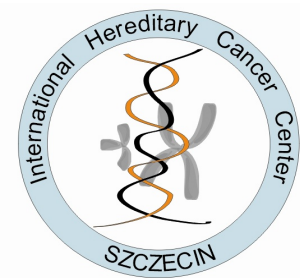
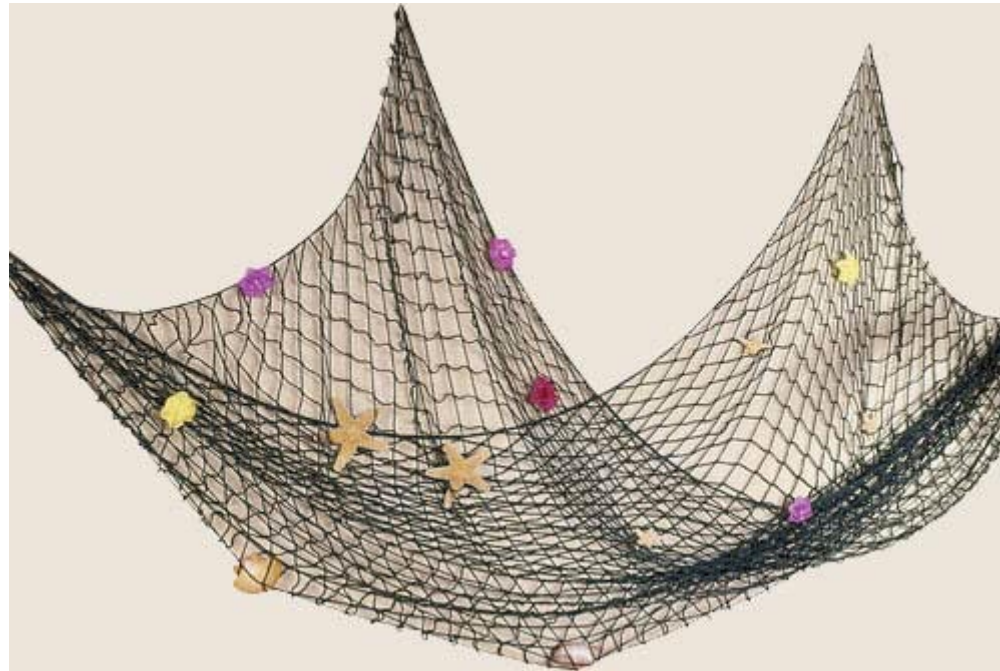


Epidemiologic traps for biotechnologists III



Dr. Pablo Serrano-Fernández
International Hereditary Cancer Center
pabloserrano.eu/biotech/

Experimental design

Epidemiology

1) Hypothesis

2) Variables

0
1
1
1
1
0
ATGTCGCCTATAACCGTACAGACAGTAGATAGCTCTGCTGACTGATCCCAATTCGGATCCGTAATGTCGCCTATATCCGTACAGACAGTAGATAGCTCTGCTGACTGAT
1
0
1
1
1
0
0
1
1
1
0
1
0
0
0
1
0
1
0
1
0
0
0
0
1
1
1
1
0
0
1
0
1
1
1

Sampling

Prospective or retrospective?

A) 1 group: before and after factor X

- keep all other conditions as constant as possible

B) 2 groups: presence / absence of factor X

- if possible do not inform of absence of factor X (e.g. placebo)
- randomize the groups (perfectly unselected)
- or apply like in C

C) 2 groups: diseased / healthy

- identify potential confounding variables
- adjust by confounding variables (groups of diff. size)
- match by confounding variables (groups of same size)

Sampling

Epidemiology

0
1
1
1
1
1
0
1
0
1
1
1
0
0
1
1
1
0
1
0
0
0
0
1
1
1
1
0
0
1
1
1
1
1

ATGTCGCCTATAACCGTACAGACAGTAGATAGCTCTGCTGACTGATCCCAATTCGGATCCGTAATGTCGCCTATATCCGTACAGACAGTAGATAGCTCTGCTGACTGAT

Problems:

- Differential recall
- Lying

Sampling

- D) 2 groups: diseased / general population sample
 - general population sample has to be large and perfectly unselected (random generators)
 - in specific cases some confounding variables may be ignored (e.g. newborns for genetic studies)

ATGTCGCCTATAACCGTACAGACAGTAGATAGCTCTGCTGACTGATCCCAATTCGGATCCGTAATGTCGCCTATATCCGTACAGACAGTAGATAGCTCTGCTGACTGAT

0
1
1
1
1
1
0
1
0
1
1
1
0
0
1
1
0
1
0
1
0
1
0
0
0
0
1
1
1
1
0
0
1
0
1
1
1

Analysis

ATGTCGCCTATAACCGTACAGACAGTAGATAGCTCTGCTGACTGATCCCAATTCGGATCCGTAATGTCGCCTATATCCGTACAGACAGTAGATAGCTCTGCTGACTGAT

ANNALS *of the* **New York Academy of Sciences**

1076: 343–354 (2006)

Pesticides and Adult Respiratory Outcomes in Agricultural Health

HOPPIN JA, UMBACH DM, LONDON SJ, LYNCH CF, ALAVANJA MCR, SANDLER DP

- Agricultural Health Study, a prospective cohort study of 89,000 licensed pesticide applicators and their spouses in Iowa and North Carolina (10 yrs).**
- Association of 40 pesticides with respiratory outcomes, including wheeze, adult asthma, farmer's lung, and chronic bronchitis.**
- Models adjusted for age, state, smoking status, and body mass index.**
- Use of chlorpyrifos for at least 20 days per year had an odds ratio of 1.48 (95% confidence interval [CI] = 1.00–2.19) for farmers, odds ratio of 1.96 (95% CI = 1.05–3.66) for commercial applicators.**

Analysis

ATGTCGCCTATAACCGTACAGACAGTAGATAGCTCTGCTGACTGATCCCAATTCGGATCCGTAATGTCGCCTATATCCGTACAGACAGTAGATAGCTCTGCTGACTGAT

Epidemiology

0
1
1
1
1
1
0
1
0
1
1
1
0
0
1
1
1
0
1
0
0
1
0
1
1
0
1
0
0
0
1
1
1
1
1
0
0
1
0
1
1
1
1

		Disease	
		+	-
Factor	+	A	B
	-	C	D

Incidence rate:

Factor + : $a/(a+b)$

Factor - : $a/(a+b)$

Analysis

ATGTCGCCTATAACCGTACAGACAGTAGATAGCTCTGCTGACTGATCCCAATTCGGATCCGTAATGTCGCCTATATCCGTACAGACAGTAGATAGCTCTGCTGACTGAT

Epidemiology

		Disease	
		+	-
Factor	+	A 20	B 80
	-	C 10	D 90

Incidence rate:

$$\text{Factor + : } a/(a+b) = 0.2$$

$$\text{Factor - : } c/(c+d) = 0.1$$

Analysis

Epidemiology

		Disease	
		+	-
Factor	+	A 20	B 80
	-	C 10	D 90

Prospective Study: e.g. Cohort study

Smokers/non-smokers (factor)

Lung cancer after 30 yrs. of study (disease)

Analysis

		Disease	
		+	-
Factor	+	A 20	B 80
	-	C 10	D 90

Prospective Study: **RELATIVE RISK (RR)**

$$\frac{\text{i. rate factor +}}{\text{i. rate factor -}} = \frac{a/(a+b)}{c/(c+d)} = 2.0$$

Analysis

		Disease	
		+	-
Factor	+	A 20	B 80
	-	C 10	D 90

Retrospective Study: E.g. Case - Control study

Smokers/non-smokers (factor)

Lung cancer until the moment of study (disease)

[adjust confounding variables]

Analysis

Epidemiology

		Disease	
		+	-
Factor	+	A 20	B 80
	-	C 10	D 90

Retrospective Study: **ODDS RATIO (OR)**

$$\frac{ad}{bc} = 2.02 \quad (\text{estimates INDIRECTLY the RR})$$

(condition: $ac \ll bd$)

Analysis

ATGTCGCCTATAACCGTACAGACAGTAGATAGCTCTGCTGACTGATCCCAATTCGGATCCGTAATGTTCGCCTATATCCGTACAGACAGTAGATAGCTCTGCTGACTGAT

ANNALS *of the* **New York Academy of Sciences**

1076: 343–354 (2006)

Pesticides and Adult Respiratory Outcomes in Agricultural Health

HOPPIN JA, UMBACH DM, LONDON SJ, LYNCH CF, ALAVANJA MCR, SANDLER DP

- Agricultural Health Study, a prospective cohort study of 89,000 licensed pesticide applicators and their spouses in Iowa and North Carolina (10 yrs).**
- Association of 40 pesticides with respiratory outcomes, including wheeze, adult asthma, farmer's lung, and chronic bronchitis.**
- Models adjusted for age, state, smoking status, and body mass index.**
- Use of chlorpyrifos for at least 20 days per year had an odds ratio of 1.48 (95% confidence interval [CI] = 1.00–2.19) for farmers odds ratio of 1.96 (95% CI = 1.05–3.66) for commercial applicators.**

Analysis

ATGTCGCCTATAACCGTACAGACAGTAGATAGCTCTGCTGACTGATCCCAATTCGGATCCGTAATGTCGCCTATATCCGTACAGACAGTAGATAGCTCTGCTGACTGAT

40	60
20	80

20	80
10	90

2	98
1	99

Epidemiology

I. Rate

Factor +

0.4

0.2

0.02

Factor -

0.2

0.1

0.01

RR

2.0

2.0

2.0

OR

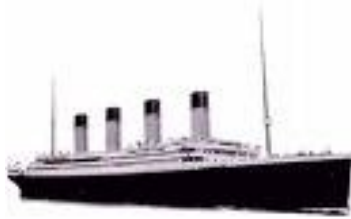
2.67

2.25

2.02

Analysis

Titanic



	Died	Survived	
Women	154	308	462
Men	709	142	851
	863	450	1313

Death incidence women: $154/462 = 0.33$

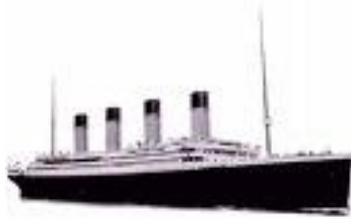
Death incidence men: $709/851 = 0.83$

RR = $0.83/0.33 = \underline{2.5}$ greater incidence of death in men.

Analysis

Epidemiology

Titanic



	Died	Survived	
Women	154	308	462
Men	709	142	851
	863	450	1313

Death incidence women: $154/462 = 0.33$

Death incidence men: $709/851 = 0.83$

RR = $0.83/0.33 = \underline{2.5}$ greater incidence of death in men.

Women: $154/308 = 0.5 = 0.5:1$ chances for dying (2:1 for surviving)

Men: $709/142 = 5 = 5:1$ chances for dying

OR = $5/0.5 = \underline{10}$ greater chances (odds) for death in men.

Analysis

ANNALS *of the* New York Academy of Sciences

1076: 343–354 (2006)

Pesticides and Adult Respiratory Outcomes in Agricultural Health

HOPPIN JA, UMBACH DM, LONDON SJ, LYNCH CF, ALAVANJA MCR, SANDLER DP

- Agricultural Health Study, a prospective cohort study of 89,000 licensed pesticide applicators and their spouses in Iowa and North Carolina (10 yrs).
- Association of 40 pesticides with respiratory outcomes, including wheeze, adult asthma, farmer's lung, and chronic bronchitis.
- Models adjusted for age, state, smoking status, and body mass index.
- Use of chlorpyrifos for at least 20 days per year had an odds ratio of 1.48 (95% confidence interval [CI] = 1.00–2.19) for farmers odds ratio of 1.96 (95% CI = 1.05–3.66) for commercial applicators.

Analysis

Population attributable risk (**PAR**)
(Fraction of people diseased due to the analysed factor)

$$\text{PAR} = \frac{\text{Prevalence (RR-1)}}{1 + \text{Prevalence (RR-1)}}$$

0
1
1
1
1
1
0
1
0
1
1
0
0
1
1
0
1
0
1
0
0
0
1
0
1
0
1
0
0
0
1
1
1
1
0
0
1
0
1
1
1
1

ATGTCGCCTATAACCGTACAGACAGTAGATAGCTCTGCTGACTGATCCCAATTCGGATCCGTAATGTCGCCTATATCCGTACAGACAGTAGATAGCTCTGCTGACTGAT

Analysis

Population attributable risk (**PAR**)
(Fraction of people diseased due to the analysed factor)

$$\text{PAR} = \frac{\text{Prevalence (RR-1)}}{1 + \text{Prevalence (RR-1)}}$$

Example:

Prevalence of smoking in Poland 32%
RR of lung cancer among smokers ~ 11

$$\text{PAR} = \frac{0.32 (11-1)}{1 + 0.32 (11-1)} = 0.762 \quad (76.2\%)$$

76.2% of lung cancers in Poland are due to smoking behaviour