

SYLLABUS

Marrakesh, Morocco, November 12-17, 2011

XXth WORLD CONGRESS OF NEUROLOGY



SOCIÉTÉ MAROCAINE
DE NEUROLOGIE

WCN Education Program
Sunday, 13 November, 2011
09:00-12:30

NEUREPIDEMIOLOGY

Chairperson: **Gustavo Roman, USA**

09:00 **INTRODUCTION TO STUDY DESIGN IN NEUROLOGY, PART 1**
Walter Rocca, USA

09:45 **INTRODUCTION TO STUDY DESIGN IN NEUROLOGY, PART 2**
Walter Rocca, USA

10:30 *Coffee Break*

11:00 **STROKE EPIDEMIOLOGY IN DEVELOPING COUNTRIES**
Gustavo Roman, USA

11:45 **EPIDEMIOLOGY OF NEUROHIV IN AFRICA**
Yomi Ogun, Nigeria

XXth WORLD
CONGRESS OF NEUROLOGY
With Africa, for Africa
Marrakesh, Morocco, November 12-17, 2011

Introduction to Study Design: Part 1

Walter A. Rocca, MD, MPH
College of Medicine, Mayo Clinic
Rochester, MN - USA

When the student is ready,
the teacher will appear

(Chinese proverb)

Structure of the presentation

- Definitions
- Complex diseases
- Epidemiology
- Causes and effects
- Study design
- Clinical trial

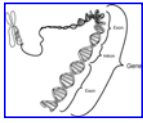
Major research areas

- Clinical research (children, men, women)
 - Diagnosis
 - Prognosis (outcomes)
 - Frequency
 - Treatment
 - Risk (risk factors)
 - Prevention
- Laboratory research (“bench” or “basic”)
 - Animals (animal models)
 - Cell cultures
 - Biologic samples (blood, CSF, etc.)
 - Genetic material
- Translational research
 - From bench to bedside (T1)
 - From bedside to practice (T2)



(Westfall et al., 2007)

Etiology of complex diseases



Susceptibility genes



Environmental factors



Constitutional and behavioral factors

Etiology of complex diseases



Conception



Birth



Adult life

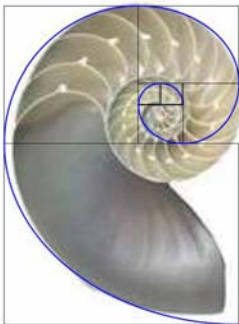


Aging



Life course

Epidemiology as the geometry of clinical research

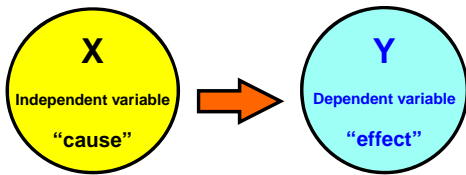


A Nautilus shell inside a Fibonacci spiral

From: Lou Marinoff
The Middle Way
New York: Sterling, 2007

Let no one ignorant of geometry enter here (Plato)

Causes and Effects



- Risk factor X → Disease Y
- Prognostic factor X → Outcome Y
- Drug X → Effect Y

Traditional laboratory experiment

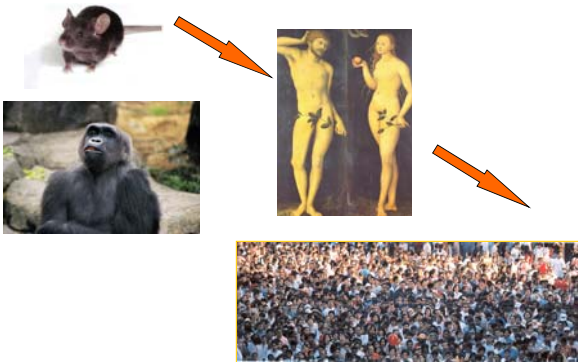
- Two key features:**
- Randomization
 - Cause before effect

Chemical X → Cancer Y

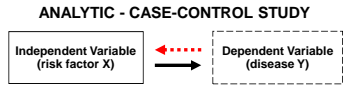
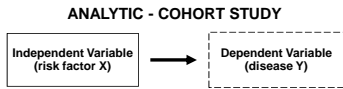
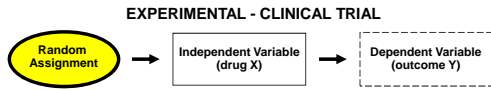
- 100 mice randomized: 50 exposed; 50 nonexposed
- Follow-up for 6 months
- Incidence rate in exposed vs. nonexposed
- Proof of causation



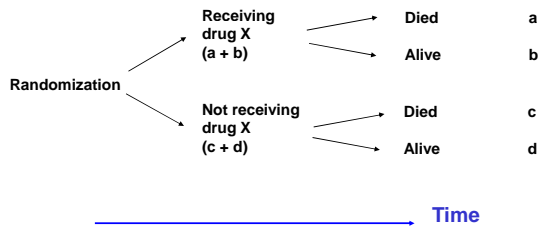
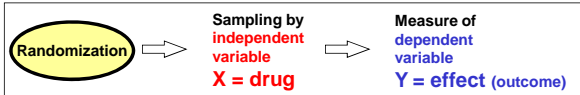
From animals to humans, to society



Clinical study design



Clinical trial design



Measures of risk

DEPENDENT VARIABLE (outcome Y)

		Died	Survived	
INDEPENDENT VARIABLE (drug X)	Drug X	a	b	a + b
	No drug X	c	d	c + d
		a + c	b + d	

Incidence: $\frac{a}{a+b}$; $\frac{c}{c+d}$

Relative risk: $\frac{\frac{a}{a+b}}{\frac{c}{c+d}}$

Summary of part 1

- Definitions
- Complex diseases
- Epidemiology **and tools**
- Causes and effects - **beliefs**
- Study design **and evidence**
- Clinical trial - **randomization**

The architecture of clinical research



Introduction to Study Design: Part 2

Walter A. Rocca, MD, MPH
College of Medicine, Mayo Clinic
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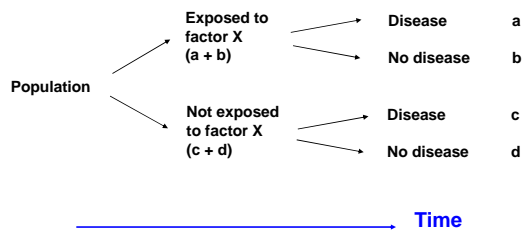
Randomization and its discontents
(Paraphrase of Sigmund Freud)

Structure of the presentation

- **When a clinical trial is not possible**
 - Observational studies
- **Cohort studies**
 - Example
- **Case-control studies**
 - Example
- **Clinical study design**
- **Closing advice**

The cohort study design

Sampling by independent variable
X = risk factor → Measure of dependent variable
Y = disease



Measures of risk

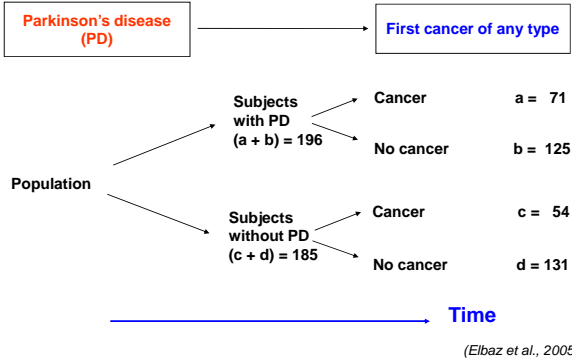
DEPENDENT VARIABLE (disease Y)

		With	Without	
INDEPENDENT VARIABLE (risk factor X)	Exposed	a	b	a + b
	Unexposed	c	d	c + d
		a + c	b + d	

Incidence: $\frac{a}{a + b}$; $\frac{c}{c + d}$

Relative risk: $\frac{\frac{a}{a + b}}{\frac{c}{c + d}}$

Parkinson's disease and cancer



Parkinson's disease and cancer

DEPENDENT VARIABLE (Cancer)

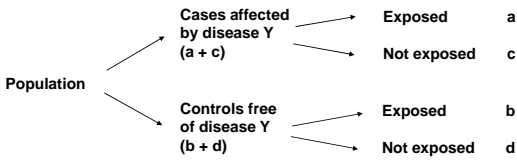
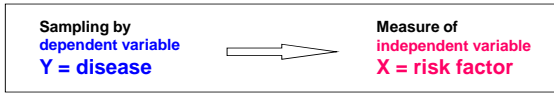
		Cancer	No cancer	
INDEPENDENT VARIABLE (PD)	PD	71	125	196
	No PD	54	131	185
		125	256	

Incidence: $\frac{71}{196}$; $\frac{54}{185}$

Relative risk: $\frac{\frac{71}{196}}{\frac{54}{185}} = 1.24$ (crude RR for cancer)

(HR from survival analysis = 1.64)
(Elbaz et al., 2005)

Case-control study design



Time ←

Measures of risk

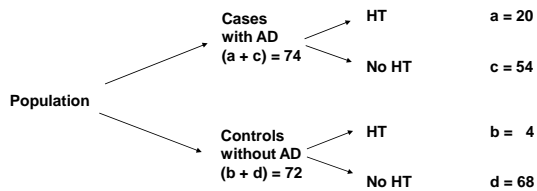
DEPENDENT VARIABLE (disease Y)

		With	Without	
INDEPENDENT VARIABLE (risk factor X)	Exposed	a	b	a + b
	Unexposed	c	d	c + d
		a + c	b + d	

Probability: $\frac{a}{a+c}$; $\frac{c}{a+c}$; $\frac{b}{b+d}$; $\frac{d}{b+d}$ Odds: $\frac{a}{c}$; $\frac{b}{d}$

$$\text{Odds ratio: } \frac{\frac{a}{c}}{\frac{b}{d}} = \frac{a \times d}{c \times b}$$

Head trauma (HT) & Alzheimer's disease (AD)



Time ←

(Mortimer et al., 1985)

Head trauma (HT) & Alzheimer's disease (AD)

DEPENDENT VARIABLE (disease)

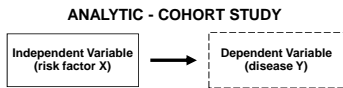
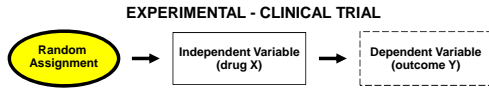
		AD	No AD	
INDEPENDENT VARIABLE (risk factor)	HT	20	4	24
	No HT	54	68	122
		74	72	

Probability: $\frac{20}{74}$; $\frac{54}{74}$; $\frac{4}{72}$; $\frac{68}{72}$ Odds: $\frac{20}{54}$; $\frac{4}{68}$

$$\text{Odds ratio: } \frac{\frac{20}{54}}{\frac{4}{68}} = \frac{20 \times 68}{54 \times 4} = 6.3$$

(Mortimer et al., 1985)

Clinical study design



Summary of part 2

- **When a clinical trial is not possible**
 - Observational studies
- **Cohort studies**
 - Parkinson's disease and cancer
- **Case-control studies**
 - Head trauma and dementia
- **Clinical study design**
 - The construction of evidence

The lesson from the lotus flower



Design the best possible study (lotus flower) despite the unavoidable uncertainties (roots in the mud at the bottom of the pond)
