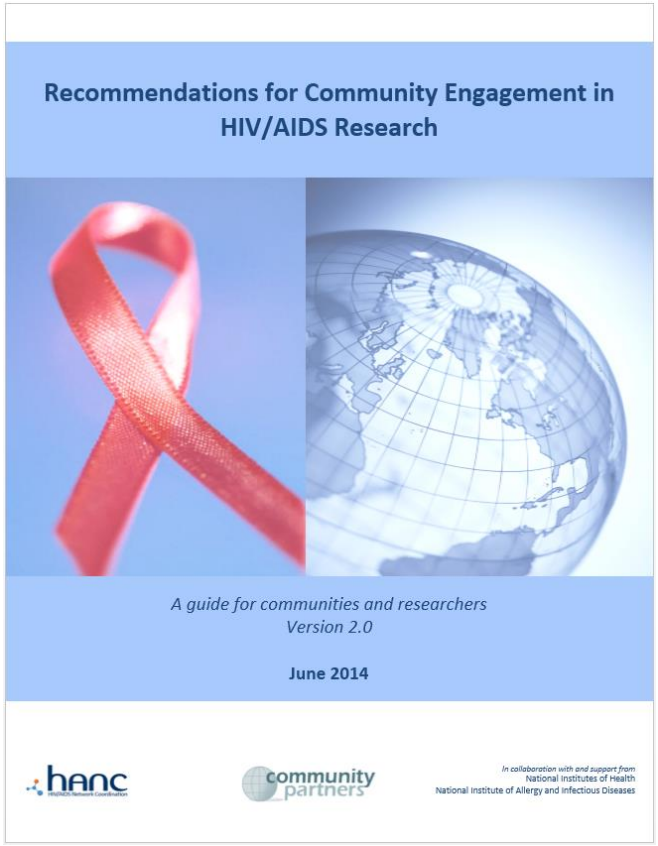
National Institute of Allergy and Infectious Diseases

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 Community Engagement Webinar

TB/HIV International Research & Community 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)

National Institute of Allergy and Infectious Diseases

TB Disease Continuum

TB exposure

TB infection

TB disease

Disease severity

- **HIV affects each step**

Death

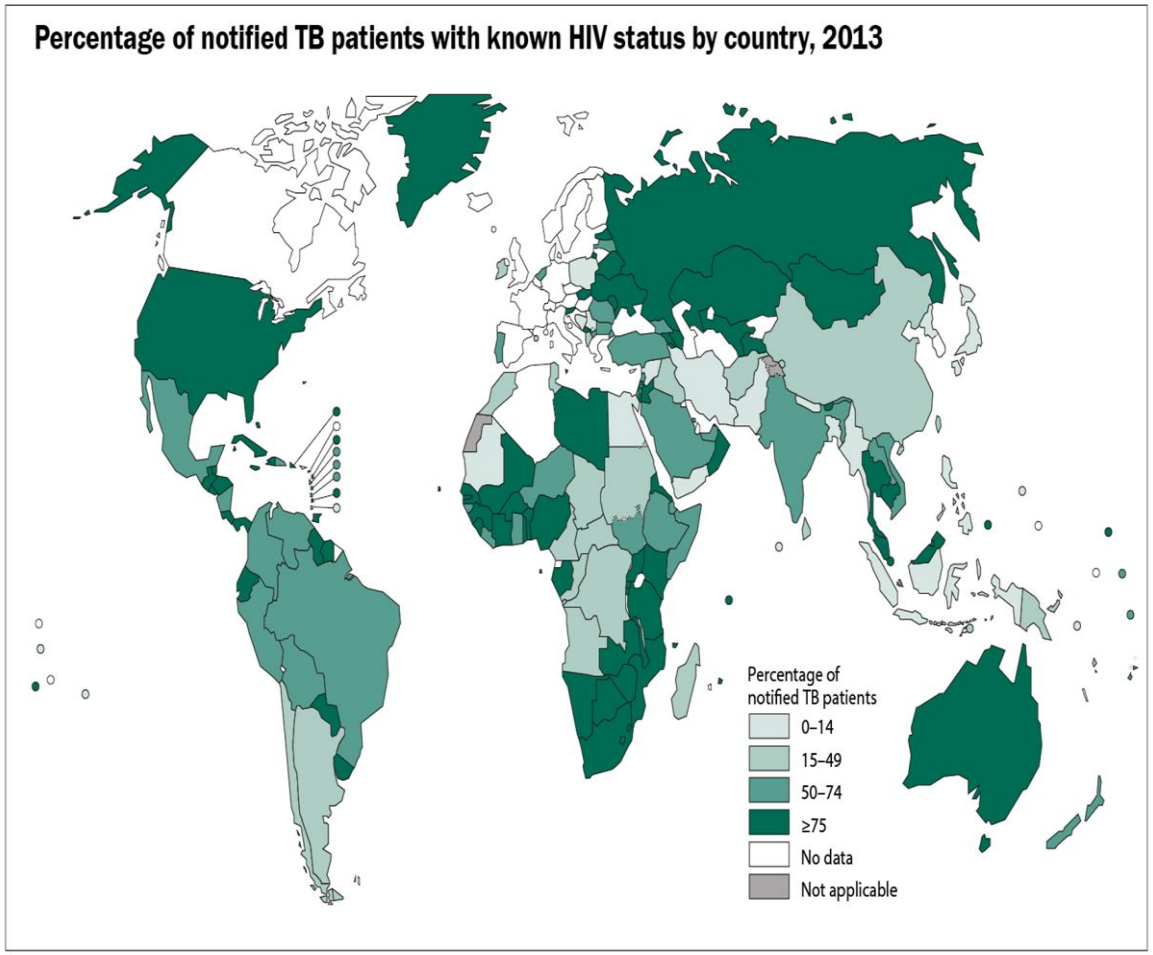
Risk factors for disease are young age, malnutrition and HIV

NIH National Institute of Allergy and Infectious Diseases

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



National Institute of Allergy and Infectious Diseases

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

Stigmatizing Language Article

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**

- Article
- Advocacy Letter
- CRAG Advocacy Campaign
- Webinar
- Community Forum

National Institute of Allergy and Infectious Diseases

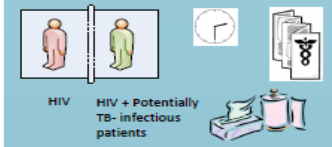
TB-HIV Infection Control Parameters

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



HIV | HIV + Potentially TB- infectious patients

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

Sputum collection

Waiting Area

- Well-ventilated
- Separate from general waiting area
- Written procedures for special precaution for individuals that may be potentially TB infectious

FACILITY Evaluation and Set-up

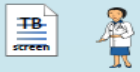
- Air Flow Assessment
- Vent System
- Air Cleaning methods: HEPA, UV Light
- Sufficient Space in Waiting Area
- Planned renovation or new construction

Space Optimization

- Use of PPE (Personal Protective Equipment)
- Use of respirators
- Written procedures for high-risk TB situations (drug-resistant, multi-drug resistant)
- Handwashing Policy
- No-Touch waste bins for tissues

FACILITY HCW (Health Care Workers)

TB Surveillance of (HCW) Health Care Workers



- TB Screening
- Isoniazid therapy availability
- Monitor TB control measures

TB Education for HCWs

- Continuous staff training
- Information (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 Control

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

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

HANC 2015

Surveys conducted under guidance of HANC TBLD-WG (TB Lab Diagnostics Working group) start: 2013. Infection Control measures are for guidance and neither mandated nor punitive.

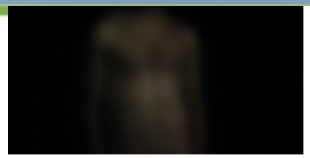
CRAG – CP Mentorship

- 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*

CRAG Resources on TAG Website

http://www.treatmentactiongroup.org/tb/community-engagement/crag



TAG
Treatment Action Group

HOME | HIV | CURE | HCV | TB | BASIC SCIENCE | POLICY | PIPELINE REPORT | TAGLINE | BLOG

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TB ONLINE

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CRAG

SHARE

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.

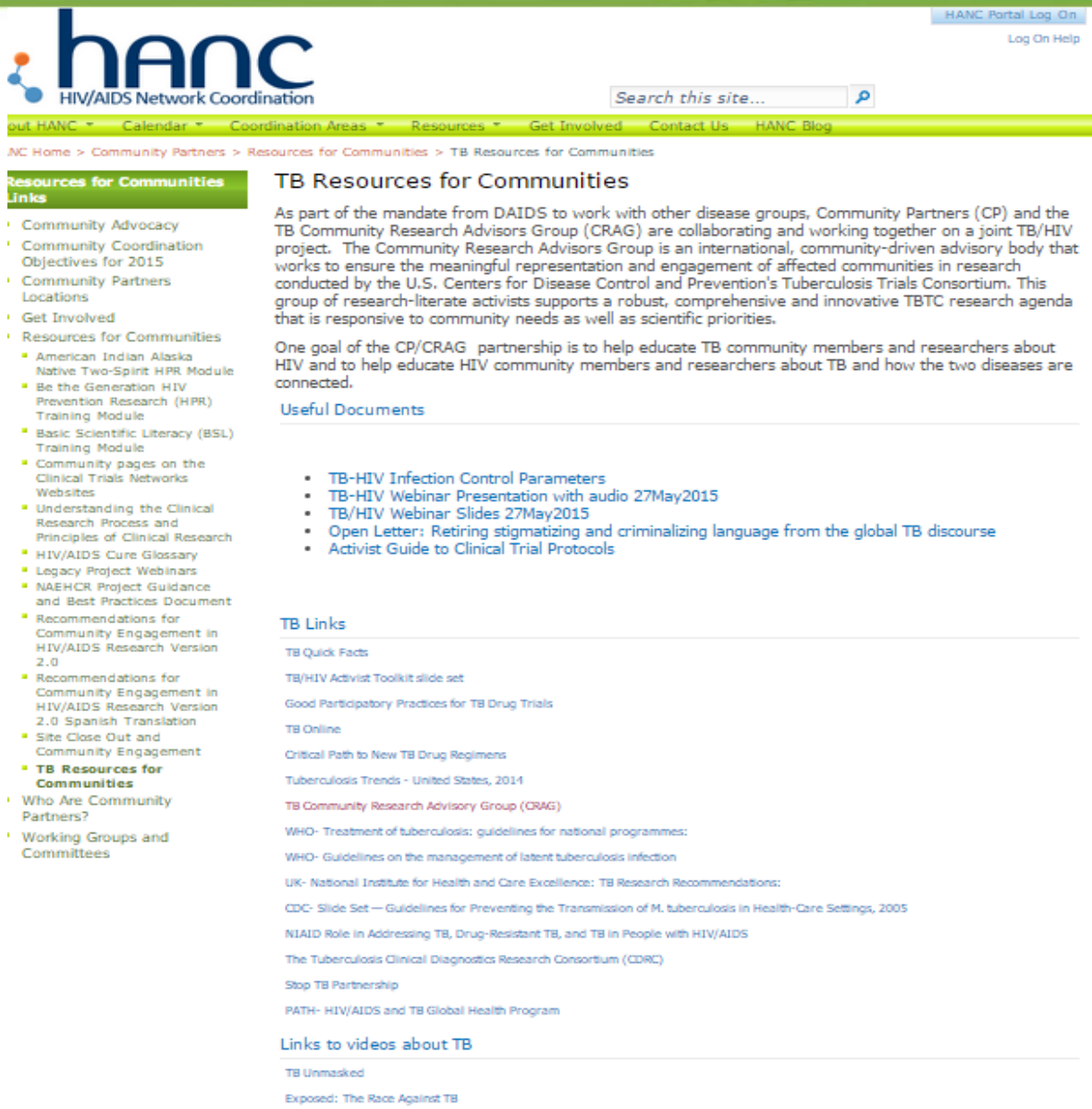
Recent accomplishments of CRAG members include:

- 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.

National Institute of Allergy and Infectious Diseases

TB Resources on HANC Public Site

www.hanc.info



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

National Institute of Allergy and Infectious Diseases

TB-HIV Assessment

USCA 2015 TB/HIV Workshop Assessment

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4.	People living with HIV are less likely to have TB outside of the lungs.	T	F	DK
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