HIV Prevention: A Global Priority

Wafaa El-Sadr, MD, MPH
ICAP, Columbia University
Pneumocystis Pneumonia — Los Angeles

In the period October 1980–May 1981, 5 young men, all active but not homosexual, were treated for biopsy-confirmed *Pneumocystis carinii* pneumonia at 3 hospitals in Los Angeles, California. Two of the patients died. All 5 patients had cytomegalovirus (CMV) infection and one had toxoplasmosis.
RARE CANCER SEEN IN 41 HOMOSEXUALS

Outbreak Occurs Among Men in New York and California — 8 Died Inside 2 Years

By LAWRENCE K. ALTMAN

Doctors in New York and California have diagnosed among homosexual men 41 cases of a rare and often rapidly fatal form of cancer. Eight of the victims died less than 24 months after the diagnosis was made.

The cause of the outbreak is unknown, and there is as yet no evidence of contamination. But the doctors who have made the
Global Number of People Living with HIV, by year

Millions

Source: Avert.org / UNAIDS
Middle East & North Africa: 460,000
Caribbean: 240,000
Eastern Europe & Central Asia & South America: 1.4 million
Central & South America: 1.4 million
North America & Western/Central Europe: 2.3 million
Asia: 4.9 million
Sub-Saharan Africa: 22.5 million

Adapted from Good magazine
Life Expectancy in Africa

UN Department of Economic and Social Affairs (2001) World Population Prospects, the 2000 Revision.
Life Expectancy in Africa

UN Department of Economic and Social Affairs (2001) World Population Prospects, the 2000 Revision.
One World One Hope

Vancouver 1996
Expansion of Treatment and Deaths from HIV in the US

HIV Treatment (% of patient-days)


Palella et al, NEJM 1998
Expansion of Treatment and Deaths from HIV in the US

Deaths

HIV Treatment

Deaths per 100 Person-Years

HIV Treatment (% of patient-days)


Palella et al, NEJM 1998
Global Scale-Up of HIV Treatment

- End of 2002
- End of 2003
- End of 2004
- End of 2005
- End of 2006
- End of 2007
- End of 2008
- End of 2009
- End of 2010

Millions

0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
Scale-Up of ART & AIDS-Related Deaths

- People receiving antiretroviral therapy
- People dying from AIDS-related causes

Deaths in PEPFAR-Supported Countries in Africa

Mortality per 1,000 adults


PEPFAR Supported

Adapted Bendavid et al. CROI2012
Deaths in PEPFAR-Supported Countries in Africa

- Deaths per 1,000 adults
- Y-axis: 0 to 9
- Line graph showing a decrease in deaths over time for PEPFAR Supported countries, with a precipitous drop starting in 2004.
- Other countries line also shows a decrease, but at a slower rate.

Adapted from Bendavid et al. CROI 2012
HIV Treatment and Worker Productivity

Average days of work / month

Months relative to initiation of HIV treatment

Adapted Larson et al, 2008
HIV Treatment and Worker Productivity

Average days of work / month vs. Months relative to initiation of HIV treatment

HIV treatment started

Adapted Larson et al, 2008
2.5 million people infected every year
7,000
New infections every day
1,000 in children
We can’t treat our way out of this epidemic
Plasma HIV RNA Levels and HIV Rates in Discordant Couples

Transmission rate per 100 Person-Years

Viral load (HIV-1 RNA copies/ml) and HIV transmission

Quinn TC, et al. NEJM 2000
Maternal ART and Perinatal HIV Transmission--US
WITS: 1990-2004

WITS Cooper et al, JAIDS 2002
ART Use and New HIV Diagnoses--
British Columbia, Canada

Adapted Montaner et al, Lancet 2010

Number of Patients on ART

Number of New HIV Diagnoses

New HIV Diagnoses (All)

On ART

New HIV Diagnoses (ever IDU)

Year

January 2004

P=0.003

P=0.954

P=0.001

P=0.002

P=0.026

January 2004
Sero-Discordant Couples
# Use of ART and HIV Incidence: Observational Studies in Discordant Couples

## Study or Subgroup | Rate Ratio (95% CI) |
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Del Romero 2010</td>
<td>0.21 [0.01, 3.75]</td>
</tr>
<tr>
<td>Donnell 2010*</td>
<td>0.08 [0.01, 0.57]</td>
</tr>
<tr>
<td>Melo 2008</td>
<td>0.10 [0.01, 1.67]</td>
</tr>
<tr>
<td>Musicco 1994</td>
<td>0.88 [0.36, 2.16]</td>
</tr>
<tr>
<td>Reynolds 2011</td>
<td>0.10 [0.01, 1.64]</td>
</tr>
<tr>
<td>Sullivan 2009</td>
<td>0.21 [0.08, 0.56]</td>
</tr>
<tr>
<td>Wang 2010</td>
<td>1.44 [0.85, 2.44]</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>0.34 [0.13, 0.92]</strong></td>
</tr>
</tbody>
</table>

* Linked transmissions

Adapted-Anglemyer et al Cochrane Reviews 2011
Genital and Plasma HIV RNA and Risk of HIV Transmission

Female-Male HIV Transmission

Male-Female HIV Transmission

Baeten et al. Sci.Transl Med 2011
HPTN 052 Study: Design

HIV-infected
CD4 350 to 550 cells/µL
HIV discordant partner

Randomization

Immediate ART
350-550 cells/µl

Deferred ART
CD4 <250>200

Couples received intensive counseling on risk reduction and use of condoms

Primary Transmission Endpoint: Linked transmissions
Primary Clinical Endpoint: WHO stage 4, Pulmonary TB, Severe bacterial infection or Death
HPTN 052 Study: Key Prevention Finding

1,763 sero-discordant couples (97% heterosexual) HIV infected partners: 890 men, 873 women

39 HIV Transmissions
- 28 linked HIV transmissions
- 11 unlinked transmissions

Immediate ART: 1 transmission
Deferred ART: 27 transmissions

☑️ 96% Protection
Early H.I.V. Therapy Sharply Curb Transmission

By DONALD G. McNEIL Jr. 
Published: May 12, 2011

The New York Times

On Thursday, Dr. F...
We can treat our way out of this epidemic
What would be the impact of treatment of discordant couples on the HIV Epidemic?
<table>
<thead>
<tr>
<th>Country</th>
<th>Population</th>
<th>HIV prevalence</th>
<th>Percent discordant couples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesotho</td>
<td>2,067,000</td>
<td>19.5%</td>
<td>13.6%</td>
</tr>
<tr>
<td>Rwanda</td>
<td>9,998,000</td>
<td>1.7%</td>
<td>3.1%</td>
</tr>
<tr>
<td>Malawi</td>
<td>15,263,000</td>
<td>7.1%</td>
<td>9.7%</td>
</tr>
<tr>
<td>Ghana</td>
<td>23,837,000</td>
<td>0.9%</td>
<td>2%</td>
</tr>
</tbody>
</table>
Effect of ART for Discordant Couples on *HIV incidence* and *Number of Infections Prevented* at Population Level

Country-Level Incidence/1000 py

<table>
<thead>
<tr>
<th>Country</th>
<th>Lesotho</th>
<th>Malawi</th>
<th>Rwanda</th>
<th>Ghana</th>
</tr>
</thead>
<tbody>
<tr>
<td>ART Coverage</td>
<td>10%</td>
<td>20%</td>
<td>30%</td>
<td>40%</td>
</tr>
<tr>
<td>Annual Number</td>
<td>10,000</td>
<td>20,000</td>
<td>30,000</td>
<td>40,000</td>
</tr>
<tr>
<td>of Infections</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prevented</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

70% Stable Partners

El-Sadr, Coburn, Blower, AIDS 2011
What would be the effect of scale-up of HIV treatment on HIV epidemic?
Could widespread use of combination antiretroviral therapy eradicate HIV epidemics?

J X Velasco-Hernandez, H B Gershengorn, and S M Blower

Modelling the effect of combination antiretroviral treatments on HIV incidence

Matthew G. Law, Garrett Prestage, Andrew Grulich, Paul Van de Ven, and Susan Kippax

Universal voluntary HIV testing with immediate antiretroviral therapy as a strategy for elimination of HIV transmission: a mathematical model

Reuben M Granich, Charles F Gilks, Christopher Dye, Kevin M De Cock, Brian G Williams

A Mathematical Model of Comprehensive Test-and-Treat Services and HIV Incidence among Men Who Have Sex with Men in the United States

Stephen W. Sorensen, Stephanie L. Sansom, John T. Brooks, Gary Marks, Elizabeth M. Begier, Kate Buchacz, Elizabeth A. DiNenno, Jonathan H. Mermin, Peter H. Kilmarx
Lower Risk of HIV Acquisition With expanded ART Coverage

- Hlabisa, South Africa: rural community with 24% adult HIV prevalence
  - 20,000 pts started on ART since 2004
- 1413 seroconversions observed; HIV incidence estimated according to time-adjusted ART coverage in local community

*Adjusted for age, sex, community-level HIV prevalence, urban vs rural locale, marital status, > 1 partner in last 12 mos, and household wealth index.

Tanser F, et al. CROI 2012
What is Needed to Achieve Population Impact of ART for Prevention

- Test HIV Positive
- Adopt safer behaviors
- Enroll in Care
- Linkage to care
- Treat
- Maintain viral suppression
- Initiation of ART
- Adherence to ART

Decrease in HIV Transmission
The Continuum of HIV Care--US

Of all with HIV infection, 850,000 individuals do not have suppressed HIV RNA (72%)

MMWR (60), 2011
## HPTN 043—Community HIV Testing

<table>
<thead>
<tr>
<th></th>
<th>Tanzania</th>
<th>Zimbabwe</th>
<th>Thailand</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBVCT Plus</td>
<td>6250</td>
<td>10,700</td>
<td>11,270</td>
</tr>
<tr>
<td>SVCT</td>
<td>6733</td>
<td>12,150</td>
<td>10.033</td>
</tr>
<tr>
<td>Population</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>size</td>
<td>6250</td>
<td>10,700</td>
<td>11,270</td>
</tr>
<tr>
<td>First time</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV test</td>
<td>37%</td>
<td>52%</td>
<td>69%</td>
</tr>
<tr>
<td></td>
<td>9%</td>
<td>5%</td>
<td>23%</td>
</tr>
</tbody>
</table>

Sweat et al. Lancet 2011
### Source of HIV Testing and CD4+ Cell Count

<table>
<thead>
<tr>
<th></th>
<th>Home-based</th>
<th>VCT</th>
<th>PITC</th>
<th>TB</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number tested</strong></td>
<td>946</td>
<td>10,261</td>
<td>8,073</td>
<td>272</td>
</tr>
<tr>
<td><strong>Percent female</strong></td>
<td>72%</td>
<td>66%</td>
<td>62%</td>
<td>50%</td>
</tr>
<tr>
<td><strong>Mean CD4+ in HIV+ (cells/mm³)</strong></td>
<td>323 (194-491)</td>
<td>217 (87-404)</td>
<td>190 (70-371)</td>
<td>136 (59-266)</td>
</tr>
<tr>
<td><strong>Missing data</strong></td>
<td>23%</td>
<td>45%</td>
<td>52%</td>
<td>38%</td>
</tr>
<tr>
<td><strong>WHO III or IV</strong></td>
<td>14%</td>
<td>38%</td>
<td>46%</td>
<td>79%</td>
</tr>
<tr>
<td><strong>Missing data</strong></td>
<td>26%</td>
<td>18%</td>
<td>23%</td>
<td>19%</td>
</tr>
</tbody>
</table>

Adapted-Wachira et al, CID 2012
CD4+ Count at Entry into Care -- HOPS

Buchacz et al, AIDS Research and Treatment 2012
Factors associated with late diagnosis

- Not being MSM OR: 1.99
- Age $\geq 35$ OR: 2.14
- Not white race/ethnicity OR: 1.45

Buchacz et al, AIDS Research and Treatment 2012
Factors Associated with Initiation of ART at Higher CD4+ cell counts- San Francisco

<table>
<thead>
<tr>
<th>At CD4&gt;500 cells/mm³</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MSM</td>
<td>0.003</td>
</tr>
<tr>
<td>Non poor</td>
<td>0.005</td>
</tr>
<tr>
<td>Diagnosed by private provider</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>At CD4&gt;350 cells/mm³</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Older</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>White</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MSM</td>
<td>0.012</td>
</tr>
<tr>
<td>Non-poor</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Truong et al. CROI 2012
Retention in ART Programs

- 36 cohorts
- 226,307 patients
- All losses except transfers

Retention:
- 6 months: 86.1%
- 12 months: 80.2%
- 24 months: 76.8%
- 36 months: 72.3%
HIV Care/Prevention Continuum

Test

HIV Positive

Link

Engage, Counsel, Monitor, and Support

HIV Care (PRE-ART)

ART Eligible

Retain, Counsel, Monitor, and Support

ART

Adherence and Viral Suppression
Test, Link to Care Plus Treat
HPTN 065 (TLC-Plus Study)
To evaluate the feasibility of an enhanced community-level HIV test, link-to-care plus treat strategy in the U.S.
HPTN 065 (TLC Plus): Study Design

- Expanded HIV Testing
  - Social Mobilization
  - Universal offer of testing in ED/hospital admission

- Linkage to Care
  - 38 Randomized HIV Test Sites to link HIV positives
  - Financial incentive plus SOC
  - Standard of care (SOC)

- HIV Care Sites

- Treat
  - Initiate ART per current guidelines

- Maintain viral suppression

- 39 Randomized HIV Care Sites
  - Financial incentive plus SOC
  - Standard of care f(SOC)

- Prevention for Positives - Select Sites

- Individual randomization
  - 660 patients in 2 communities
  - CARE plus Standard of Care
  - Standard of Care
<table>
<thead>
<tr>
<th>Study</th>
<th>HPTN 071 (PopART)</th>
<th>Iringa /JHU Study</th>
<th>TasP-ANRS</th>
<th>Botswana/HSPH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Principal investigator</td>
<td>• Richard Hayes (PI)</td>
<td>• David D. Celentano (PI)</td>
<td>• Francois Dabis &amp; Marie-Louise Newell PIs</td>
<td>• Max Essex (PI)</td>
</tr>
<tr>
<td>Funder</td>
<td>• NIAID, NIMH, OGAC, BMGF</td>
<td>• USAID, OGAC</td>
<td>• ANRS</td>
<td>• CDC, OGAC</td>
</tr>
<tr>
<td>Country</td>
<td>Zambia &amp; South Africa</td>
<td>Tanzania</td>
<td>South Africa</td>
<td>Botswana</td>
</tr>
<tr>
<td>Design</td>
<td>Cluster RCT</td>
<td>Cluster RCT</td>
<td>Cluster RCT</td>
<td>Paired cluster-RCT</td>
</tr>
<tr>
<td>Clusters</td>
<td>• 24 (15 Zambia, 9 in SA)</td>
<td>• 24 total clusters</td>
<td>• 34 total clusters</td>
<td>• 30 total clusters</td>
</tr>
<tr>
<td></td>
<td>• ~55,000 per cluster</td>
<td>• ~10,000 per cluster</td>
<td>• 1,250 per cluster</td>
<td>• 5,000 per cluster</td>
</tr>
<tr>
<td>Study arms</td>
<td>Three arm</td>
<td>Two arm</td>
<td>Two arm</td>
<td>Two arm</td>
</tr>
<tr>
<td>Interventions</td>
<td>• Home-based C&amp;T, mobile &amp; clinic-based C&amp;T</td>
<td>• HIV testing, care and ART for CD4&lt; 350</td>
<td>• Home-based C&amp;T</td>
<td>• Home-based C&amp;T</td>
</tr>
<tr>
<td></td>
<td>• Male circumcision</td>
<td>• Male circumcision</td>
<td>• Immediate ART initiation for all</td>
<td>• ART for CD4&lt;350, WHO I/II or HIV RNA &gt;10,000</td>
</tr>
<tr>
<td></td>
<td>• Risk reduction counseling &amp; condom provision</td>
<td>• Cash transfer - women</td>
<td>• ART for CD4&lt;350, WHO I/II or HIV RNA &gt;10,000</td>
<td>• Male circumcision</td>
</tr>
<tr>
<td></td>
<td>• Immediate ART to all HIV+</td>
<td>• BCC</td>
<td>• Key groups FSW, MSM)</td>
<td>• PMTCT (option B)</td>
</tr>
<tr>
<td>Primary outcome</td>
<td>HIV incidence over 2 yrs</td>
<td>HIV incidence at 2 yrs</td>
<td>HIV incidence at 2 yrs</td>
<td>HIV incidence 2 yrs</td>
</tr>
<tr>
<td>How measured</td>
<td>Prospective cohort</td>
<td>Prospective cohort</td>
<td>Prospective cohort</td>
<td>Prospective cohort</td>
</tr>
<tr>
<td>Estimated annual HIV incidence</td>
<td>1.17% (Zambia), 1.49% (SA)</td>
<td>1.0 per 100 py</td>
<td>2.5%</td>
<td>±1.5% (15-49 yrs)</td>
</tr>
</tbody>
</table>
Examples of clusters
Red dots = health clinics
Purple dots = hot spots (bars, truck stops, hotels)
Striped areas = PMTCT catchment areas
Location: Southwest central Tanzania
Iringa District, Iringa Region, Tanzania

Botswana- CDC

Iringa Study- USAID

TASP- Africa Centre ANRS

HPTN 071 –NIH PopART
Balancing the Individual and Society

PLWH

Society

Risks versus Benefits

Health Systems
Ethics
Equity
Resources

Risks versus Benefits
DHHS Guidelines Guidelines, 2012: When to Start

- ART recommended for all HIV-infected patients; strength of recommendation varies according to CD4+ cell count.

<table>
<thead>
<tr>
<th>CD4+ Cell Count</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 350 cells/mm³</td>
<td>Start ART (AI)</td>
</tr>
<tr>
<td>350-500 cells/mm³</td>
<td>Start ART (AII)</td>
</tr>
<tr>
<td>&gt; 500 cells/mm³</td>
<td>Start ART (BIII)</td>
</tr>
</tbody>
</table>

Strength of recommendation:
- A: Strong
- B: Moderate
- C: Optional

Quality of evidence:
- I: ≥1 randomized controlled trials
- II: ≥1 well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes
- III: Expert opinion

DHHS Guidelines for Antiretroviral Therapy in Adults and Adolescents. March 27, 2012.
HIV Disease Progression and Death by CD4+ cell Count

Rate, events per 100 person/years

Death, AIDS, or severe non-AIDS
Death or AIDS
Death

Anglaret et al. CID 2011
HIV Disease Progression and Death by CD4+ cell Count

Rate, events per 100 person/years

- Death, AIDS, or severe non-AIDS
- Death or AIDS
- Death

Anglaret et al. CID 2011
HPTN 052 Study: Key Finding

1,763 sero-discordant couples (97% heterosexual) HIV infected partners: 890 men, 873 women

105 Clinical Events

Immediate ART: 40 Events
Deferred ART: 65 Events

41% Reduction in Clinical Events

TB (17 versus 33 cases)
Extrapulmonary TB (3 versus 17 cases) ($P = .002$)

START Study

HIV-infected
ART-naïve
CD4+ count > 500 cells/mm³

Early ART Group
Initiate ART immediately
N=2,000

Deferred ART Group
Defer ART until the CD4+ count declines to < 350 cells/mm³ or AIDS
N=2,000

Endpoints: Serious AIDS Event
Non-AIDS Events or Death

Strategic Timing of AntiRetroviral Treatment
In all, 238 Clinical Research Sites in 35 countries
With 68 sites in US and Puerto Rico
68 Clinical Research Sites in the U.S. and Puerto Rico
Clinical Trials for Prevention of Sexual Transmission of HIV

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Positive Effect</th>
<th>Adverse Effect</th>
<th>No Effect</th>
<th>Number of trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Behavioral</td>
<td>-</td>
<td>7</td>
<td></td>
<td>7</td>
</tr>
<tr>
<td>Structural</td>
<td>1</td>
<td>2</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>Male circumcision</td>
<td>3</td>
<td>1</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>STI treatment</td>
<td>1</td>
<td>8</td>
<td></td>
<td>9</td>
</tr>
<tr>
<td>Vaccine</td>
<td>1</td>
<td>3</td>
<td></td>
<td>4</td>
</tr>
<tr>
<td>PrEP (Topical microbicides)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non ARVs</td>
<td>-</td>
<td>1</td>
<td>11</td>
<td>12</td>
</tr>
<tr>
<td>ARVs</td>
<td>1</td>
<td></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>PrEP (Systemic, oral)</td>
<td>3</td>
<td>3</td>
<td></td>
<td>6</td>
</tr>
</tbody>
</table>

Adapted Padian et al. Lancet 2011
Pre-Exposure Prophylaxis (PrEP)
Efficacy of Topical and Oral PrEP

- Oral FTC/TDF and Oral TDF for HIV serodiscordant couples (Partners PrEP) in Kenya, Uganda: 73% (49; 85)
- Oral FTC/TDF for young heterosexuals (TDF2) in Botswana: 63% (22; 83)
- Oral FTC/TDF for MSM (iPreEx) in Americas, Thailand, SA: 44% (15; 63)
- 1% tenofovir vaginal gel in SA: 39% (6; 60)
- Oral FTC/TDF for women (FEM-PrEP) in Kenya, SA, Tanzania: 0% (-69; 41)

Adapted, Abdool Karim 2011
FDA Advisory Committee Supports Approval of Gilead’s Truvada® for Reducing the Risk of Acquiring HIV
Published: May 11, 2012

Taking Truvada to Prevent H.I.V. Also Comes With Risks
Published: May 14, 2012

U.S. debates recommending drug for AIDS prevention
Adherence and HIV Acquisition-- iPrEx

<table>
<thead>
<tr>
<th>Group</th>
<th>HIV Conversions per PY (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>4.2%</td>
</tr>
<tr>
<td>BLQ</td>
<td>3.6%</td>
</tr>
<tr>
<td>Above BLQ</td>
<td>0.5%</td>
</tr>
<tr>
<td>Overall</td>
<td>2.4%</td>
</tr>
</tbody>
</table>

Birnkrant, FDA 2012
Relative risk in reduction

- Never measurable: -6.5%
- Sometimes measurable: 58.9%
- Always measurable: 93.9%
- Overall: 75.1%

TFV Level

Adherence and HIV Acquisition–Partners PrEP Study

Birnkrant, FDA 2012
Infected *Cases* and Matched *Controls* with ≥10 ng/ml Tenofovir in Plasma at Visits Defining Infection Windows

**Time of infection**

- **Window Start**
  - Cases: ?
  - Controls: ?
  - P = 0.63

- **Window End**
  - Cases: 25.9%
  - Controls: 21.2%
  - P = 0.12

- **Both Visits**
  - Cases: 25.7%
  - Controls: 35.1%
  - P = 0.60

Adapted Van Damme et al, CROI 2012
Pre-Exposure Prophylaxis (PrEP)
HIV Prevention Continuum
HIV Negative Individuals

Test

- Negative

Link

Engage, Counsel, and Support

Counsel, Intervene, Monitor and Support

Support Adherence, Monitor, Repeat HIV testing

- Pre-Exposure Prophylaxis, Male Circumcision, Condoms
Efficacious Interventions

**Effectiveness and Safety of Tenofovir Gel, an Antiretroviral Microbicide, for the Prevention of HIV Infection in Women**

Quarraisha Abdool Karim, et al.

*Science* 329, 1168 (2010)

DOI: 10.1126/science.1193748

**PIVOTAL STUDY FINDS THAT HIV MEDICATIONS ARE HIGHLY EFFECTIVE AS PROPHYLAXIS AGAINST HIV INFECTION IN MEN AND WOMEN IN AFRICA**

**Prevention of HIV-1 Infection with Early Antiretroviral Therapy**

Myron S. Cohen, M.D., Ying Q. Chen, Ph.D., Marybeth McCauley, M.P.H., Theresa Gamble, Ph.D., Mina C. Hosseinipour, M.D., Nagalingeswaran Kumarasamy, M.B., B.S., James G. Hakim, M.D., Johnstone Kumwenda, F.R.C.P., Beatriz Grinsztejn, M.D., Jose H.S. Pilotto, M.D., Sheela V. Godbole, M.D., Suresh Mah煅ndih, M.D., Swamth Shrivastava, M.D., P. Rose, P. Santos, M.D., Kenneth H. Mayer, M.D.
Combination Prevention

Leadership and scaling up of treatment/prevention efforts

Highly active HIV prevention

Behavioural change

Treatment/antiretroviral/STI/antiviral

Biomedical strategies

Social justice and human rights

Community involvement

Coates et al. Lancet 2008
Contribution by Key Populations to the HIV Epidemic

UNAIDS, 2010

Percent new infections

Lesotho  |  Kenya  |  Swaziland  |  Uganda  |  Zambia

Other  |  Sex Work  |  IDU  |  Prison population (measured only in Kenya)  |  MSM  |  Multiple partners  |  Stable heterosexual couples
Conclusions-I

• Substantial achievements in the response to the HIV epidemic
• New prevention tools offer promise for control of HIV transmission
• Further efforts are needed to define how best to use these interventions:
  – Defining risks and benefits for individuals
  – Optimizing every step of the continuum of care and prevention
  – Determining efficacy of various interventions in specific populations
Conclusions-II

• Need for other efficacious interventions (vaccine, structural, behavioral)

• Research design challenges ahead
  – Design of studies in key hard to reach populations
  – Defining the population impact of various prevention interventions
  – Assessment of impact of combination strategies for prevention
  – Defining which interventions to be prioritized by various communities and countries

• Much remains to be done:
  – 6 million people need ART now for their own health
  – 2.5 million new infections annually
Thank you