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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

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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

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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

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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.

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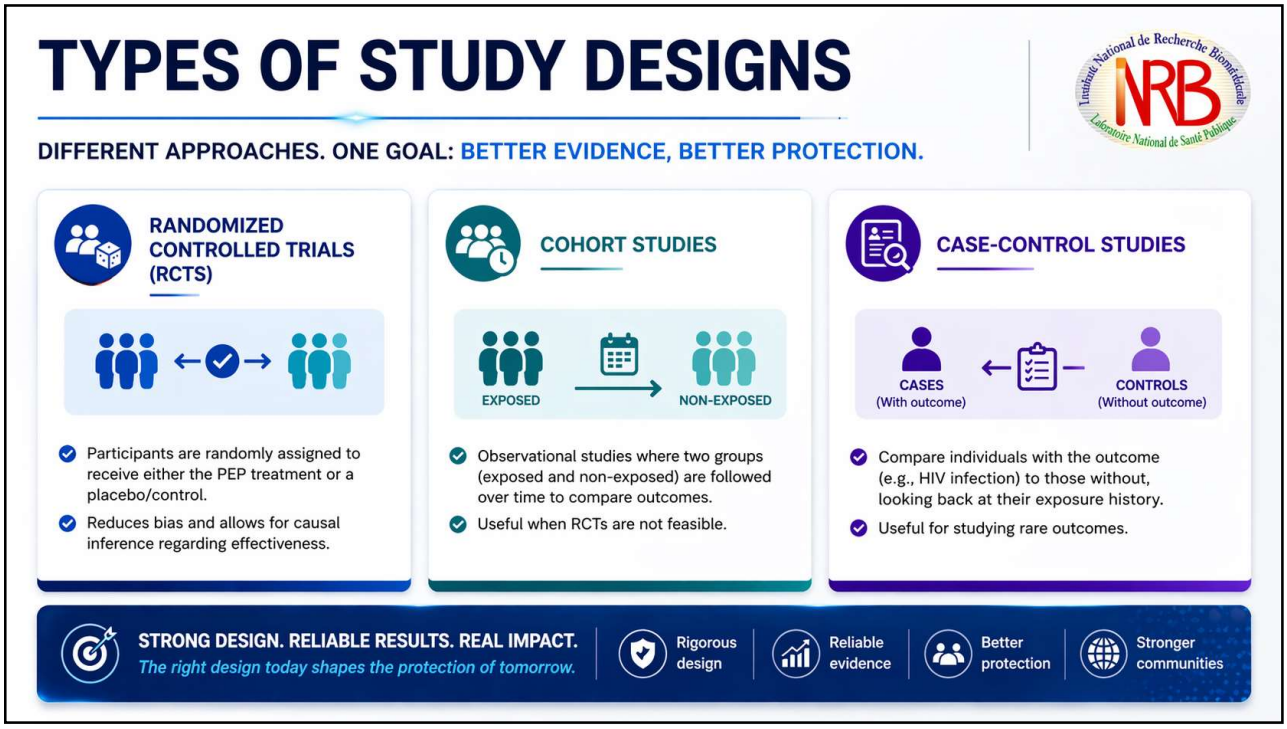

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Key Components of Trial Design

- **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.

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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.

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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.

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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.

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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.

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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

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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**

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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.

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Q&A

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