The HIV Prevention Trials Network (HPTN) and the International Maternal Pediatric Adolescent AIDS Clinical Trials Group (IMPAACT)

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Research Advocacy Workshop
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Notes: NIAID has the most money of the NIH groups, and funds these trial networks: It's recently been restructured. Some of the leading lights such as the MTN (microbicides) split, and the Mother-to-child transmission and the pediatric treatment people ran off together (IMPAACT).

IMPAACT

- merger of the Pediatric AIDS Clinical Trials Group (PACTG) and the Perinatal Scientific Working Group of the HIV Prevention Trials Network (HPTN).
- mission is to significantly decrease the mortality and morbidity associated with HIV disease in pregnant women, children, and adolescents in the US and worldwide by:

1) Developing and evaluating safe and cost effective approaches for the interruption of mother-to-infant transmission
2) Evaluating treatments for HIV-infected children, adolescents, and pregnant women, including treatment and prevention of co-infections and co-morbidities
3) Evaluating vaccines for the prevention of HIV sexual transmission among adolescents

There has been some grumbling about IMPAACT maintaining a full roster of domestic sites given small numbers of pediatric/adolescent cases and decreased maternal-to-child transmission in the US

Notes: HPTN doesn't have a lot of money. There are some grumbling about IMPAACT, not much perinatal transmission in the U.S. anymore, why do they still need so many sites? There are still a lot that needs to be investigated around the world, such as breast milk substitutions.

HPTN

- Worldwide collaborative clinical trials network that develops and tests the safety and efficacy of primarily non-vaccine interventions designed to prevent the transmission of HIV.

Notes: HPTN is what's left, after the other networks splited off. I call it the "everything else prevention network", or the 'Stigma Network" -- sex and drugs. That may be one of its problems.

HPTN in the US

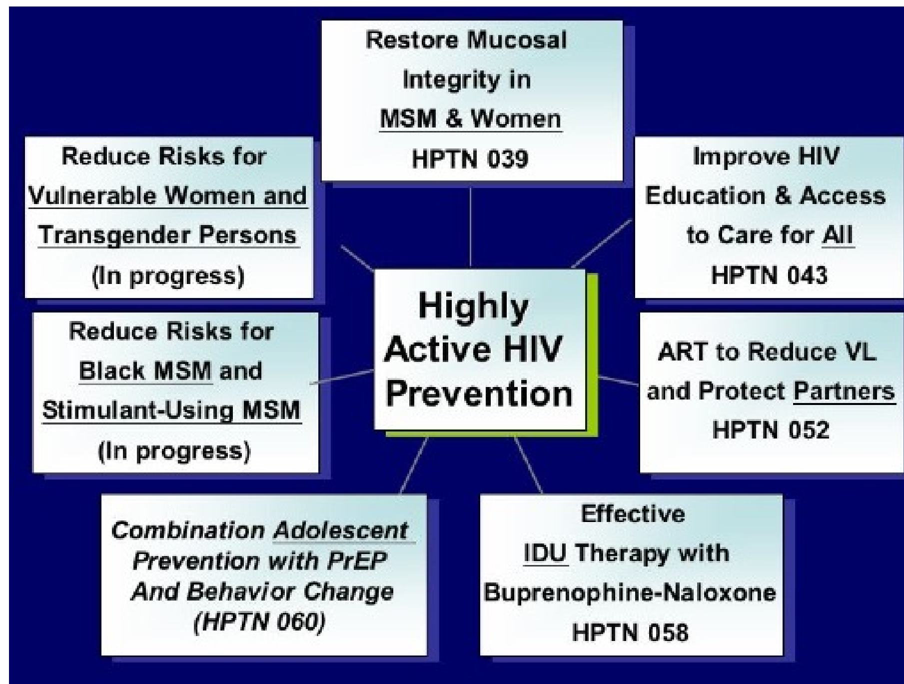
- ❖ In the refunding process, all but one US site were eliminated
- ❖ Other sites were approved as “qualified reserves” that could be eligible for studies but that have no continuity or maintenance funds
- ❖ Two sites -- Boston and NYC -- were later given some funds to coordinate process of proposing domestic research
- ❖ The HPTN has been working with other NIH institutes and CDC to develop proposals for a domestic agenda

Notes: In the US, after the other trial networks split off, there was a refunding process. HPTN was left with one site in Seatlle. LA, SF, Atlanta don’t have sites anymore, they were closed. Some prevention sites are OK to have trials but there is not money to maintain the site, pay staff, etc. They are called “Qualified reserves” -- sort of like being pre-qualified for a mortgage because your credit is good, but you don’t have any money. These sites looks good, can probably do a trial, except they don’t have a trial, and no money for maintenance and upkeep. So they are all sub-primed out.
After protest by CHAMP and others, two sites were given some money to follow along and make proposals.

They need to fork over money for prevention research. As advocates we shouldn’t have to say, “take the money from something else.” We need them to put more money in. This is what prevention justice is about, one of the 3 Rs is Research.

HPTN Domestic Agenda

Excerpts from the HPTN Domestic Prevention Working Group presentation to the HPTN Executive Committee
November 1, 2007
Thank you to Sten Vermund for sharing these slides



Notes: This is their concept of how to do prevention.
HPTM proposals for trials (mostly outside of the United States) –
domestic adolescent women and young MSM (killed because it needs a lot of money, and we don't know if PREP works yet and you want to try it in adolescents? It also combines multiple major ideas into one in a way that might not work),
stimulant-using MSM (this was killed because it is too much about gay and drugs).
Based on CHAMP and others bugging them, they have integrated transwomen as a category recently. This is evidence that advocacy works.

What Do We Know?

- Localized rather than generalized epidemic
- Evidence of recent infection
- Populations at risk for HIV without reported high risk behaviors
- Populations most severely affected unlikely to be aware of HIV status
- Blacks with known HIV infection, less likely to benefit from advances in ART

Building a Domestic Agenda

- Need to focus on key populations at risk defined by:
  - Geographic "hot spots"
  - Specific behaviors (e.g. MSM)

- Rather than focusing on identifying individuals as per their risk behaviors, need to emphasize characteristics of their partners and sexual networks

Control of HIV in context of a concentrated US epidemic

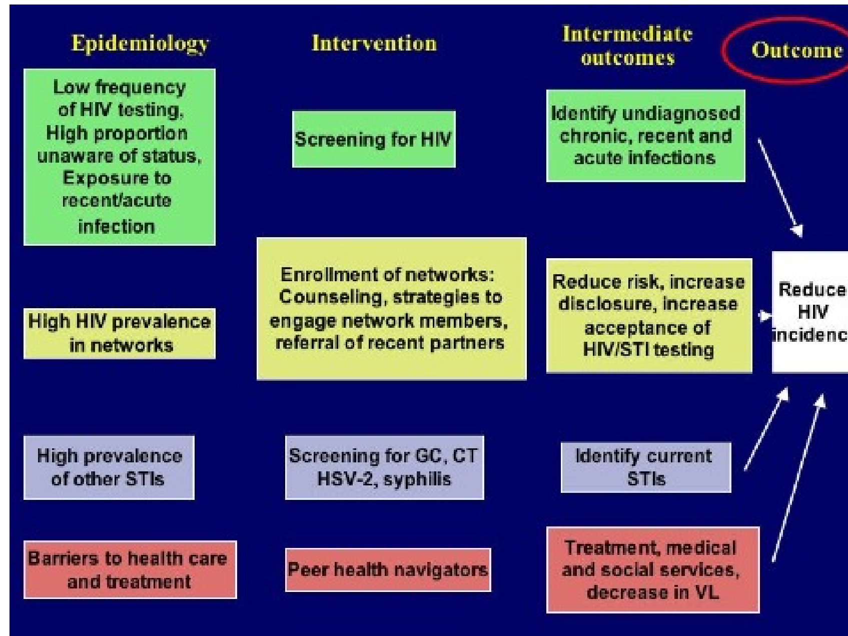
- Target high risk persons
- Tailor interventions specifically:
  - Black MSM
  - *Stimulant-using MSM (italics added)*
  - Black and Hispanic highest risk women and transgender population
  - *Adolescent MSM (HPTN 060 with ATN) (italics added)*

Notes: Italics means it's not happening.

U.S. has one of the worst epidemics in the world. But it's unrecognized because it's in geographic hot spots, neighborhoods and people who are stigmatized. Despite not having more risky acts or even as many sex partners. Rather than focusing on individual behaviors, What environmental factors contribute to higher risk?

They are looking at research into risk of Black MSM, Black and Latina highest risk women and trans people.

Feasibility study of a community-level, multi-component intervention for Black men who have sex with men



Notes: Why do Black MSM have higher risk? One of their answers is # unaware of status, so they do testing, does that reduce incidence? This hasn't even been tried to see if it works yet. So little has been done and this population is so unattended, we know so little. Formative research on basic information has to be done before we can decide what the big study should be in Black MSM.

HIV System Navigation: An Emerging Model to Improve HIV Care Access
- Bradford et al, AIDS Patient Care & STDs 21: 2007

HSN's have been shown to increase engagement in care resulting in improved clinical outcomes

What is Health System Navigation

A Health System Naviga-

Can be a...	But is *not*
✓ Buddy	✓ Case manager
✓ Sounding board	✓ Mental health specialist
✓ Facilitator to health care	✓ Permanent solution
✓ Guide	
✓ Coach	
✓ Advocate	
✓ Case finder	
✓ Resource	
✓ Someone who "teaches you how to fish"	

Overview of 4 Stages

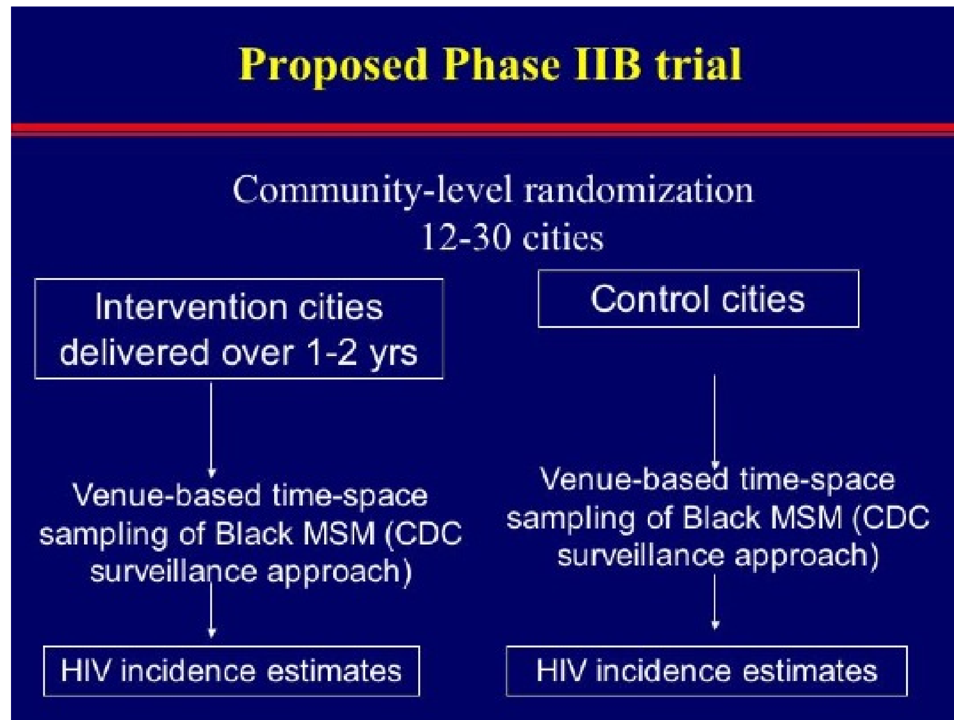
Stage 1 Engage
1. Identify clients
2. Introduce Health System Navigation to Clients
3. Introduce the SPNS research study to clients
4. Prescreen clients for eligibility

Stage 2 Assessment
5. Enroll client into the SPNS study
6. Review intake to get the big picture
7. Help them create an Action Plan

Stage 3 Action Plan
8. High intensity Action Plan intervention
9. Low intensity Action Plan intervention

Stage 4 Monitoring
10. Follow-up on progress, help if needed

Proposed Phase IIB trial
Community-level randomization 12-30 cities



Notes: One proposal idea is to have control cities instead of control groups. One city gets the intervention and another doesn't.

What needs to be known before initiating a Phase IIB Study?

- Will it be possible to mobilize sufficient numbers of Black MSM to join the study?
- What will motivate Black MSM to join?
- Will Black MSM refer their network partners, and will the referred partners enroll?
- How will recruitment strategies be adapted in different communities: NYC vs North Carolina vs. Atlanta?
- What are the best estimates of intervention effect?
- Will the intervention be feasible and acceptable to Black MSM?
- Will Black MSM accept HIV & STI testing?
- Will peer health system navigators be acceptable to Black MSM resulting in increased utilization of services?
- Is STI treatment and Counseling acceptable in this setting?
- Will research centers partner effectively with local CBOs in this intervention?
- Will community leadership locally and nationally be supportive?

Notes: There are a lot of initial questions that needs to be answered first. What they're proposing to do next – smaller study (feasibility study) working with small community-based orgs to get more information. Who else do you hang out with? Find out more about their lives. Bring your friends in. Social network to find out how to do the work with these groups as a clinical trial.

Feasibility Study

- Each site to enroll 100 Black MSM over 6 months, focusing on those likely to have undiagnosed HIV infection, working closely with Black MSM NGO's
  - Venue based outreach
  - Key informants, opinion leaders

- Enrollment Criteria
  - 18 or older; UAI with a man in last 6 months

- Participants would fill out a questionnaire asking about sexual practices, types of partners, substance use, social and sexual networks, and be tested for HIV/STI.
- Index participants would be asked to enumerate up to 20 social and sexual network members
- More detailed questions about each network member
- The first 25 HIV+ and the first 25 HIV- men at each site would be asked to bring in up to 5 of their network members who are Black MSM
  - Questionnaire about motivators/barriers to referrals
  - Training for index on how to engage network members
- These network members will be offered participation in the study with similar questionnaire and HIV/STI testing
- All participants with new clinical and social problems would be offered the assistance of a peer health system navigator
- Three month follow-up visit would be scheduled.

Feasibility Study Could determine:
Intervention practicality:

- Enrollment
- Number of network members completing a visit
- Acceptance of HIV/STI testing
- Identification of undiagnosed HIV/STI infections
- Performance of peer navigators and pilot training modules
- Uptake of treatment and other services

Estimates of intervention effectiveness:

- % of HIV- men who have exposure risk through network members
- % HIV+ identified and linked into care and risk reduction
- Change in sexual risk behaviors over 3 mos.

Many US CTUs are well-situated to do this trial
HPTN Qualified Reserve Sites in cities with large Black MSM populations (N >250,000)
Can also engage other CRS with large Black MSM communities

Atlanta	27,923	Baltimore	46,438
Boston	7,234	Los Angeles	28,577
Memphis	11,408	New York	82,825
Philadelphia	28,112	RT/Wake Co.	6,247
San Diego	4,253	San Francisco	12,494

Notes: Back to the "Qualified Reserved sites" - These are where black gay men are!

Women's ISIS (HIV seroincidence study)

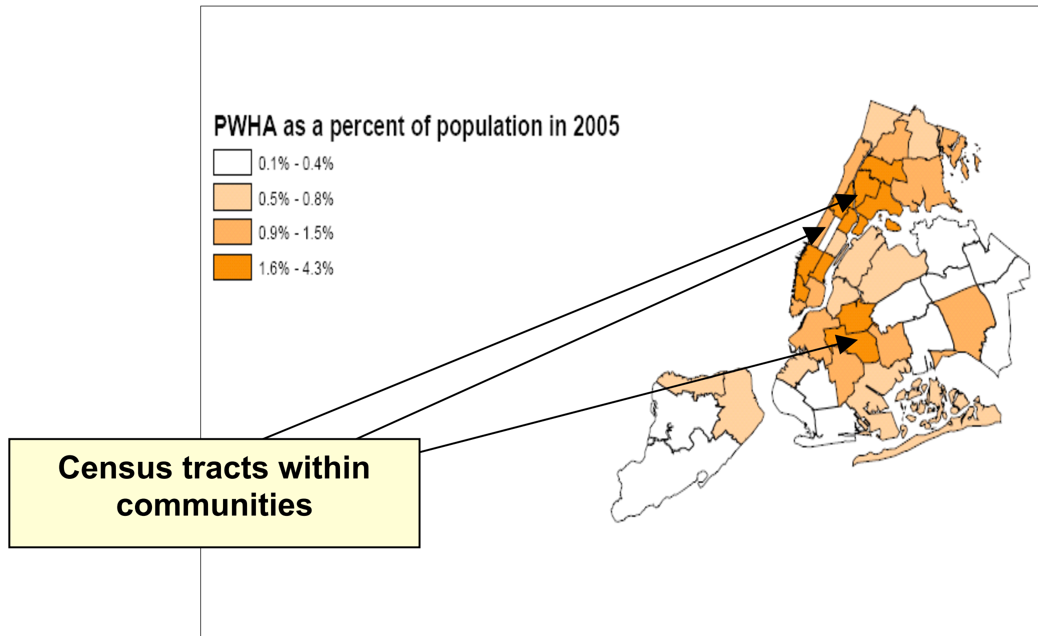
- ❖ Limited HIV incidence data exist for U.S. women, impeding design of rigorous HIV prevention studies
  - o Assess feasibility of HIV seroincidence as 1º endpoint for any US prevention study

- ❖ Choice of communities guided by CDC National HIV Behavioral Survey using census tracts based on mingling of poverty levels and high HIV prevalence

- ❖ Communities selected on census tracts (CDC National HIV Behavioral Survey) where high poverty levels intersect high HIV prevalence

- ❖ Enrollment criteria for women from selected census tracts to include individual and partner characteristics

Notes: Women's study – also a feasibility study, even less is known. They know very little about who are the highest risk groups. One of the leading concept is to look at formerly incarcerated women. This is an example from NYC. Census-tracked neighborhoods of high HIV incidence. Within these communities, look at enrollment criteria (individual characteristics and that of their partners) What are next steps in having feasibility studies? Hope to have an idea of the full study based on the findings from the feasibility studies, in 2009-2010.



Next Steps

Feasibility studies in MSM will focus on…

- ❖ working through specifics of intervention
- ❖ assessment of feasibility of recruiting and retaining elusive populations of African American and Substance-using MSM

For ISIS…

- ❖ Consultation with HVTN/MTN in Seattle next week (HVTN meeting) and further design development

Anticipate full Phase 3 trial proposals in 2009-10

Notes: Only $3 million for these feasibility studies have been pledged. Maybe enough to do one of these studies. None of it through NIAID, which has the most money. (it's coming from NIMH, mental health). Wafah El-Sadr is planning the women's study (ISIS). They don't even know what they're researching yet. So women from NYC, I would encourage you to get involved in that, it's an opportunity to get involved in planning on the ground floor.

Black MSM trials are a little further along, and are having conference calls.
You've got to be in the game to play.

We've got to have resources and coordination to do research advocacy. CHAMP doesn't have the capacity to do that now, but it needs to be done. If you want to help think that through and you know funders or networks that want to be part of that, please talk to us. It can happen if we make it happen. When I started doing prevention activism, I was shocked how little prevention activism there was. Now I'm newly shocked about how little is known in prevention research. If we don't even know the incidence we're starting with, how do we know if we're getting anywhere? As community advocates, it's okay if we don't have all the answers. Part of the answers will come from research and part will come from social revolution.