Approaches to assessing coronary heart disease risk: Statistical and Epidemiological Issues

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Artemis Hotel

Amsterdam, Netherlands

Program

- **Session I: Goals and Objectives**
- **Session II: Background**
  - **Objective: understand the role of cohort analyses**
- **Session III: Missing Data and Data Imputations**
  - **Objective: methods for defining and handling missing data**
- **Session IV: Risk Ratios and Multiple Testing**
  - **Objective: understanding the public health significance**
- **Session V: Access and Replication**
  - **Objective: methods for confirmation**
- **Session VI: Adjustment for Confounding**
  - **Objective: identify new methods for adjustment**

RCT / observational studies

- Do not address the same question
  - For AE, trials are usually to small without enough follow-up
- When used to claim beneficial effect, observational studies have not performed well in several examples
  - Vitamin, HRT, …
- For AE, however the situation is slightly different

Questions

- Role of cART
- Role of traditional risk factors
- Role of HIV infection

Background

- D:A:D
  - Specific cohort study
- FHDH ANRS CO4
  - Nested case-control study within the cohort
- GSK trials
  - Observational analyses of trials except when restricting to those where abacavir was randomized
- ACTG
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Methods

- Traditional (parametric) models
  - Accounting for potential confounders
  - Sensitivity analyses for factors thought to be on the causal pathway
- Novel techniques (Machine learning- data mining techniques)
  - Recursive partitioning
  - Non parametric Super learner
- Theoretically appealing, but no proofs of a different results in the context of HIV and CVD

Additional problems

- Study design and data collection are still critical as
  - Only measured confounding can be accounted for
    - Time-dependent confounding
      - IPWT
- Sample size needed for such techniques
- No straightforward implementation

Multiplicity issue ?

- Look at estimates and confidence intervals rather than p-value
- Test and hold out dataset
- Replication studies

A way forward ?

We need a way to deal with unexpected findings

- A systematic approach to proceeding that is rigorous and yet allows the unexpected signal to get through

Various sources of discrepancies

- Clear delineation of the research question
  - Studies find different findings because they ask different questions
  - What is the patient population, what is the outcome, what is the exposure?
- Confounding issues
  - Systematic review of the confounders of interest and what was included in the study
- Estimation methods
  - Methods used – a systematic approach to evaluating findings using different methods for the same study population, outcome, exposure, confounders, etc. - DATA SHARING