



HIV PREVENTION TRIALS NETWORK

NIMH Project Accept (HPTN 043)

**A CLUSTER-RANDOMIZED TRIAL OF COMMUNITY
MOBILIZATION, MOBILE HIV TESTING, POST-TEST SUPPORT
SERVICES, AND REAL-TIME PERFORMANCE FEEDBACK FOR
HIV PREVENTION IN ENTIRE COMMUNITIES**



It's Been a Remarkable Few Years for HIV Prevention

Study

Treatment for prevention

(Africa, Asia, Americas)

PrEP for discordant couples

(Partners PrEP)

PrEP for heterosexuals

(Botswana TDF2)

Medical male circumcision

(Orange Farm, Rakai, Kisumu)

PrEP for MSMs

(Americas, Thailand, South Africa)

STD treatment

(Mwanza)

Microbicide

(CAPRISA 004 tenofovir gel)

HIV Vaccine

(Thai RV144)

Effect size (CI)

96% (73; 99)

73% (49; 85)

63% (21; 48)

54% (38; 66)

44% (15; 63)

42% (21; 58)

39% (6; 60)

31% (1; 51)



NIMH Project Accept (HPTN 043) Ushers in A New Era of HIV Prevention Research

- HIV prevention in entire communities and not only in study cohorts—beyond proof of concept to community effectiveness
- Combination prevention bringing together synergistic and not antagonistic elements
- Saturating communities with interventions likely to reduce HIV transmission
- Ensuring that saturation takes place
- Providing convincing data that the entire communities, and not just specially recruited cohorts, are affected
- Maintaining effects (should they be achieved) over time

What We Found

Comparing intervention vs. control communities we found that:

- **Rates of testing were higher in intervention communities**
 - Especially among men and young people
- **Number of sexual partners and multiple partners were lower in intervention communities**
 - Especially among HIV-infected individuals
 - And among HIV-infected men
- **Diagnoses of HIV infection (and especially previously undiagnosed HIV infections) were higher in intervention communities**
- **Social norms regarding the importance of testing were higher in intervention communities**
- **Modest reductions in HIV incidence occurred in intervention vs. control communities**
 - Especially among women in the 24-32 age range

Implications

NIMH Project Accept (HPTN 043) demonstrated that it is possible to:

- **Implement interventions in entire communities and to see those effects**
- **Achieve process goals**
 - Although it takes a fair bit of effort and attention and cannot be expected to occur “because we provide it and they will come”
- **Produce outcomes for entire communities**
 - And not just for those enrolled in cohorts

Implications

NIMH Project Accept (HPTN 043) demonstrated that it is possible to:

- **Reach men and young people with HIV preventive interventions—a major problem in sub-Saharan Africa**
- **Increase testing and identification of previously undiagnosed cases of HIV infection**
- **Produce reductions in HIV incidence—giving hope that combination prevention approaches may be able to reduce HIV incidence**

Two Approaches to HIV Voluntary Counseling and Testing (VCT)

Community-based VCT (CBVCT)

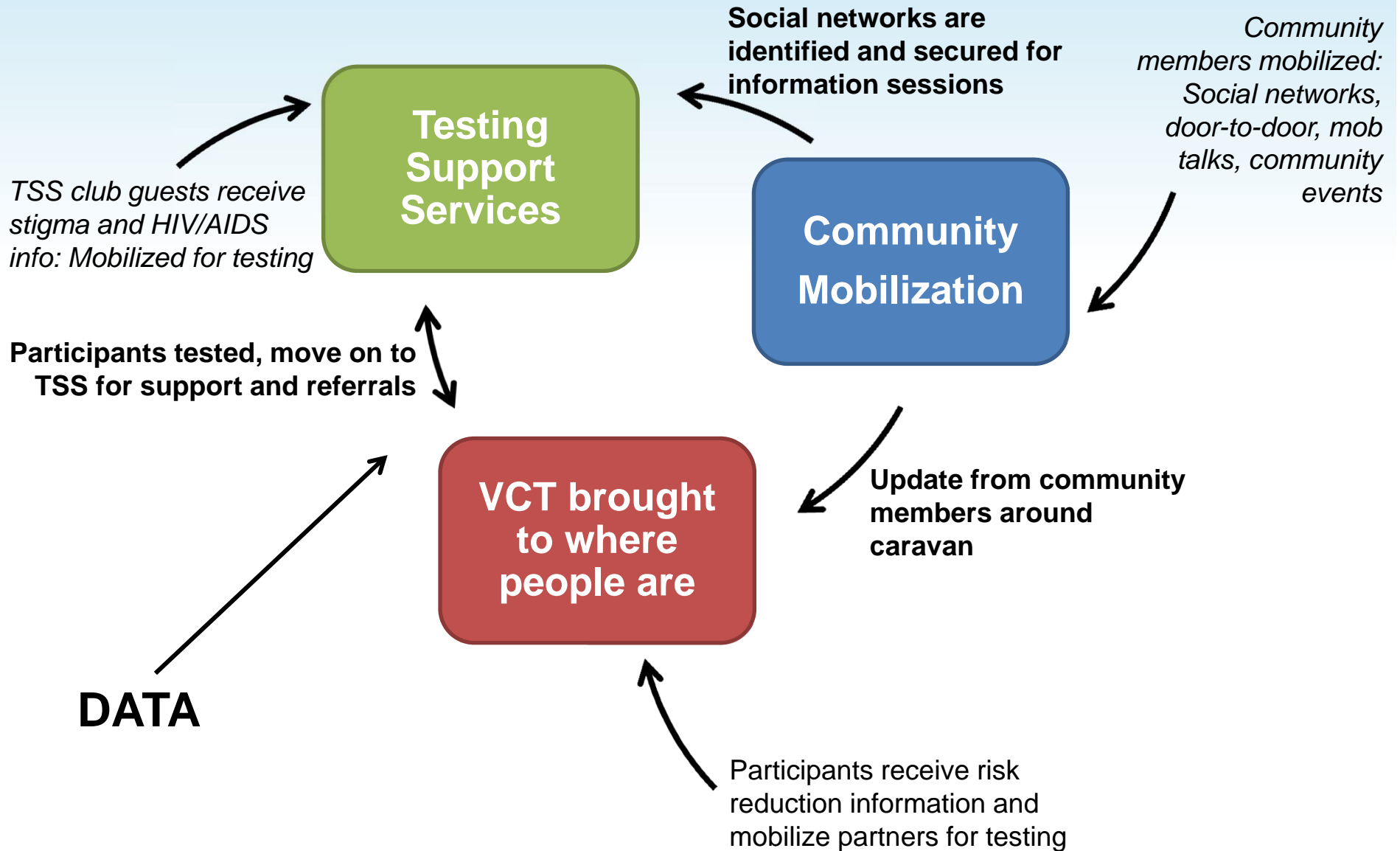
1. Community preparation, outreach, mobilization
2. Mobile VCT
3. Post-test support services
 - a. Stigma-reduction skills training
 - b. Coping effectiveness training
 - c. Ongoing counseling
4. Ongoing data feedback and field adjustments

Standard VCT (SVCT)

1. Clinic-based VCT
2. Standard VCT services normally provided in that community

Van Rooyen et al, AIDS and Behavior, 2012

THE COMPLETE INTERVENTION PACKAGE





1. Community Mobilization

The intervention was designed to change community norms related to HIV awareness, particularly the benefit of knowing one's HIV status.

2. Increased Access to VCT

The intervention was designed to remove barriers to knowing one's HIV status and to reinforce the goal of making testing more normative.



3. Post-test Support Services

The intervention was designed to increase safety and minimize the potential negative consequences of testing by providing various types of support.



4. Real-Time Performance Feedback

The intervention was designed to ensure that milestones were set for each of the intervention components, and that utilization data was continuously examined to ensure that milestones were being met as the intervention components were implemented.



NIMH PROJECT ACCEPT (HPTN 043) STUDY SITES



Study Sites (N = 48 communities)

Kisarawe District, Tanzania

- Very rural
- 10 communities; SVCT provided by project

Hill Tribe Areas near Chiang Mai, Thailand

- Very rural SNF2
- 14 communities; SVCT from available clinics

Vulindlela, KwaZulu-Natal, South Africa

- Rural
- 8 communities; SVCT from available clinics

Soweto, South Africa

- Urban
- 8 communities; SVCT from available clinics

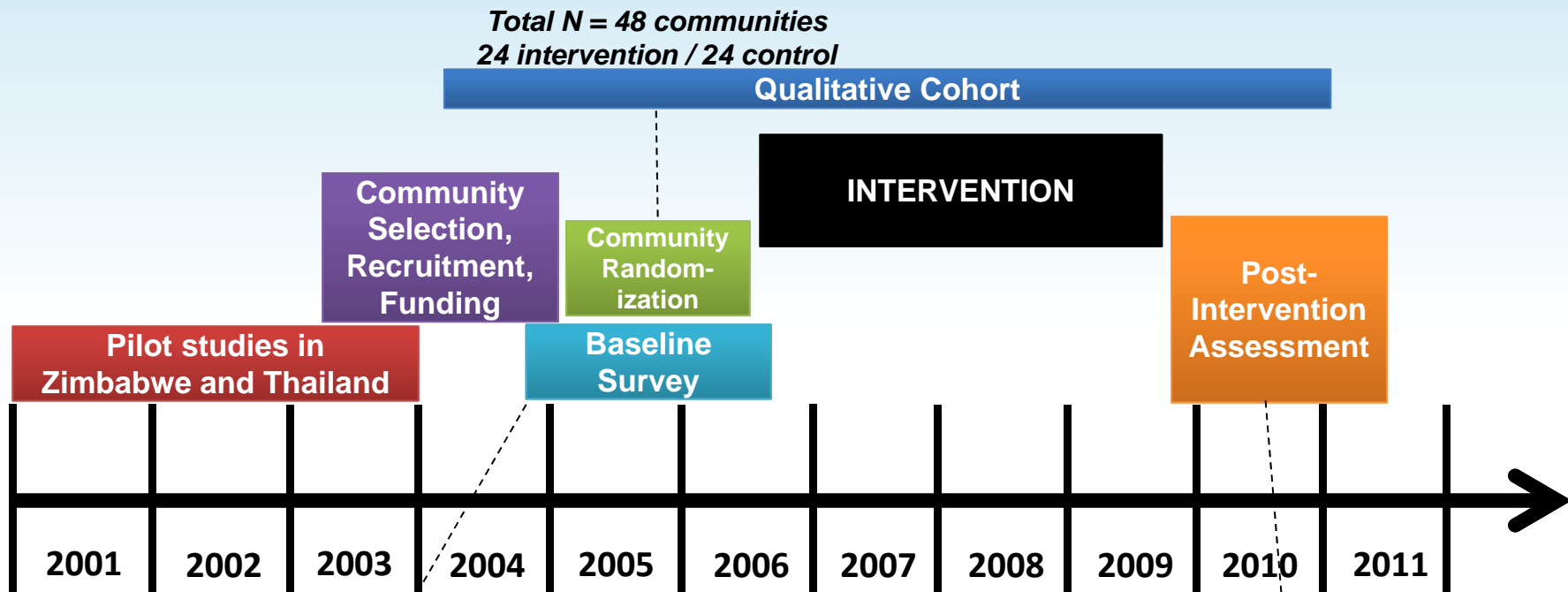
Mutoko, Zimbabwe

- Very rural
- 8 communities; SVCT provided by project

Study Sites: Randomization

- Communities were matched into pairs based on socio-demographic, cultural, and infrastructure characteristics available from preliminary formative research.
- Within each pair, one community was randomly assigned to intervention and one to comparison conditions.
- The randomization was performed centrally and the assignment was not blinded due to the nature of the intervention.

Study Design: Timeline



- *Probability sample of 18-32 year olds*
- *Survey only*

- *Assessment of a random sample of 18-32 year olds in each intervention and control community*
- *Behavioral survey*
- *Biologic assays to estimate HIV incidence*

ALL OF THIS RESULTED IN:

86,720 HIV tests

**69,987
in CBVCT
communities**

**7,636
in SVCT
communities**

**50,000 individuals
when repeat tests are excluded**

140,755 post-test support visits

Study Design

- Outcomes were evaluated among a probability sample of community residents of 18 to 32 years of age, not only those who participated in the intervention

Overall results

Country	Prevalence	Incidence	Total Site Population
South Africa--Soweto	14.1		302,500
South Africa--Vulindlela	30.8		133,300
Mutoko, Zimbabwe	12.9		169,600
Kisarare, Tanzania	5.9		109,800
Thailand	1.0		205,700

Validation Sample Set Used to Select a Testing Algorithm

- Samples and data from 7 clinical studies
- Known infecting subtypes: A, C, and D
- 5,325 samples from 3,436 individuals
 - Known duration of infection (1 month to >10 years)
 - CD4+ cell count data available
- Tested with the BED-CEIA and an avidity assay
- Subset tested for HIV viral load

Analysis of Study Samples

- HIV rapid testing and CD4 testing performed in country
- Further testing performed at the HPTN Network Laboratory
 - >30,000 samples shipped and analyzed
 - Quality assurance testing
 - Confirmation of HIV status
 - Identified contamination problem in Soweto
 - HIV subtyping (confirmed low prevalence of subtype D in Tanzania)
 - >7,600 HIV-infected samples identified
 - BED-CEIA, avidity, viral load, and ARV testing
- Incidence estimate based on BED-CEIA, avidity, VL, CD4
- ARV-positive samples excluded from incidence calculation

Evaluation of HIV Incidence

- Incidence estimated by a multi-assay incidence algorithm (MAA) that included BED-CEIA, avidity assay, viral load, and CD4
 - Developed, validated, and evaluated for this purpose
- HIV rapid testing and CD4 testing performed in country
- Further testing performed at the HPTN Network Laboratory
- ARV-positive samples excluded from incidence calculation
- Thailand excluded from incidence analysis (low prevalence)

Statistical Methods

- Incidence estimated by the MAA in each community (window period 0.71 years)
- Overall intervention effect estimated by weighted average of log incidence ratios between matched pairs of intervention and control communities
 - Weights were proportional to the harmonic mean of the number of recent infections in the paired communities
 - Pairs with larger number of recent infections get larger weight in the analysis
- Intervention effect tested by weighted paired t-test on log incidence
- Confidence intervals were based on the weighted paired t-statistic

Overall results (89% response rate)

Subgroup	Effect ^a	95% CI	p-value
All participants	0.86	0.73 – 1.02	0.0822
Women	0.88	0.73 – 1.06	0.1691
Men	0.81	0.57 – 1.15	0.1934
Age 18-24 years	0.98	0.80 – 1.22	0.8554
Age 25-32 years	0.75	0.54 – 1.04	0.0777
Women, age 18-24 years	1.00	0.78 – 1.28	0.9833
Women, age 25-32 years	0.70	0.54 – 0.90	0.0085
Men, age 18-24 years	0.95	0.64 – 1.40	0.6934
Men, age 25-32 years	0.78	0.41 – 1.47	0.3914

^a Relative risk of infection (CBVCT vs. SVCT); weighted incidence ratio

What We Found

Incidence Reduction

- There was an overall reduction in incident HIV infections of 13.9%
 - Relative Risk [RR] = 0.86
 - 95% confidence interval [CI]: 0.72-1.02
 - $p = 0.08$

What We Found:

Incidence Reduction

- The reduction in incidence in women over 24 years of age was 30.2%
 - RR = 0.70
 - 95% CI: 0.54 – 0.90
 - $p < 0.01$
- There was no change in HIV incidence among women under 24 years of age (RR = 0.98)

What We Found

Increased Testing and Case Finding

- The intervention increased HIV testing by 45% among men and 15% among women
 - Rates of testing were highest among men and young people
 - Many women had been tested in antenatal clinics but the increase was still significant

What We Found:

Increased Testing and Case Finding

- The intervention produced an almost 4-fold increase in the detection of previously undiagnosed HIV cases
 - This was true at all of the 3 sites where differential utilization could be assessed

What We Found:

Reductions in Unprotected Sex

- The intervention reduced the number of sexual partners reported by HIV-infected individuals by 8%
 - 95% CI: 1% - 16%
 - $p = 0.03$
- This effect was primarily due to an 18% reduction in number of sexual partners among HIV-positive *men* (95% CI = 5% to 28%, $p = .009$).

1. What We Found: Reductions in Unprotected Sex

- Multiple sexual partners were reported less frequently among HIV-infected individuals in the intervention
 - RR = 0.70
 - 95% CI: 0.54 – 0.92
 - $p = 0.01$

 - Among HIV-infected men
 - RR = .71
 - 95% CI: 0.57 to 0.89
 - $p = .0006$

What We Found:

The Intervention was Safe

- The intervention was safe
- There was no increase observed in negative effects of the intervention in communities
 - This included no increase in violence towards women as a result of learning their HIV status

Implications

NIMH Project Accept (HPTN 043) demonstrated that it is possible to:

- Implement interventions in entire communities
- To evaluate results for the entire community
 - Not just those enrolled in cohorts

Implications

NIMH Project Accept (HPTN 043) demonstrated that it is possible to:

- Effectively engage men in community-based HIV testing programs
 - In fact, the intervention was especially effective in reaching men, with both increased HIV testing and greater reductions in HIV risk behavior among HIV-positive men (compared to control).

Implications

NIMH Project Accept (HPTN 043) demonstrated that it is possible to:

- Achieve process goals
 - Although this requires a fair bit of attention and effort

Implications

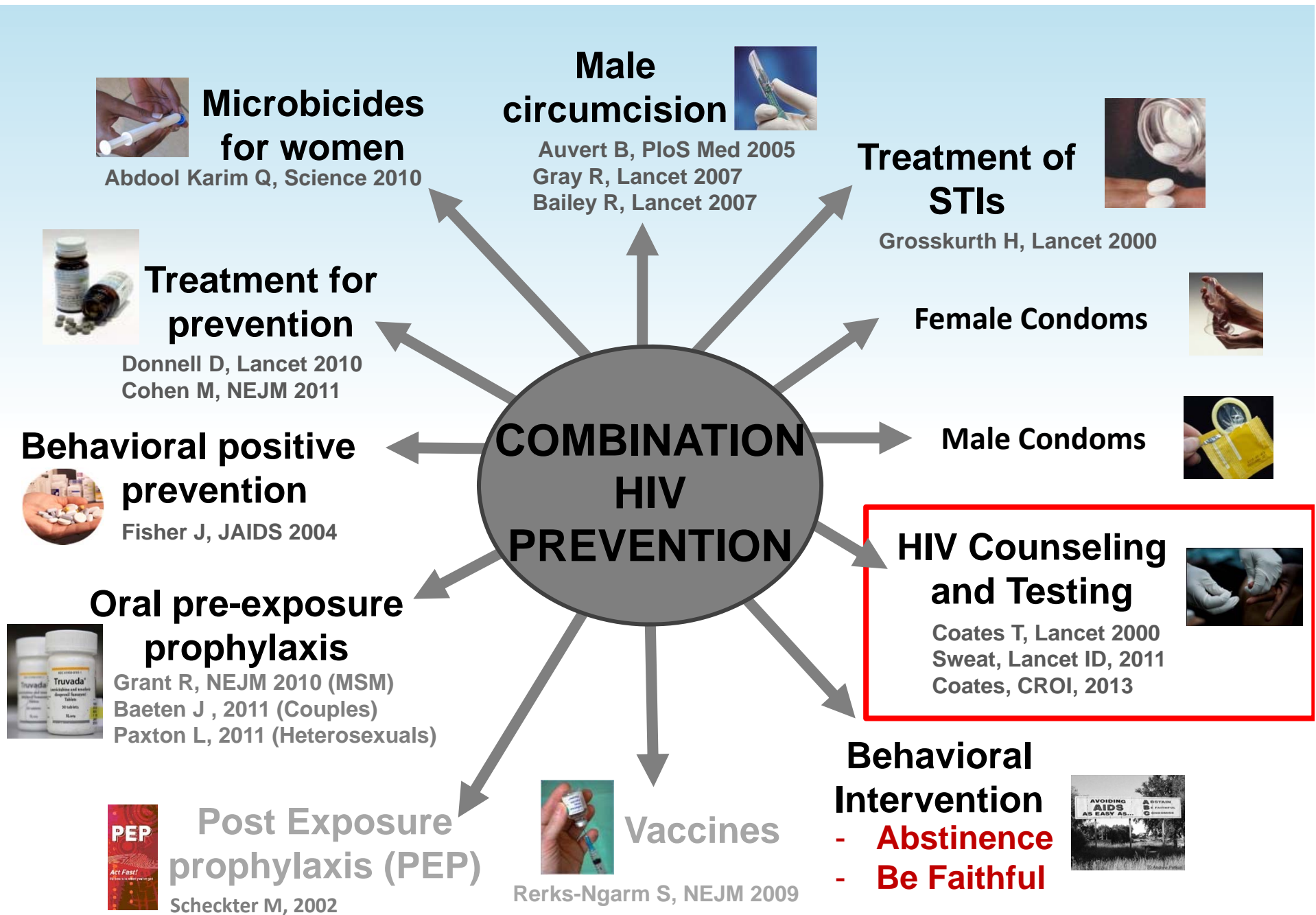
NIMH Project Accept (HPTN 043) demonstrated that it is possible to:

- Increase testing and identification of previously undiagnosed cases of HIV infection
 - Especially among men and young people

Implications

NIMH Project Accept (HPTN 043) demonstrated that it is possible to:

- Produce modest reductions in HIV incidence
 - This suggests that the addition of other components — referral and maintenance in care, early treatment, male circumcision, pre-exposure prophylaxis — might be successful in achieving greater reductions in HIV incidence in entire communities.



Note: PMTCT, Screening transfusions, Harm reduction, Universal precautions, etc. have not been included – this is focused on reducing sexual transmission

Collaborators: NIMH Project Accept (HPTN 043)

- Principal Investigators
 - Soweto, South Africa: Thomas Coates / Glenda Gray
 - Tanzania: Michael Sweat / Jessie Mbwambo
 - Thailand: David Celentano / Suwat Chariyalertsak
 - Vulindlela, South Africa: Thomas Coates / Linda Richter / Heidi van Rooyen
 - Zimbabwe: Steve Morin / Alfred Chingono
- NIMH Cooperative Agreement Project Officer: Chris Gordon
- Core Lab: Susan Eshleman/Estelle Piwowar-Manning
- Statistical Core: Michal Kulich, Deborah Donnell

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