Sex and gender differences in ARV-based HIV prevention research

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Sex and gender are biological and physiological characteristics that define men and women. Economic, social, political and cultural attributes, constraints and opportunities associated with being a woman or a man.

**Issues**

What is the optimal combination prevention approach for early treatment as prevention or pre-exposure prophylaxis (PrEP) in women? Are the HIV prevention benefits of antiretroviral (ARV) drugs as evident in women as they are in men and, if not, why not? What questions concerning the gender and sex aspects of ARV-based prevention are outstanding?

**Methods**

The Industry Liaison Forum (ILF) of the International AIDS Society (IAS) convened an affiliated event at the 20th Conference on Retroviruses and Opportunistic Infections (CROI) in Atlanta, US, in March 2013 to address the topic of sex and gender differences in antiretroviral (ARV)-based HIV prevention research. [Agenda and presentations are available at: http://www.iiasociety.org/illf.aspx]

Data were reviewed from trials of early treatment for prevention (before national eligibility criteria are reached) and pre-exposure prophylaxis, as well as from a study of the impact of antiretroviral treatment (ART) scale up in populations at risk of HIV acquisition. In vitro and preclinical evidence of potential sex-based differences and similarities in ARV-based prevention were considered, along with differences between men and women in trial endpoints: seroconversion, safety and tolerability, adverse event profiles, drug resistance and adherence. Social science perspectives included the importance of gender with respect to acceptability and risk compensation on ARV-based prevention. Potential areas of collaboration are between preclinical, clinical and social science disciplines. Promising ARV-based prevention products in the pipeline were reviewed. A formal lively debate addressed the subject: it resolved that with respect to antiretroviral-based prevention of sexual transmission, treatment is enough for women.

**Results**

An optimal “combination prevention” approach for ARV-based interventions should consider the broader context of women’s lives, including their socioeconomic and behavioural vulnerability to HIV, as well as biological aspects, in order to address immediate risks, underlying vulnerabilities and the pathways that link them. Macaque studies reveal higher levels of ARV drug penetration in rectal tissues compared with vaginal tissues, suggesting one reason that clinical trials of oral tenofovir (TDF)-based interventions have demonstrated greater efficacy in men who have sex with men (MSM) than in heterosexual women. When conditions simulating perfect adherence are met, drug penetration and protection thresholds vary, depending on the compound, dosage, site (e.g., vaginal or rectal mucosa) and other factors. Conflicting clinical trial efficacy data and significant gaps between self-reported measures of adherence and actual plasma concentrations are observed among both men and women.

**Key conclusions**

- Data disaggregation and analysis by sex and gender are needed to more fully understand the relative benefits for women and men of ARV-based HIV prevention.
- Conflicting data among clinical trials evaluating ARV-based prevention for women underscore the need for studies to further explore the social, behavioural and biological variables that affect efficacy and effectiveness.
- Knowledge of the nature, extent and significance of sex and gender differences in ARV-based prevention is essential to inform future policy and programming.

**Consensus Statement**

**ASKING THE RIGHT QUESTIONS: Advancing an HIV Research Agenda for Women and Children**

**Recommendation 3:** Research data should be disaggregated by sex to ensure opportunities for gender-based analyses using a variety of indicators, such as retention in ART programmes, morbidity and mortality, loss to follow up, and pharmacokinetic (PK) and pharmacodynamic (PD) parameters.

**References**


**Competing interests**

The Industry Liaison Forum (ILF) is an initiative of the International AIDS Society (IAS) with a mission to accelerate scientifically promising, ethical HIV research in resource-limited countries, with a particular focus on the role and responsibilities of industry as sponsors and supporters of research. The authors declare that they have no competing interests.

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**Combination prevention context for antiretroviral-based prevention**

- Evidence-informed, human rights-based and context-specific, tailored to local epidemics and needs.
- Fully engages affected communities, promoting human rights and gender equality.
- Operates synergistically on multiple levels: individual, family and society.
- Invests in decentralized and community responses.
- flexible: adapts to changing epidemic patterns and rapidly deploys innovations.
- Combines biomedical, behavioural and structural elements to address immediate risks, underlying vulnerabilities and pathways that link them.