

INSTITUT NATIONAL DE RECHERCHE BIOMÉDICALE
NRB
LABORATOIRE NATIONAL DE SANTÉ PUBLIQUE

EVALUATION OF POST-EXPOSURE PROPHYLAXIS: TRIAL DESIGN

A COMPREHENSIVE OVERVIEW

PROTECT Lives | **EVIDENCE Driven** | **SCIENCE In Action** | **STRONGER Together**

Prof. Placide Mbala Kingebeni
MD, MSc, PhD

Research today. Protection tomorrow.

1

INSTITUT NATIONAL DE RECHERCHE BIOMÉDICALE
NRB
LABORATOIRE NATIONAL DE SANTÉ PUBLIQUE

Introduction

- **Definition of PEP:**
 - Post-exposure prophylaxis (PEP) refers to the use of specific medications after potential exposure to the pathogen to prevent infection.
- **Key Example:** HIV PEP → must be started within 72 hours for optimal effectiveness
- **Importance of PEP:**
 - Essential for **high-risk exposures and populations**
 - Examples:
 - ✓ Healthcare workers (e.g., needlestick injuries)
 - ✓ Newborns of infected mothers (Ebola, Marburg)
 - ✓ Individuals exposed through sexual contact

2



Objectives of the Presentation

1. **Clinical Trial Designs for PEP:** Review key trial designs used to evaluate post-exposure prophylaxis
2. **Efficacy and Safety Assessment:** Understand how PEP effectiveness and safety are measured in trials
3. **Ethical Considerations in PEP Research:** Highlight major ethical challenges in conducting PEP trials

3

Types of study designs

- **Observational studies :**
 - **Case-control studies :** compare prior PEP exposure (infected vs non-infected)
 - **Cohort studies :** Prospective studies → Follow exposed individuals → safety & infection outcomes
- **Interventional studies :**
 - **Open-label / extension studies :** Evaluate new PEP strategies
 - **Preference designs :** Hybrid approaches allowing individuals to choose between different PEP products or choose to be randomized.
 - **Randomized controlled trials :** Participants are randomly assigned to receive either PEP or placebo → Gold standard for efficacy


4

Types of study designs

▪ Implementation science/Other methods :


- **Qualitative studies** : Interviews and focus groups exploring barriers and facilitators for PEP uptake and completion.
- **Cross sectional surveys** : Assessing the feasibility and acceptability of PEP protocols among target populations.

5




TYPES OF STUDY DESIGNS


DIFFERENT APPROACHES. ONE GOAL: BETTER EVIDENCE, BETTER PROTECTION.




RANDOMIZED CONTROLLED TRIALS (RCTS)




- ✓ Participants are randomly assigned to receive either the PEP treatment or a placebo/control.
- ✓ Reduces bias and allows for causal inference regarding effectiveness.




COHORT STUDIES




- ✓ Observational studies where two groups (exposed and non-exposed) are followed over time to compare outcomes.
- ✓ Useful when RCTs are not feasible.




CASE-CONTROL STUDIES




- ✓ Compare individuals with the outcome (e.g., HIV infection) to those without, looking back at their exposure history.
- ✓ Useful for studying rare outcomes.




STRONG DESIGN. RELIABLE RESULTS. REAL IMPACT.
The right design today shapes the protection of tomorrow.




Rigorous design



Reliable evidence



Better protection



Stronger communities

6



Key Components of Trial Design

Population:

- Define the target population based on exposure risk (e.g., healthcare workers, sexual assault survivors, babies born from infected mothers).
- Consider inclusion/exclusion criteria to ensure a homogeneous study group.

Intervention:

- Specify the PEP regimen (e.g., antiviral, combination of drugs or vaccine).
- Consider dosage, duration, and administration method.

Endpoints:

Primary Endpoints:

- Rate of new infections within a specified time frame.

Secondary Endpoints:

- Incidence of side effects, adherence rates, quality of life assessments.

7



Sample Size Calculation

Importance:

- A well-calculated sample size is crucial for achieving reliable results and statistical significance.

Factors Influencing Sample Size:

- Expected event rate (e.g., incidence of EVD in control group).
- Desired power (commonly 80% or 90%).
- Significance level (commonly set at 0.05).

Formula Example:

- Use standard formulas for calculating sample size based on the above factors.

8



Randomization Methods

Different Methods:

- **Simple Randomization:** Randomly assign participants to groups, may lead to imbalances.
- **Stratified Randomization:** Ensures balance across key characteristics (e.g., age, gender).
- **Block Randomization:** Creates blocks of participants to ensure equal group sizes.

Importance of Blinding:

- Blinding participants and researchers reduces bias in reporting and assessing outcomes.

9



Ethical Considerations



Informed Consent:

Participants must understand the risks, benefits, and purpose of the trial.

Special considerations for vulnerable populations (e.g., minors, those incapacitated).



Monitoring for Adverse Effects:

Continuous safety assessments throughout the trial.

Ethical obligation to halt the study if severe adverse effects occur.



Data Safety Monitoring Boards (DSMBs):

Independent committees that monitor patient safety and treatment efficacy during the trial.

10



Data Analysis



Statistical Methods:

Use intention-to-treat analysis to account for dropouts and non-compliance.

Statistical tests (e.g., chi-square tests for categorical data, t-tests for continuous data).



Handling Missing Data:

Use imputation sensitivity analysis to address missing data.

11

CHALLENGES & LIMITATIONS

Recognizing realities. *Strengthening evidence.*





COMMON CHALLENGES

- 
Recruitment difficulties
 Stigma, low awareness of PEP and fear of disclosure limit participation.
- 
Adherence issues
 Side effects, pill burden and socioeconomic barriers can lead to incomplete PEP regimens.



LIMITATIONS OF TRIAL DESIGNS

- 
RCTs may not reflect real-world scenarios
 Controlled conditions and high adherence in trials may overestimate effectiveness.
- 
Observational studies are prone to confounding
 Cohort and case-control studies may be limited by unmeasured confounders and biases.

Bridging the gap between efficacy and real-world effectiveness remains a **key challenge.**

12



PEP Trials: Key Evidence

1. HIV PEP / Prevention Trials

- Evidence from HPTN 083 & 084
- Demonstrate high efficacy in preventing infection
- Inform global prevention strategies and guidelines

2. Rabies PEP

- Proven high effectiveness when administered promptly
- Remains a life-saving intervention

3. EBOPEP Project(Ongoing):

- **Objective:** "Evaluate PEP strategies to prevent Ebola after high-risk exposure."
- **Planned Design (RCT):** Arm 1: Ervebo / Arm 2: Ervebo + Inmazeb
- **Operational Experience – Bulape (16th EVD, DRC)**
 - Rapid field deployment
 - Establishment of PEP center
 - Integration with ETU, mobile labs, and response teams
- **Key Lessons Learned**
 - Feasibility challenges in declining outbreaks
 - Logistical and cold chain constraints
 - Need for **adaptive trial designs** in outbreak settings

13



Conclusion

▪ Key Points:

- **Robust trial design** is essential to evaluate PEP effectiveness
- **Ethical considerations** must guide all study approaches

▪ Future Directions:

- Need for **innovative and adaptable designs** → To address **emerging infections and evolving public health needs**

14

Future directions

- **From “emergency treatment” to “continuous prevention”**

- Shift from infection-only outcomes → drug protection levels
- Focus on sustained protection over time

- **Radical Simplification (“Single Treatment”)**

- Evaluation of the safety and efficacy of “full distribution at first contact” models without mandatory in-clinic follow-up visits, thanks to remote monitoring.

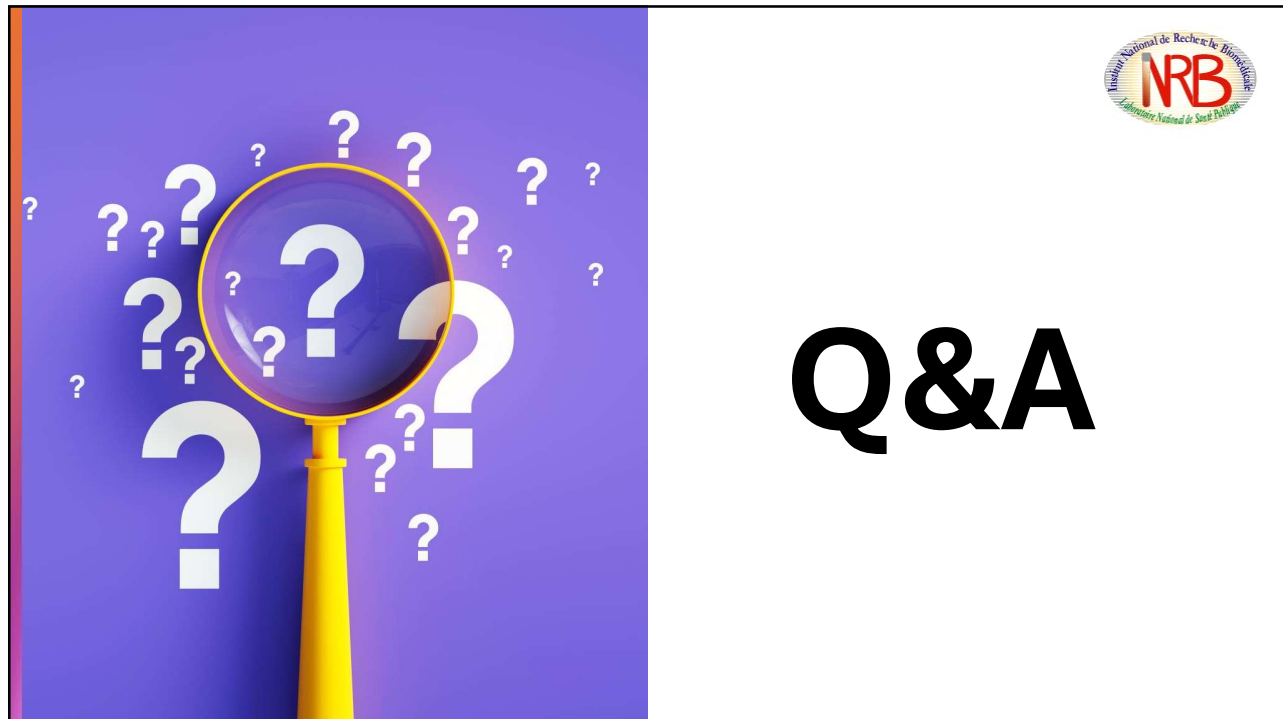
- **New Distribution Models (Health)**

- Direct access at pharmacies, self-sampling kits, etc. : evaluating the impact of removing geographical barriers and the stigma associated with hospitalization on the use of post-exposure prophylaxis (PEP) among key populations.

- **Statistical Innovation / Modelling**

- Since the use of a placebo is ethically unacceptable, future evaluations rely on synthetic comparators.
- Mathematical models and local prevalence data allow researchers to estimate the number of infections that would have occurred without post-exposure prophylaxis (PEP), thus validating the efficacy of new drugs.

15



Institut National de Recherche en Santé Publique
NRB
Agence Nationale de Santé Publique

Q&A

16