

Test and treat: strategies for both higher and lower resources settings

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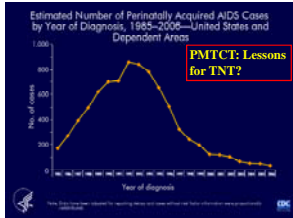
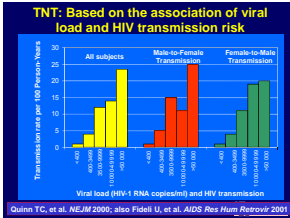
HIV Prevention Trials Network

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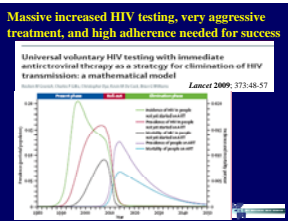


Introduction

- Quinn et al (*N Engl J Med* 2000) and Fideli et al (*AIDS Res Hum Retrovir* 2001) showed that viral load of an infected sexual partner predicted transmission to the uninfected partner
- PMTCT success demonstrates the value of reducing maternal VL with ART to prevent transmission to a child



3. Does HIV therapy started earlier than current standard of care (SOC) benefit the patient in the long run? **HPTN 052/ACTG 5345; INSIGHT START trial**
 - Observational data suggest benefits of earlier ART
 - Kithaha MM et al. *USA N Engl J Med* 2009; 360: 1815-26
 - Reynolds S et al. Uganda, CROI 2009, Abst. 52a
 - Sullivan P et al. Rwanda & Zambia, CROI 2009, Abst. 52bLB
 - When to Start Consortium. 18 cohorts. *Lancet* 2009; 373: 1352-63
 - HOWEVER: Unmeasured confounders likely when including persons who want therapy and whose care providers agreed → RCTs needed
 - International RCT in Haiti: 350 CD4+ cells/μL star had better outcomes than starting at 200 cells (GHESKIO, IAS 2009)



4. Can we better engage hard-to-reach populations? HPTN 061 & 064 in the USA

BROTHERS: Community-Based, Multi-component HIV Prevention Intervention for Black MSM

ISIS HIV Seroincidence Study in Women

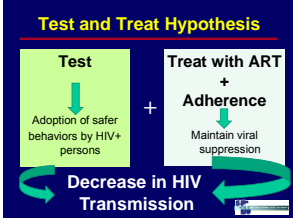
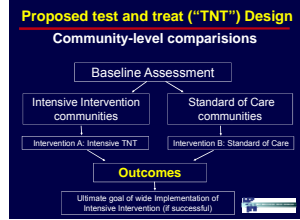
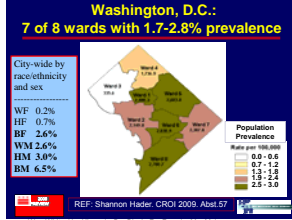
HIV System Navigation (HSN): An Emerging Model to Improve HIV Care Access

- Near peers
- Structured training as per HRSA evaluation
- Finding at-risk persons for testing
- Engagement in testing, bridging to care, adherence to care, retention in care

Methods

GOAL: Decrease in HIV transmission from virally suppressed persons

- Identification of HIV+ persons unaware of their HIV status
 - Risk reduction in HIV+ persons ("Positive Prevention")
- Active bridge to HIV care for ART
 - Both newly diagnosed and any others out-of-care
 - ART eligibility from current guidelines
 - May evolve to earlier ART with results of current work
- Achieve and maintain high ART adherence rates
 - Goal of maximal RNA suppression with high coverage



Discussion

CURRENT EFFORTS HAVE INADEQUATE COVERAGE

- Testing efforts must be expanded substantially
- Linkage of HIV+ to care/sites needs to be ensured
- Achievement & maintenance of viral suppression needs to be enhanced
- Positive prevention efforts must be included
- Measurement of the effectiveness of a package of "TNT" interventions needs careful evaluation
- Comparator communities and evaluations of different approaches are needed

Interventions Needed

- FIND PERSONS WITH HIV AND GET THEM INTO CARE
 - Massive expansion of HIV testing built on existing initiatives
 - Excellent bridging to care
 - Peer navigators or coupon (reward)-based system
 - Aggressive use of ART within current guidelines
- KEEP PERSONS IN CARE BY PROVIDING THE SUPPORT THAT THEY REALLY NEED
 - Positive prevention counseling within the clinic
 - Strong adherence support essential
 - Intervene with co-morbidities to secure needed treatments: alcohol, substance use, mental health, STI/OIs, nutrition

Possible Outcomes

- Primary Outcome for preliminary work:
 - Change in proportion of individuals with suppressed HIV RNA
- Secondary Outcomes (selected):
 - Proportion of risk population tested
 - Change in median CD4+ cell count
 - Change in proportion of newly identified HIV+ engaged in care within 6 months
 - Change in proportion of HIV+ with concomitant diagnosis of HIV and AIDS
 - Estimated HIV incidence (modeled or measured)

Preparatory Activities

- Learn feasible strategies from community members → garner community support
- Estimate the number that need to be tested in each intervention community to have impact
- Map the testing sites and the care and treatment sites → expansions for coverage
- Recruit and train peer workers
- Review data sources → utility for evaluation
- Establish system for sample collection/storage

Test and Treat (TNT)

- A major research-service-training partnership is needed to achieve results
- A PEPFAR/Global Fund partnership would make this research more feasible
- This research agenda is important for both resource-limited settings
- A study of the risks and benefits of much earlier ART is essential

ART for prevention: Some key Research Questions

1. Does expanded HIV testing reduce HIV transmission in a given community?
2. Does ART reduce transmission of HIV to a seronegative sexual partner?
3. Does HIV therapy started earlier than current SOC benefit the patient in the long run?
4. Can we better engage hard-to-reach populations?
5. Can combined testing expansion and bridging to good HIV/AIDS care suppress viral load and reduce HIV incidence?

Work in Progress

HIV PREVENTION TRIALS NETWORK (HPTN)

Project ACCEPT, HPTN 052/ACTG 5245, HPTN 061/HPTN 064, New "test and treat" proposal

1. Does expanded HIV testing reduce HIV transmission in a given community? HPTN 043

A Phase III RCT of Community Mobilization, Mobile Testing, Same-Day Results, and Post-Test Support for HIV in sub-Saharan Africa and Thailand (HPTN 043)

- 48 Communities Randomized to intensive VCT advocacy or standard VCT
 - 36 in rural Zimbabwe, Tanzania, & South Africa
 - 6 in urban South Africa; 14 in northern Thailand
- Massive community mobilization
 - >56,000 samples for seroconversion estimates in the full intervention
 - Study completion in 2010

2. Does ART reduce transmission of HIV to a seronegative sexual partner? HPTN 052

- RCT of ART to prevent the sexual transmission of HIV in serodiscordant couples (12 sites, Africa/Asia)
 - Randomize persons with 350-550 CD4+ T lymphocytes to early treatment vs. SOC
 - N=1750 couples; 65% enrolled to date
 - Outcome: Seroconversion in primary sexual partners
 - Study fully accrued in early 2010