Combination prevention for HIV
How to evaluate whether it works?

Marie Laga
Institute of Tropical Medicine
Antwerp, Belgium
Preventing HIV includes...

Create an enabling environment

Reduce Exposure
behavior change

Reduce Transmissibility
condoms, ART, mc..

Empowerment
Norms & laws

Services & Systems

Stigma reduction
HIV prevention: human behaviour at the center

• Negotiating and using condoms
• Adopting safer sex
• Accepting to be tested for HIV
• Adhering to ART, PrEP or condom use
• Seeking health care for Male circumcision
• Overcoming stigma to seek care
UNAIDS (2010) provides the following definition of combination HIV prevention:

“The strategic, simultaneous use of different classes of prevention activities (biomedical, behavioral, social/structural) that operate on multiple levels (individual, relationship, community, societal), to respond to the specific needs of particular audiences and modes of HIV transmission, and to make efficient use of resources through prioritizing, partnership, and engagement of affected communities.”
The biomedical approaches robust RCT evidence

Randomized, Controlled Intervention Trial of Male Circumcision for Reduction of HIV Infection Risk: The ANRS 1265 Trial
Bertran Auvert et al, Plos 2005
"What works" in Behaviour change or Community Empowerment?
Community RCTs on impact of multi-component behavioral Interventions : no effect on HIV incidence


Possible Explanations for flat results in c-RCT?

- Control group: *Compared to what?*
- The intervention too “weak”? *The trial design lead to fit the intervention to the trial*
- The power to detect an effect? *HIV rare event*
- Low or heterogeneous “uptake” of the interventions?
- Long and complex pathway between interventions and endpoint?
- Context specificities

Is intervention truly ineffective or evaluation method inappropriate?
The evidence dilemma

- “Scientific rigour = good quality RCT” require tightly defined interventions, preferably with a short impact pathway, which tends to limit HIV prevention to biomedical approaches only.

- Combination prevention including also social movements, advocacy, education, social mobilisation, are likely to be more powerful, but impractical to prove evidence, because less-well-defined and longer more complex impact pathway.
The Evidence dilemma

• C-RCT : gold standard for evaluation of combination prevention programs?

• Absence of evidence does not mean absence of effectiveness

• More negative trials add to the “confidence crisis in HIV prevention”

• Balance cost of prevention trials versus cost of preventing infections

• Alternative methods to obtain “rigorous evidence”?
Evaluating HIV prevention effectiveness: the perfect as the enemy of the good

Marie Laga\textsuperscript{a}, Deborah Rugg\textsuperscript{b}, Greet Peersman\textsuperscript{c} and Martha Ainsworth\textsuperscript{d}

There is a need to better understand the effectiveness of HIV-prevention programs. Cluster randomized designs have major limitations to evaluate such complex large-scale combination programs. To close the prevention evaluation gap, alternative evaluation designs are needed, but also better articulation of the program impact pathways and proper documentation of program implementation. Building a plausible case using mixed methods and modeling can provide a valid alternative to probability evidence. HIV prevention policies should not be limited to evidences from randomized designs only.

\textit{AIDS} 2012, \textbf{26}:779–783
Dealing with “complexity”
Need for Program Theory or Logic

• Spelling out the different steps
• Makes the connections explicit

• More work needed here to desentangle steps and components of HIV prevention programs!
Example: Water quality

SITUATION

Priorities

Staff
Money
Materials
Partners
Research

INPUTS

OUTPUTS

Activities
Participation

Outcomes - Impact

Short Term
Medium Term
Long Term

Increased knowledge of link between cattle diet and water quality

Increased understanding of recommended phosphorus levels

Monitor phosphorus levels in feed, manure, soil

Make appropriate adjustments to cattle feed

Improved water quality

EDUCATIONAL WORKSHOPS

Set up record keeping systems to track phosphorus

Farmers at risk of overfeeding phosphorus

On-farm visits

ASSUMPTIONS

1. Reducing phosphorus saves time and money
2. Low phosphorus feed is readily available

EXTERNAL FACTORS

Government programs regulate and offer incentives; Other sources reinforce use of high-phosphorus diets

Feed cost savings

Reductions in phosphorus use
# Levels of Evidence in public health program evaluation

<table>
<thead>
<tr>
<th>Type of evidence</th>
<th>Type of statement</th>
<th>Compared to what</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adequacy</td>
<td>The expected change occurred (but no causality)</td>
<td>-No control group&lt;br&gt;-Predefined criteria, or absolute or incremental value</td>
</tr>
<tr>
<td>Plausibility</td>
<td>Program seemed to have effect over &amp; above external influences&lt;br&gt; <em>based on a step by step ruling out of other confounding factors</em></td>
<td>-A non-random control group (historical, external, internal, simulated)</td>
</tr>
<tr>
<td>Probability</td>
<td>-The program has an effect&lt;br&gt;-(P&lt;x% that the difference between program &amp; non-program were due to confounding / bias)</td>
<td>Randomised control group or cluster</td>
</tr>
</tbody>
</table>

*from Habicht et al*
Effectiveness by “Plausible attribution”

- Triangulation of data sources: survey’s, surveillance, program data, context

- Mixed methods needed

- Causality considerations: Bradford Hill criteria

- Modelling to simulate control groups and predict impact
Has Prevention worked?

Working backwards
• Making sense of national trends
• Showing effectiveness of ongoing, real life programs

Prospective Evaluations
• Evaluating “new programs”
Declining HIV prevalence trends observed in many African countries: what does it mean?

**Eastern Africa**

![Graph showing declining HIV prevalence in Ethiopia and Kenya](chart)

**Source:** UNAIDS Report on the global AIDS epidemic, 2008
Understanding National Trends: Impact of Prevention
The example of Zimbabwe

Ref Halett T et al, 2010
Declining HIV incidence/prevalence in Zimbabwe

- **HIV prevalence decline**
  - 1998: 29.3 %
  - 2007: 15.6 % (adults 15-49)

- **Emigration of PLWHA**

- **Mortality**
  - Increased mortality among persons with high infection risk

- **HIV incidence decline**
  - Behaviour change

- **Emigration of persons with riskier behaviours**

- **Reasons for prevalence decline**
  - Increased mortality among persons with high infection risk

- **Behaviour**
  - **Abstinence**
    - No clear trend
    - Age of debut high since 1980s

  - **Partner Reduction**
    - Decrease in mean number of partners

  - **Condom use**
    - High levels of condom use with non-regular partners
  
  - Other programs:
    - STI treatment, blood safety

- **Programmes**
  - Focus on delayed debut: FBOs, NGOs, education system
  - Some focus on partner reduction and prevention in marriage within ABC
  - Strong public sector & social marketing condom programs
  - HIV awareness: media, IPC, schools, clinics, churches

- **Other factors**
  - Reduced ability to afford multiple partners
  - Personal experience of morbidity and mortality
  - Relatively high levels of education/social capital
High Coverage of ART Associated with Decline in Risk of HIV Acquisition in Rural KwaZulu-Natal, South Africa

Frank Tanser,¹* Till Bärnighausen,¹,² Erofili Grapsa,¹ Jaffer Zaidi,¹ Marie-Louise Newell¹,³

SCIENCE VOL 339 22 FEBRUARY 2013

HIV Prevalence 2005 to 2011

ART Coverage 2005 to 2011
Avahan case study

A prospective impact evaluation using “plausibility“ design
Avahan footprint, coverage, services in first 5 years..

**Source:** Avahan routine monitoring data

### Core group programs
- 200,000 FSW (35-45%)
- 70,000 MSM (45-70%)
- 20,000 IDU (25%)

### Men at risk programs
- 5 million men
- 100 towns, 17 transshipment locations

#### Towns covered
- Dec 03: 376
- Jun-04: 408
- Dec-04: 465
- Jun-05: 531
- Dec-05: 578
- Jun-06: 598
- Dec-06: 604
- Jun-07: 605

#### Peer educators
- Dec 03: 240
- Jun-04: 2300
- Dec-04: 4000
- Jun-05: 5000
- Dec-05: 6200
- Jun-06: 7200
- Dec-06: 7100
- Jun-07: 7500

#### Core groups covered
- (figure in thousands)

#### Condoms distributed and sold per month
- (figure in millions)

---

**States (6)**

**Districts (83)**

**Intervention sites**
<table>
<thead>
<tr>
<th>Area</th>
<th>Questions</th>
<th>Methods &amp; Data Sources</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scale/coverage/quality of</td>
<td>Are geographic footprint, quality of coverage and service uptake adequate</td>
<td>Analysis of 2 rounds of Integrated Behavioral &amp; Biologic Assessments or surveys (IBBA)</td>
</tr>
<tr>
<td>services</td>
<td>(~80% of population) over time? What were the costs associated with</td>
<td>of core/bridge (29/83 districts)</td>
</tr>
<tr>
<td></td>
<td>implementation over time?</td>
<td>Mathematical modeling informed by very limited general population surveys for</td>
</tr>
<tr>
<td></td>
<td></td>
<td>generating “infections averted”</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Synthetic analysis associating trends in HIV prevalence among young antenatal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>attendees with coverage and intensity of core and bridge group prevention interventions</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Program monitoring; routine financial reports; costing studies; estimated cases</td>
</tr>
<tr>
<td>Epidemic Outcomes &amp; impact</td>
<td>Has there been an increase in condom use in high-risk groups (HRGs)?</td>
<td>averted</td>
</tr>
<tr>
<td></td>
<td>Has there been a reduction in STI and new HIV infections in HRGs?</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Have there been a reduction in HIV infection in the general population?</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Can these changes be attributed to HRG interventions?</td>
<td></td>
</tr>
<tr>
<td></td>
<td>What was Avahan’s contribution to these changes?</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cost effectiveness</td>
<td>What was the cost effectiveness of population (HRG) reach?</td>
<td></td>
</tr>
<tr>
<td></td>
<td>What was the cost effectiveness of infections averted (HRG, general</td>
<td></td>
</tr>
<tr>
<td></td>
<td>What was the cost efficiency of the various service components?</td>
<td>population)?</td>
</tr>
</tbody>
</table>
Assessment of the population-level effectiveness of the Avahan HIV-prevention programme in South India: a preplanned, causal-pathway-based modelling analysis

Michael Pickles, Marie-Claude Boily, Peter Vickerman, Catherine M Lowndes, Stephen Moses, James F Blanchard, Kathleen N Dearing, Janet Bradley, Banedakoppa M Ramesh, Reynold Washington, Rejatashwara Adhikary, Mander Mainkar, Ramesh S Paranjape, Michel Alary

Summary

Background Avahan, the India AIDS initiative of the Bill & Melinda Gates Foundation, was a large-scale, targeted HIV prevention intervention. We aimed to assess its overall effectiveness by estimating the number and proportion of HIV infections averted across Avahan districts, following the causal pathway of the intervention.

Methods We created a mathematical model of HIV transmission in high-risk groups and the general population using data from serial cross-sectional surveys (integrated behavioural and biological assessments, IBBAs) within a Bayesian framework, which we used to reproduce HIV prevalence trends in female sex workers and their clients, men who have sex with men, and the general population in 24 South Indian districts over the first 4 years (2004–07 or 2005–08 dependent on the district) and the full 10 years (2004–13) of the Avahan programme. We tested whether these prevalence trends were more consistent with self-reported increases in consistent condom use after the implementation of Avahan or with a counterfactual (assuming consistent condom use increased at slower, pre-Avahan rates) using a Bayes factor, which gave a measure of the strength of evidence for the effectiveness estimates. Using regression analysis, we extrapolated the prevention effect in the districts covered by IBBA to all 69 Avahan districts.

Findings In 13 of 24 IBBA districts, modelling suggested medium to strong evidence for the large self-reported increase in consistent condom use since Avahan implementation. In the remaining 11 IBBA districts, the evidence was weaker, with consistent condom use generally already high before Avahan began. Roughly 32,700 HIV infections (95% credibility interval 17,900–61,600) were averted over the first 4 years of the programme in the IBBA districts with moderate to strong evidence. Addition of the districts with weaker evidence increased this total to 62,800 (32,000–118,000) averted infections, and extrapolation suggested that 202,000 (98,300–407,000) infections were averted across all 69 Avahan districts in South India, increasing to 606,000 (290,000–1,193,000) over 10 years. Over the first 4 years of the programme 42% of HIV infections were averted, and over 10 years 57% were averted.

Interpretation This is the first assessment of Avahan to account for the causal pathway of the intervention, that of changing risk behaviours in female sex workers and high-risk men who have sex with men to avert HIV infections in these groups and the general population. The findings suggest that substantial preventive effects can be achieved by targeted behavioural HIV prevention initiatives.

Funding Bill & Melinda Gates Foundation.
Evaluation of Combination Prevention
Conclusions

• Redefine meaning of “What works in Combination prevention?” Evidence based Prevention programming cannot rely solely on RCT evidence

• Lower expectations about need for probability evidence; When and why is precise estimate of impact needed?

• Plausibility designs, improved program data and mixed methods and mathematical models get us a long way to provide answers on “whether, why and how?..”

• Shift towards analyzing National Program Successes, and real-time program evaluation

• Clear need for collaboration and cross fertilization between Researchers, Evaluators and Program Implementers