

# Principles and Structure of a Research Protocol

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The Union

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*Health solutions for the poor*



**LuxOR**  
Luxembourg Operational Research

# BASIC STRUCTURE

- **Background and rationale to study**
- **Aim and objectives (the research question)**
- **Methods (includes ethics submission)**
- **Budget and time lines**
- **Justification**

# **Background and Rationale**

- **Country / context in which study is to be done**
- **The problem and what is known about it**
- **Are there knowledge gaps?**
- **Will this study fill those knowledge gaps?**

# Aim and Objectives

- **Aim is broad**
- **Objectives are more specific**

# For example: (1)

## **AIM**

To document the management and outcome of new smear-positive Pulmonary TB patients who fail first line treatment in Malawi

# For example: (2)

**Specific Objectives** are to determine:-

1. The number of new smear-positive PTB patients who failed treatment
2. The management of patients who failed
3. Their treatment outcomes on Re-Rx regimen
4. The culture and drug sensitivity results of those who failed and in relation to treatment outcomes

# Methods

- **Study design** (descriptive, case-control, cohort)
- **Setting – general and study site**
- **Participants** (and study period)
- **Data variables to be collected:**
  - exposure and outcome variables
  - data collection instrument (when data collected)
  - data validation
- **Sources of data**
- **Analysis and statistics** (sample size, if needed)
- **Ethics approval**

# Recurrent Tuberculosis in Malawi



# BACKGROUND: NTP in Malawi (1)

- Model “DOTS” Programme
- Management by District TB officers
- Excellent Monitoring and Evaluation, using Registers and quarterly cohort reporting
  
- 27,000 cases of TB registered per annum
- HIV-prevalence in TB patients = 70%

# The problem and rationale (2)

Between 1987 to 1999:

- **% Patients registered nationally with Relapse smear-positive PTB in Malawi declined from 6% to 3%**
- **No reported cases of recurrent smear-negative TB**

**BUT**

- **HIV-prevalence in TB patients increased from 30% to 70%**
- **Research literature from Africa (4 studies) showed that recurrent TB increases as HIV-prevalence increases**

# Annual TB recurrence

**HIV+ve**

**HIV-ve**

Zaire

18%

6%

(Perriens et al 1991)

Kenya

17%

0.5%

(Hawken et al 1993)

Zambia

22%

6%

(Elliott et al 1995)

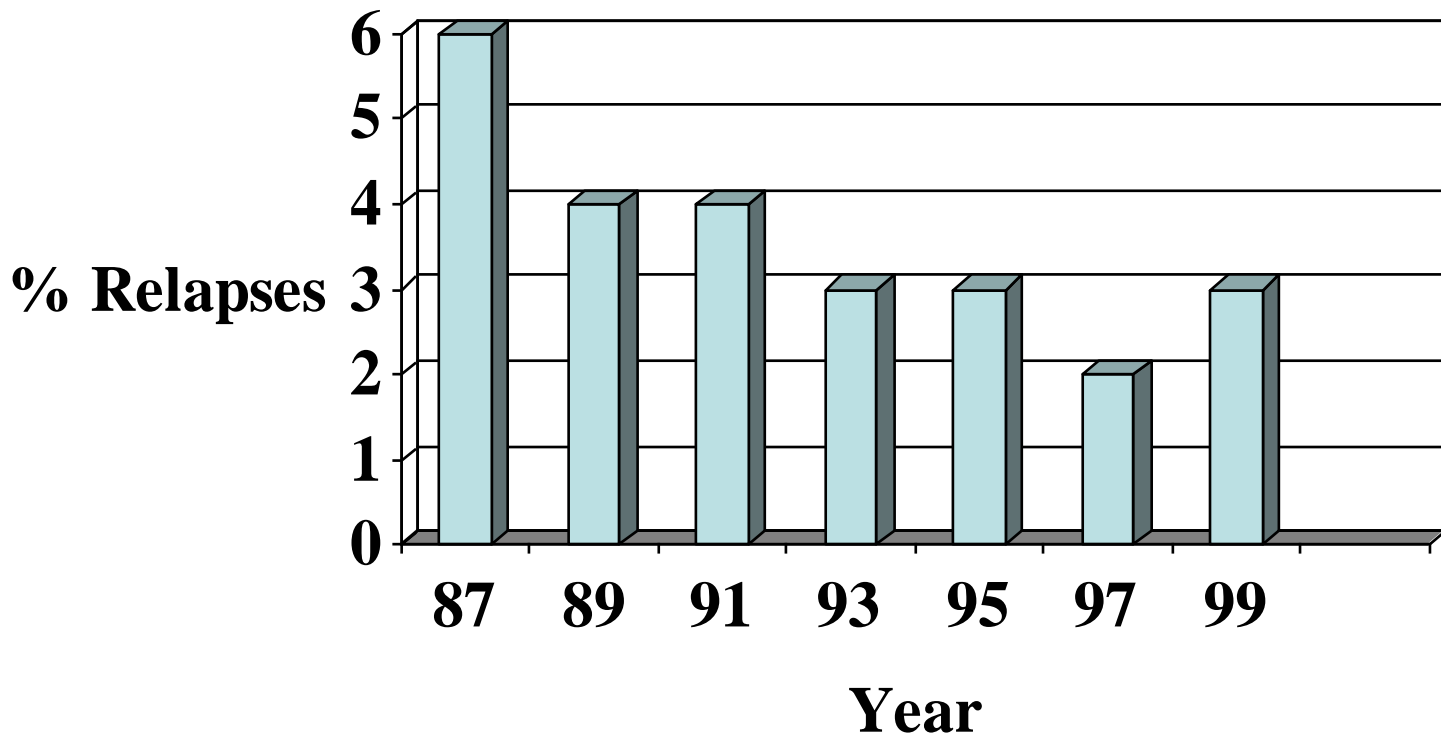
S.Africa

16%

6%

(Sonnenberg et al 2001)

# **% Patients registered nationally with relapse smear-positive PTB in Malawi**



# HIV and TB in Malawi

<u>Year</u>	<u>Site</u>	<u>No. TB</u>	<u>% HIV-positive</u>
<b>1986</b>	<b>Zomba</b>	<b>125</b>	<b>26</b>
<b>1993</b>	<b>Mzuzu</b>	<b>167</b>	<b>67</b>
<b>1994</b>	<b>Blantyre</b>	<b>665</b>	<b>75</b>
<b>1995</b>	<b>Zomba</b>	<b>793</b>	<b>77</b>
<b>2000</b>	<b>Malawi</b>	<b>512</b>	<b>77</b>

# The research question:

Is the Malawi NTP missing recurrent tuberculosis under routine programme settings?

# AIM of the Study

**To determine whether patients who have been registered as “New TB” have been previously diagnosed and treated as relapse smear-positive Pulmonary TB and recurrent smear-negative TB?**

# METHODS



# Design

- This will be a cross-sectional study involving a structured interview of TB patients

*[study designs include descriptive, cross-sectional, case-control, and cohort – either prospective or retrospective]*

# Setting and site visits

- General: Malawi is a small country in Africa with high HIV and TB burden. There is a country-wide DOTS Programme and all patients spend the first two months of TB treatment in hospital receiving initial phase therapy
- Site visits: **All** hospitals in the country that register and treat patients with TB will be visited. These include 3 central hospitals, 22 district hospitals and 18 mission hospitals
- Timing of the visits: These hospitals will be visited between January and June 1999 as part of the routine NTP supervision

# Participants (patients)

- **All** patients who are in hospital receiving treatment during the initial phase and who have been registered as “New TB” will be interviewed using a structured questionnaire
- Patients will be identified by going round the TB wards (all patients are admitted to TB wards) in a set fashion and this will include all patients in their beds

*Patients not in their beds at the time will not be interviewed: a record will be made of TB registration number, age, sex, and type of TB*

# Variables, data collection and validation

- Variables to be collected include: -TB registration no., age, sex, type of TB, **previous history of TB**
- Those with previous history of TB will be asked: when, what type of TB, was treatment completed
- Data to be collected into a structured questionnaire
- Validation of data on previous TB will be done using TB identity cards wherever possible

# Sources of data:

- All patients in their TB beds will be interviewed
- Patients who are out of the TB ward and cannot be traced will not be included  
*[however, their age, sex and type of TB will be listed and compared with those in bed to ensure the two groups are similar]*

# Analysis and statistics

- Data will be entered into EPI-INFO software
- The chi-square test will be used to compare differences in proportions between groups (odds ratios with 95% confidence intervals)
- Differences at 5% level ( $p < 0.05$ ) to be regarded as significant

# Sample size

Not calculated because this is a national study involving all patients in hospital at the time of the visit

# Ethics approval

- Study to be approved by the TB programme management group
- Ethics approval to be obtained from the Malawi National Health Science Research Committee



# BUDGET

<b>Research Activity</b>	<b>Costing (USD\$)</b>
Two NTP operational research officers for hotel accommodation and daily per diems	450
Stationary	50
<b>TOTAL</b>	<b>500</b>

*Research piggy-backed onto routine supervision and therefore less costly*

# JUSTIFICATION

If hypothesis is correct, and previously treated patients are incorrectly registered as “new patients”, then:-

- Incorrect treatment is administered
- Incorrect data are reported to WHO
- We need to find out why and educate District TB Officers about proper management