

EVALUATING EVIDENCE OF HIV PREVENTION INTERVENTIONS

THAT WORK

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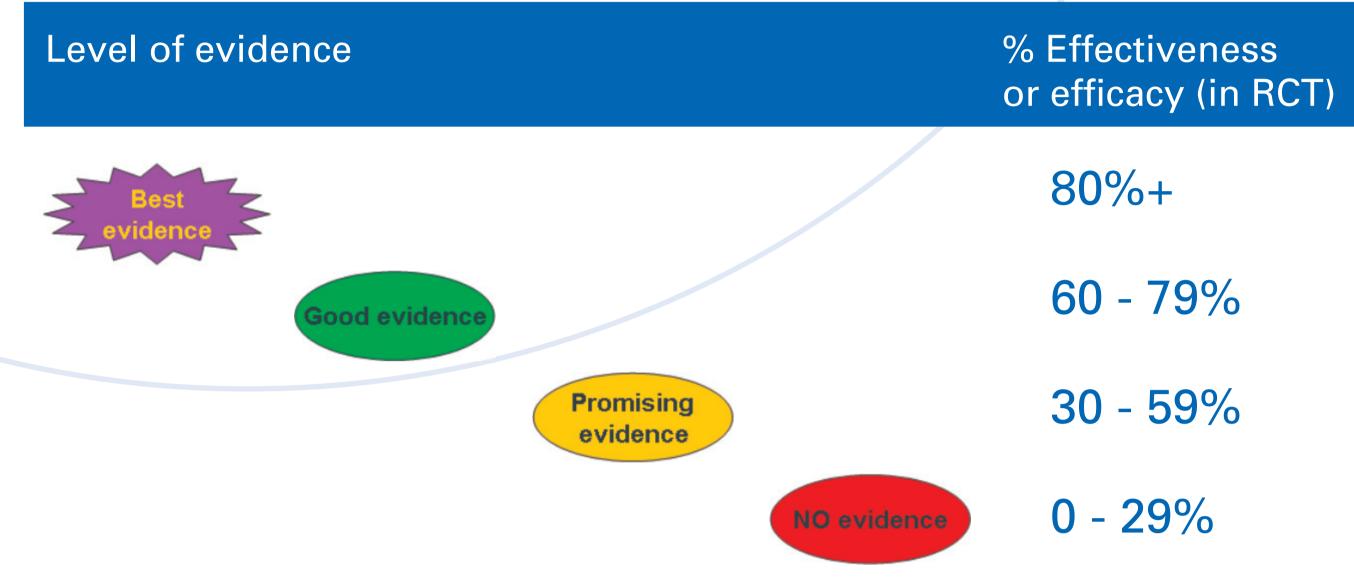
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HUMAN SCIENCES RESEARCH COUNCIL

PROPOSED LEVELS OF EVIDENCE



MALE CIRCUMCISION (MC)

RCTs on MC in South Africa, Uganda, and Kenya¹:

• "Compelling evidence that MC is 65% effective in reducing the risk of acquiring HIV in circumcised men..."

Cochrane review of trials in SA, Uganda, and Kenya between 2002 and 2006 that enrolled 11,054 males

- "Research on effectiveness of MC for preventing HIV in heterosexual men is conclusive"
- **No further trials are required** to establish that HIV infection rates are reduced in heterosexual men for at least the first two years after circumcision.²

HIGHLY ACTIVE ANTIRETROVIRAL THERAPY (HAART)

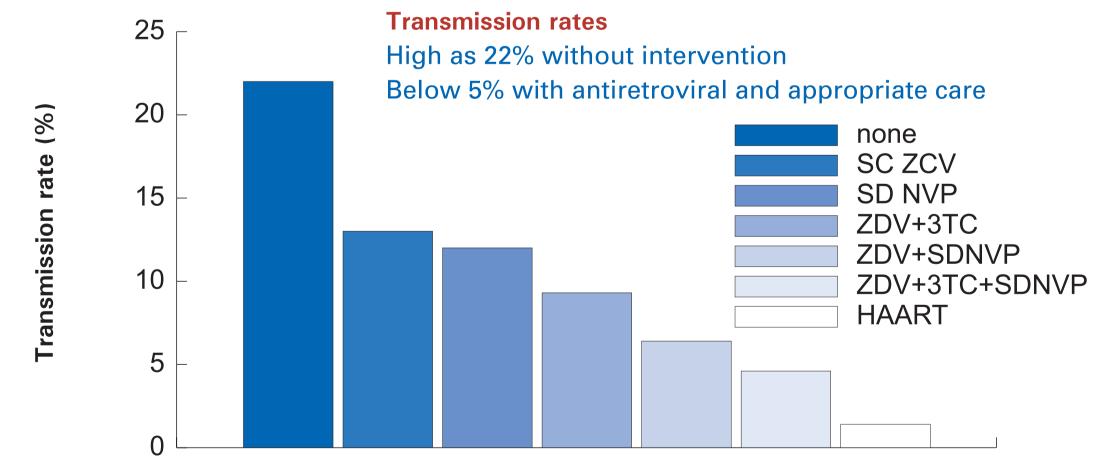
RCTs on HAART³

 Reported 60% to 80% reductions in new AIDS illnesses, hospitalizations and deaths

Meta-analysis of 54 antiretroviral clinical trials⁴

- Using one antiretroviral reduced progression to AIDS or death by 30% against placebo.
- Using two antiretrovirals reduced progression to AIDS or death by 40% against one antiretroviral
- Using three antiretrovirals reduced progression to AIDS or death by 40% against two antiretrovirals

PREVENTING MOTHER-TO-CHILD TRANSMISSION (PMTCT) OF HIV



CONDOMS

Meta-analysis commissioned by UNAIDS⁵:

Male condom use is 90% effective in preventing HIV transmission. Family Planning Programs:

"Evidence from Family Planning programs over many years makes it abundantly clear that the condom is a safe and relatively effective method..."

Laboratory and clinical evidence

US FDA approved the **female condom** as **94-97% effective** in reducing the risk of HIV infection, if used correctly and consistently.⁶

STI TREATMENT

Cluster RCT in Mwanza & Tanzania⁷:

- Improved STI treatment services shown to reduce HIV transmission by about 40%.
 Two trials (Mwanza & Rakai)
- No evidence for substantial benefit from STI treatment of all community members.

7 Schulze KF (2004) Population-based interventions for reducing sexually transmitted infections, including HIV infection. The WHO Reproductive Health Library; Geneva

Gray, H. et al. (2007). MC for HIV prevention in young men in Rakai: A RCT.Lancet 369:657-66.
Siegfried N, Muller M, Volmink J, Deeks JJ,. MC for prevention of heterosexual acquisition of HIV in men. Cochrane Database of Systematic Reviews, Issue 4, 7 October 2009
Jordan et al. (2002) Systematic review and meta-analysis of evidence for increasing numbers of drugs in antiretroviral combination therapy. BMJ 2002;324:757
http://www.bmj.com/cgi/content/full/324/7340/757
Palella et al. (1998) Declining morbidity and mortality among patients with advanced HIV infection. NEJM, 338:853-860.
Hearst N and Chen S, Condom promotion for AIDS prevention in the developing world: is it working? Studies in Family Planning, 2004, 35(1):39-47. http://www.usp.br/nepaids/condom.pdf
AVERT, "The Female Condom" fact sheet, available online at http://www.avert.org/femcond.htm

Cochrane Reviews⁸

• Limited evidence from the RCTs indicates that STI control serves as an effective HIV prevention strategy.

MICROBICIDES AND CERVICAL BARRIERS

- Early-generation microbicides Studies: failed to detect prevention benefit
- disappointing results reported on HIV prevention potential of female diaphragms.
 THPTN 035: A multi-centre clinical trial conducted at 7 sites (6 in Africa) with 3,099 participants to evaluate safety and effectiveness of two candidate microbicides, BufferGel and PRO 2000:-
 - PRO 2000 was 30% effective compared with no gel
 - BufferGel had no detectable effect on preventing HIV infection.
- Topical microbicides: Not performed well in human HIV prevention studies
 - 10 trials of surfactant and polyanionic compounds yielded negative results

HIV VACCINE

- Thai Phase III HIV vaccine clinical trial (RV 144),
 - Tested "prime-boost" combination of two vaccines: ALVAC® HIV vaccine the prime), and AIDSVAX® B/E vaccine (the boost).
 - Vaccine combination based on HIV strains commonly in Thailand.
 - Trial demonstrated that the vaccine regimen was safe and modestly effective in preventing HIV infection.
 - Prime-boost combination lowered the rate of HIV infection by 31.2%9

HIV Vaccine Trials Network (HVTN)

- A first large-scale study to evaluate a candidate clade B HIV HIV vaccine.
- Phase IIb or "test of concept" efficacy trial with 3,000 participants at 5 sites in South Africa.
- Trials halted in September 2007 owing to vaccine's lack of efficacy

SUMMARY: EVIDENCE OF BIOMEDICAL HIV PREVENTION INTERVENTIONS

Interventions	% Effectiveness or efficacy
Male Condoms	80-95% [Natural experiment]
Female Condoms	94-97% [Natural experiment]
PMTCT [Dual & triple therapy]	92-98% [RCTs]
HAART	60-80% [RCTs]
Male Circumcision	65% [3 RCTs]
HPTN 035 (PRO 2000)	30% [1 RCT]
STI treatment	40% [1 RCT]
RV 144 Thai vaccine trial	31.2% [1 RCT]
HIV Vaccine Trials Network (HVTN)	No efficacy [RCT]
Early-generation microbicides & topical microbicides	Failed [RCTs] and negative results [10 RCTs]

HIV COUNSELING AND TESTING (HCT)

- Meta-analysis: 11 studies on impact of counseling and testing for PLWH/A¹⁰
 - 68% reduction in high risk sexual behaviors with partners not already HIV+ (95% CI: 59% 76%)
 - Very similar findings for men and women
- Meta-analysis: 27 studies¹¹
 - No significant impact of "counseling and testing" bundle on behavior relative to the untested

SUMMARY: BEHAVIOURAL AND STRUCTURAL HIV PREVENTION INTERVENTIONS THAT WORK

Interventions	% Effectiveness or efficacy
HCT for PLWHA	68% reduction in high risk sexual behaviors [1 comm RCT]
Stepping Stones	Lowered the risk of HSV-2 by 34.9 per 1000 people exposed;
IMAGE study	less IPV and less transactional sex [comm RCT]
	IPV was reduced by 55% [comm RCT].
Abstinence-only interv's	7/13 reported sex [SR]
HCT on untested	no impact of C&T on behavior of untested
Stepping Stones	did not lower incidence of HIV-1
IMAGE	No effect on HIV incidence [comm RCT]
Concurrency	No conclusive evidence

CONCLUSION

No "Magic Bullet" for HIV

"It is critical to note that there is no "magic bullet" for HIV prevention. None of the new prevention methods currently being tested is likely to be 100 percent effective, and all will need to be used in combination with existing prevention approaches if they are to reduce the global burden of HIV/AIDS."

Source: Global HIV Prevention Working Group (2008)

Wilkinson D, Rutherford G. Population-based interventions for reducing sexually transmitted infections, including HIV infection. *The Cochrane Library*, Issue 1 2003. *Rerks-Ngarm R, Pitisuttithum P, Nitayaphan S, Kaewkungwal J, Chiu J et al*. Vaccination with ALVAC and AIDSVAX to Prevent HIV-1 Infection in Thailand. NEJM 20 October 2009

Marks G et al. JAIDS 2005;39:446-453.

Weinhardt LS et al. *Am J Public Health*. 1999;89:1397-1405.