Imperial College London

How to address relevant global health problems with correct study design

Practical session

Global Health Course

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TB as occupational hazard

Since early ’50s TB has been viewed as an occupational hazard to HCWs

In high-income countries the occupational risk among HCWs substantially decreased

- The progressive introduction of control measures against TB transmission
- The introduction of effective anti-tuberculosis treatment
- The concurrent long-term downward trends of tuberculosis incidence

In low and middle income countries the occupational risk of tuberculosis has remained unchanged.

TB control in Health Care Settings

Probability of transmission of tuberculosis to HCW depends on

- the number of patients with active tuberculosis in contact with a worker
- the infectiousness of the index case
- the ventilation rate of the worker
- the duration of exposure
- the air-exchange rate in the interior space.

Measures to decrease the risk of TB transmission

- reducing the delay in diagnosing / isolation of potentially infectious cases
- adoption of adequate therapeutic protocols
- safety of procedures causing aerosolization of tubercule bacilli (such as cough-induction, bronchoscopy, etc…)
- adoption of personal protection devices (such as HEPA masks)
- engineering solution to ensure adequate ventilation

Case Study Scenario

You are part of a team asked to

– assess the magnitude of the problem in a specific area

– assess the risk associated to specific occupations and workplaces

– identify and test potential preventive measures

How would you proceed?

Framing the questions-Exposure

Where / When HCWs are exposed to TB infection?

- How many potentially infectious TB cases is a HCWs exposed to?
- For how long?
- Are all the TB cases equally infectious at any time?

Classification of the working activities in terms of TB exposure?

The exposures of interest are chosen in order to answer the right question → workplaces & working activities are defined accordingly.

- Doctor, Nurses, Lab Technicians, Cleaners, Students.
- Chest clinics, Surgery, Pathology, Outpatient services.

Framing the questions-Outcome

How much TB do we have among the HCWs?

How much TB transmission is occurring in the HCS?

- Prevalence of tuberculosis among HCWs?
- Incidence of tuberculosis among HCWs?

- Prevalence of tuberculosis infection among HCWs?
- Incidence of tuberculosis infection among HCWs?

The outcome of interest is chosen in order to answer the right question → the testing protocol is defined accordingly.

- Chest X-Rays
- TB Skin Test single step
- TB Skin Test two steps

Study design: Cross Sectional

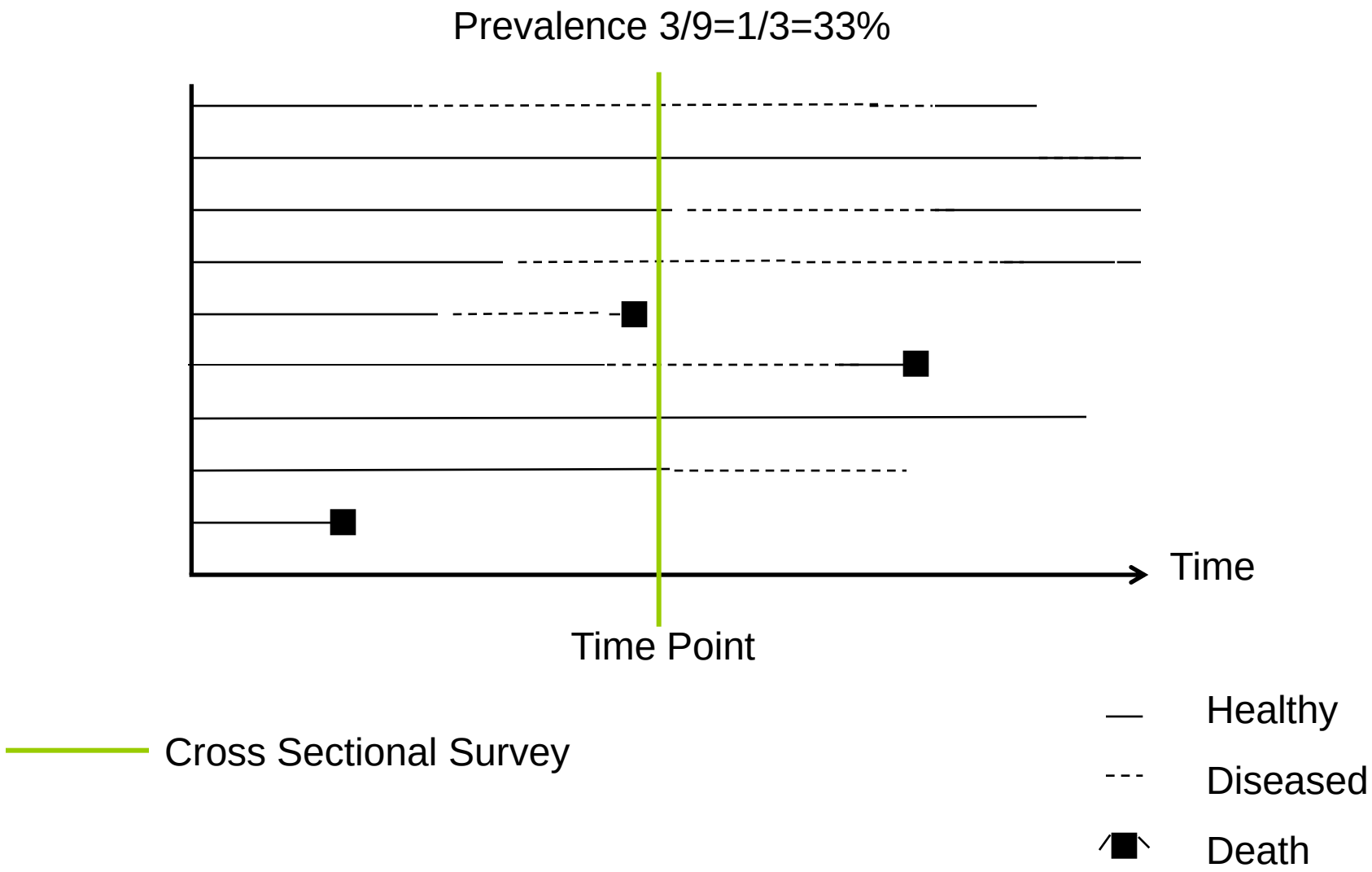
To assess

- Prevalence of TB or LTBI (latent TB infection) among HCWs.
  - Gender
  - Age
  - Workplace & Working activities

- Number of TB cases attending HC facilities.
  - TB definition
  - Infectiousness
  - Time spent in the facility

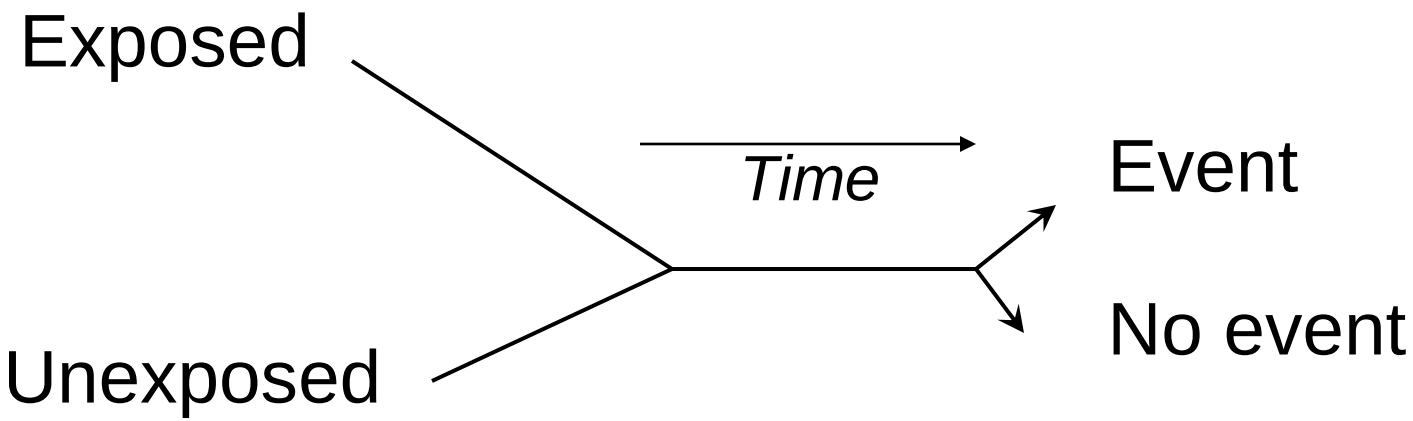
- TB control measures adopted.
  - Administrative measures and safety protocols
  - Individual protection measures
  - Engineering solution to ensure adequate ventilation

Time (Prevalence)



Analytical studies

*Investigating the **(causal)** association between **exposure** and **outcome** of interest*



Study design: Analytical studies

To investigate the causal relationship between

- Exposure
  - Workplace & Working activities as proxies.
- Outcome
  - Incidence of LTBI
- Confounders:
  - Age
  - Gender
  - Time since employment/ Years of training

Measuring exposure and outcome

Exposure: the **independent** variable within the ***causal pathway*** .

- Usually characterized by **intensity**, **duration** and **dose.**
- Examples: year of birth, age, employment status, employment site, smoking habits, genotype, etc...
- Assessment: questionnaire, administrative datasets, instrumental measurements , etc...

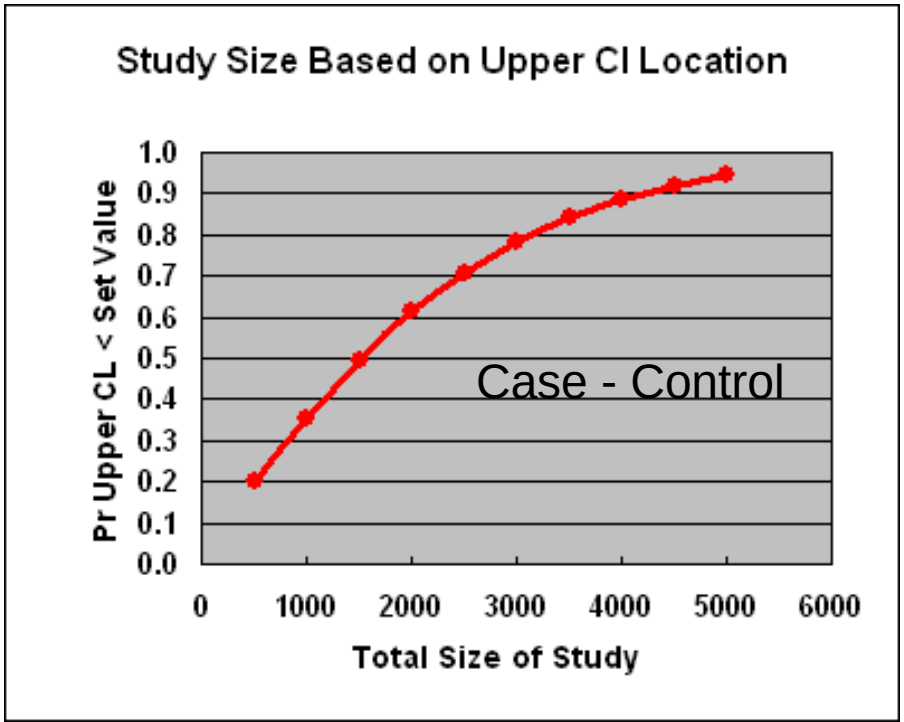
Outcome: the **dependent** variable within the ***causal pathway*** .

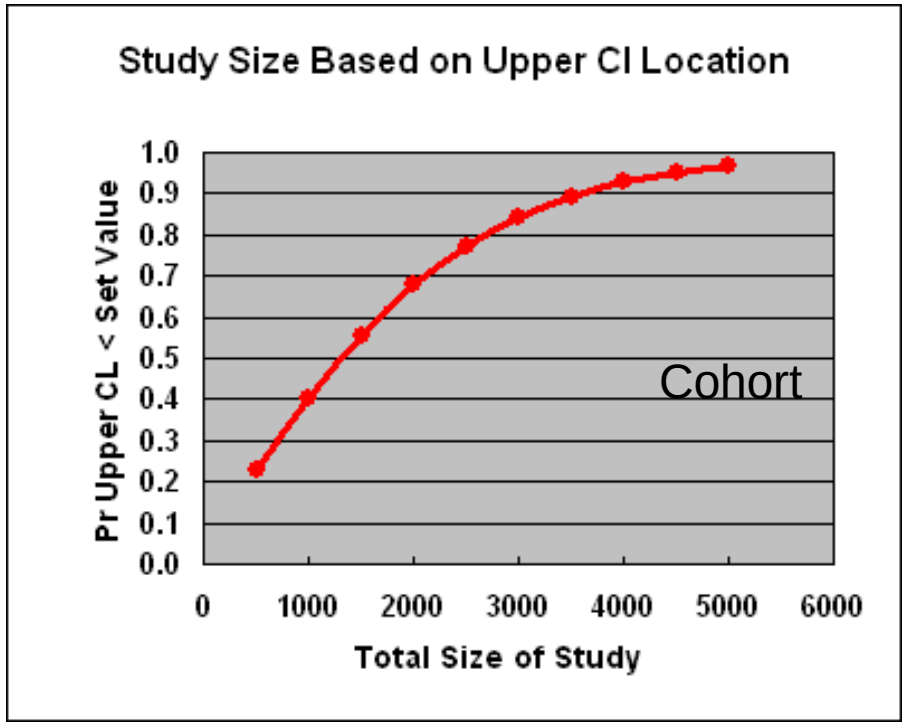
- Usually explicitly described by a **"case definition"**
- Examples: clinical signs or symptoms, height, weight, physical or psychological performances, etc...
- Assessment: questionnaire, administrative datasets, instrumental measurements , etc...

Sample size & Power Calculation

How large should be the sample to capture a significant effect of exposure (avoid type II error)?

- Expected risk among unexposed (e.g. 5%)
- Expected effect of exposure & variability (e.g. RR 2; RR Upper Bound 3)
- Type I error level (e.g. 95%CI or 90%CI)





Data analysis

Cohort analysis	Exposed (HCWs)	Unexposed (Administrative)
Events	180	60
Person-years	4700	4500
Rate	0.037	0.013

IRR: (180/4700) / (60/4500) = 2.87 (95%CI 2.1- 3.7)

Unexposed and exposed subjects have the same **sampling fraction (10%)**

Cases	180	60
Controls	470	450

OR: (180/470) / (60/450)= (180*450) / (470*60) = 2.87 (95%CI 2.07-4.02)

Study design: RCT

What single or combination of preventive measure should be adopted?

- Administrative measures
- Safety protocols
- Individual protection
- Engineering solution

Design a randomized controlled trial: cluster sampling, factorial design, how many units would be involved?

Study design: RCT

So far no RCT has been published.

Mathematical Models simulations

Cost – effectiveness analysis based on observational studies

References

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