

**Ethics & HIV Pre-Exposure
ChemoProphylaxis (PrEP)**

A Thesis Project

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OUTLINE

- Background
- Objectives
- Methods
- Implications to Stakeholders

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Background Objectives Methods Implications

Effective HIV Prevention

- Sexual abstinence
- Condoms
- Circumcision
- Safe medico-surgical practices

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Background Objectives Methods Implications

Prevention Methods: Limitations

- social/moral acceptability
- persistent risk-taking behaviors
- limited access to condoms and ARVs
- stigma
- imbalanced gender roles
- limited access to/use of safe medico-surgical practices

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Background Objectives Methods Implications

Recent Setbacks in HIV Research

- microbicides trials: nonoxynol-9 (1999)
 - vaginal irritation
 - increased infection risk
- vaccine trials: STEP (2004-2007)
 - increased infection risk

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Background Objectives Methods Implications

Novel Approach: PrEP

Pre-Exposure chemoProphylaxis

- Nevirapine trials
 - reduced mother-to-child transmission (Jackson 1999)
 - safely tolerated in seronegative subjects (Jackson 2003)
- Tenofovir trials
 - double-blind randomized trials, female sex workers
 - studies halted (Cambodia 2004, Cameroon 2005)
- Some issues raised
 - community acceptability
 - post-trial treatment
 - long term toxicity

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Background Objectives Methods Implications

Objectives

Summarize / analyze:

- evidence on effectiveness and harm
- scientific validity of methods
- ethical questions (appropriateness)

in HIV PrEP trials

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Background Objectives Methods Implications

Methods

Bad Science is Unethical

1. Systematic review
2. Critical scientific appraisal
3. Critical ethical appraisal
4. Synthesis

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Background Objectives **Methods** Implications

1. Systematic Review

- Sources of trials
 - Published primary reports
 - Electronic databases
 - Selected internet websites
 - Specialty journals (hand search)
 - Unpublished primary reports
 - Pharmaceutical industry
 - HIV research sponsors
 - Field experts

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Background Objectives **Methods** Implications

1. Inclusion Criteria

Population sexually active seronegative adults
Intervention administration of an antiretroviral drug
Comparator “standard of care”
Outcome seroconversion
Study design any trial (prospective controlled study)

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Background Objectives **Methods** Implications

2. Scientific Appraisal

- Justification and rationale for trial
 - study question
 - treatment, dose, frequency
 - population
- Risk of bias
 - sequence generation, allocation concealment, blinding
 - incomplete outcome data
 - selective outcome reporting
- Quality of report (standardized assessment tools)
 - CONSORT
 - NOS

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Background Objectives **Methods** Implications

2. Scientific Internal Validity

- funding
- research team (competences)
- study design
- comparator
- outcome measures
- sample size and power
- compliance
- contamination

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Background Objectives **Methods** Implications

2. Scientific External Validity

- mechanism of action of drug
- target viral clade
- target population
- setting/healthcare system

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Background Objectives **Methods** Implications

4. Ethical Appraisal: Survey

- *What is critical in HIV research?*
- *What is largely ignored in HIV research?*
 - > justification of study
 - > protocol development
 - > funding
 - > conduct
 - > post-trial

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Background Objectives **Methods** Implications

4. Ethics Internal Factors

- value of research question
- local consultations/contribution
- study design & choice of comparator
- investigators recruitment & conflict of interest
- patients selection
- informed consent process & compensation
- risk-benefit ratio
- management of incident infection & trial-related harm
- compliance and contamination

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Background Objectives **Methods** Implications

4. Ethics External Factors

- ethics review process
- dissemination
- exiting the field (ownership,...)
- persistent tensions (stigma, politics,...)

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Implications to Stakeholders

- investigators
- sponsors and funding agencies
- local scientific community
- local legal authorities
- study participants
- media
- healthcare centres

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Implications to Stakeholders

This project will help establish:

- the benefits and harms of HIV PrEP
- how well/poorly ethical issues are handled
- how to orient future HIV PrEP research

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QUESTIONS / COMMENTS



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