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HIV PREVENTION STRATEGIES

Over the past two decades, scientific research has identified a range of effective strategies for preventing all routes of HIV transmission – sexual, blood borne and mother to child. However, fewer than one in five people at high risk for HIV have access to effective prevention worldwide.

Unfortunately there is no single solution. In this edition of 'Taleletso' we review some of the prevention strategies that show most promise.

PREVENTING SEXUAL TRANSMISSION What Works?

1. HIV Testing: HIV testing is vital to HIV prevention. Studies have shown that people who know their HIV status are more likely to protect

themselves and others from infection.

2. STD Screening: Infection with other STIs increases the risk of HIV acquisition by 2-5 times. Promptly detecting and treating STDs can help reduce risk. A study in Tanzania found that treating STDs can reduce the rate of HIV infection by 38% ^[Garnett 1993]

3. Behavioral Modifications: Newly infected persons are 26 times as infectious than later in the asymptomatic phase. Therefore it's important that they adopt risk reducing behaviors. Effective behavioral interventions include:

- Remaining sexually abstinent or delaying initiation of sexual activity
- Condom skills education
- Group-based interactive HIV prevention intervention
- Motivational interviewing for HIV and partner violence risk reduction

- Safer sex skills building & decreasing the number of sexual partners

4. Financial incentives: What is the role of financial incentives to prevent HIV?

In Malawi, school girls aged 13-22 years were given small cash incentives (up to US\$15) for achieving high levels of school attendance, and study results showed that girls who received the incentive had a 60% reduction in HIV infection. In Tanzania, young adults were given incentives (up to US\$60 over a year) to avoid indulging in unsafe sex, and the results showed a 25% reduction in HIV incidence. Delaying sexual debut may not be as important in Botswana. Current data suggests 68.6% for females in Botswana become sexually active by age 19, and by 24 years 96.7% female becomes sexually active.

SUMMARY OF SUCCESSFUL STRATEGIES

Condoms

Used properly, condoms are up to 87% effective in preventing HIV

Male Circumcision

Male acquisition of HIV can be reduced by circumcision by as much as 60%

Oral PrEP

One study in Botswana found that truvada reduced HIV transmission by 62%. Other studies in heterosexuals have failed to demonstrate this level of efficacy

Topical PrEP

Vaginal Tenofovir has been demonstrated to reduce risk of HIV by 39% when used pre & post coitally

Treatment as Prevention

For patients in serodiscordant sexual relationships ARV reduces risk transmission by 96%

Vaccines

RV144 Vaccine trialed in Thailand was shown to reduce risk of HIV by 31%

Combination

No single strategy is enough—a combination approach to prevention could significantly reduce HIV transmission.

SUPPORTIVE POLICIES

HIV prevention is most effective when it is supported by strong and visible political leadership, and by policies that address the root causes of vulnerability to HIV, including:

Anti-stigma measures that prevent discrimination against people with HIV and vulnerable groups

Gender equality initiatives, including programs to enhance women's education and economic independence, and laws to combat sexual violence and trafficking

Involvement of communities and HIV-infected individuals in educating people about HIV, and in developing, implementing, and evaluating prevention programs

5. Male Condoms: Consistent and correct use of male condoms has been reported to be 87% effective for prevention of HIV but may be as low as 60% or as high as 95%.^[Davis 1999]

Condom effectiveness rates may be lower in real-life settings than those reported in these studies because participants in study settings are instructed in proper condom usage and are provided with high-quality condoms that may be less likely to fail. So why aren't condoms more successful?

- People don't like using them – they reduce sensation
- Lack of spontaneity
- Lack of partner cooperation
- Requires male erection

6. Male Circumcision: Three important randomized trials have demonstrated that male acquisition of HIV can be reduced by circumcision:

- Rakai, Uganda - 51% reduction^[Bailey 2007]
- Kisumu, Kenya – 53% reduction^[Gray 2007]
- Orange Farm, RSA – 61% reduction^[Awert 2005]

Male circumcision also reduces the incidence of trichomoniasis, bacterial vaginosis, and genital ulcers in women, which could in turn reduce a woman's risk of HIV acquisition.^[Gray 2009] Although male circumcision provided some benefits to women, it has not been shown to reduce HIV transmission from infected men to uninfected women.^[Wawer 2009; Baeten 2010]

7. Nonspecific Microbicides: Non-specific microbicides were developed for the prevention of HIV and other sexually transmitted pathogens but do not contain an antiretroviral agent.

However, nearly 20,000 HIV-negative women have participated in randomized, placebo-controlled trials of nonantiretroviral-containing microbicides. None of these nonspecific products has demonstrated any level of effectiveness in reducing HIV infection in women.

8. Oral Pre-Exposure Prophylaxis (PrEP) – Recent research has showed that oral antivirals may be an important means of reducing the risk of infection for HIV negative serodiscordant couples (where one partner is positive and the other is not):

TDF2 study: Botswana based study randomized heterosexually active adults to emtricitabine/tenofovir (truvada) or placebo for \geq 12 months of follow-up. The overall protective efficacy of emtricitabine/tenofovir was 62.6% (95% confidence interval: 21.5% to 83.4%; $P = .0133$)^[Thigpen 2011] The reduction in HIV acquisition was observed in both men and women, and medication adherence was similar between the study arms.

FEM-PREP Study: FEM-PREP trial (Kenya) of PrEP in heterosexual African women at high risk of HIV infection failed to show that PrEP reduced the risk of HIV acquisition and the study was closed early.

9. Topical Pre-Exposure Prophylaxis: The CAPRISA 004 study assessed the efficacy of tenofovir 1% gel for the prevention of HIV in 889 women in Durban, South Africa. ^[Sokal 2010]

In this study, women were instructed to use a vaginal gel applying the gel 12 or fewer hours before sex and again up to 12 hours afterward.

The results of the study demonstrated that the tenofovir gel was associated with an overall 39% reduction in the risk of acquiring HIV compared with placebo ($P = .017$).

A sub-analysis of efficacy according to adherence showed that among women with adherence rates > 80%, the protective effect was greater, with a 54% reduction in the rate of acquisition of HIV infection.

This represents the first time that a vaginal microbicide preparation could be used by a woman to protect herself against the risk of acquiring HIV infection during sexual intercourse has been shown to confer benefit.

10. ART for Prevention: The use of antiretroviral therapy in pregnancy has dramatically reduced the incidence of perinatally acquired HIV infections. ^[Dorenbaum 2002] Indeed, mother-to-child transmission of HIV has reduced from approximately 20% without intervention to < 2% with HAART. ^[Cooper 2002]

Decreases in HIV-1 RNA are also associated with decreased heterosexual transmission of HIV. ^[Quinn 2000]

For this reason, it has long been speculated that effective antiretroviral therapy may also reduce sexual transmission of HIV by lowering levels of HIV in the genital tract. This was confirmed in 2011 by a very important trial, HPTN 052

11. Vaccines: The RV144 vaccine was trialed in Thailand, and employed a prime-boost vaccine strategy composed of the “prime” vaccine and a “booster” gp120 B/E vaccine

The investigators reported that 74 out of 8198 volunteers who did not receive the vaccine became infected with HIV vs only 51 out of 8197 volunteers who did, which correlates to a 31% reduction in risk (95% confidence interval: 1.1-51.1). ^[NIAID 2009]

These findings suggest that vaccines may have a role in further prevention strategies – but are not the miracle cure that once was hoped for....

HPTN 052 study¹

This was a phase III randomized trial designed to evaluate the role of HAART in the prevention of HIV transmission among serodiscordant couples ^[Cohen 2011a]

Within each couple, the HIV-infected partners (who had CD4+ cell counts of 350-550 cells/mm³ at baseline) were randomized either to immediate therapy or delayed therapy (when the CD4+ cell count fell to ≤ 250 cells/mm³).

This trial was stopped early because a very clear benefit was demonstrated in the immediate treatment group: Out of the 28 genetically linked transmissions that occurred among study subjects, 27 were in the control arm vs only 1 in the intervention arm ($P < .001$), representing 96% efficacy.

41% reduction in HIV-related clinical events were observed in HIV-infected patients randomized to the immediate vs delayed therapy arm. ^[Grinsztejn 2011]

RECOMMENDATIONS ON PrEP*

Where Oral Pre-Exposure Prophylaxis (truvada) is available for HIV negative persons in serodiscordant couples, recommendations for use *might* include:

Determine eligibility

Document negative HIV antibody test(s) immediately before starting PrEP medication
 Test for acute HIV infection if patient has symptoms consistent with acute HIV infection
 Confirm that patient is at substantial, ongoing, high risk for acquiring HIV infection
 Confirm that calculated creatinine clearance is ≥ 60 mL/min/1.73 m²

Other recommended actions

Screen for hepatitis B infection; vaccinate against hepatitis B if susceptible, or treat if active infection exists, regardless of decision about prescribing PrEP
 Screen and treat as needed for STIs

* From USA, not from Botswana



A COMBINATION APPROACH TO HIV PREVENTION...

There is an increased recognition by most HIV prevention researchers that a combination of prevention approaches will be needed and that the 'package' of interventions implemented will likely depend on the specific characteristics of a community, such as the prevalent modes of HIV transmission and the larger biomedical infrastructure in the community, as well as the support services needed in order to effectively roll out an intervention.

Got a clinical question about a complicated medical patient or a patient with HIV?
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