From Research to Practice: Training in Sexual and Reproductive Health Research

Strategies for data analysis: case-control studies

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UNDP/UNFPA/WHO/World Bank Special Programme of Research, Development and Research Training in Human Reproduction
World Health Organization

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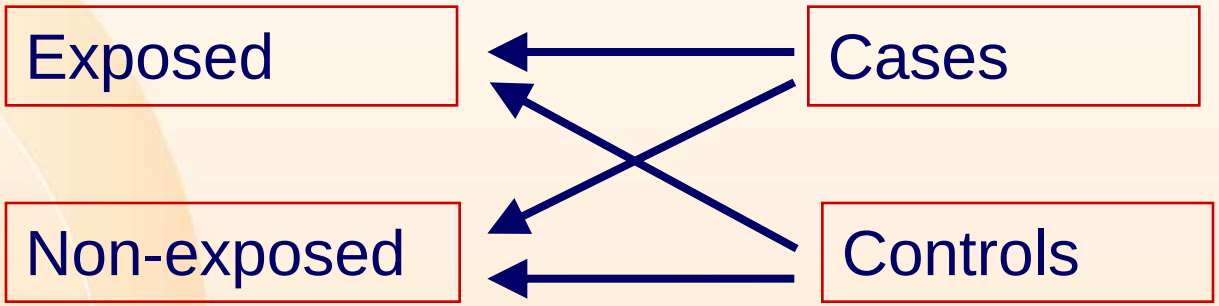
Design of case-control studies: retrospective



Then measure exposure

First select

Examples of topics investigated by case-control studies

Exposure	Outcome
Use of oral contraceptives	Breast cancer
Recent use of oral contraceptives	Myocardial infarction
Large doses of folate and iron in pregnancy	Microcephaly
Phyto-oestrogens	Breast cancer
Male condom use	Genital warts

Examples of topics investigated by case-control studies

Exposure	Outcome
Body mass index	Pancreatic cancer
Physical disability	Earthquake mortality
Hiatus hernia	Reflux oesophagitis
Paracetamol use	Ovarian cancer

Prevalence of disease is fixed by design

	Cases	Controls
Exposed	a	b
Non-exposed	c	d
	a+c	b+d

Fixed margins

Prevalence of disease is fixed by design

	Cases	Controls
Exposed	20	10
Non-exposed	80	90
	100	100

Prev=20/30?

No!

Fixed margins

Prevalence of disease is fixed by design

	Cases	Controls
Exposed	20	20
Non-exposed	80	180
	100	200

Prev=20/40?

No!

Fixed margins

Prevalence of exposure in cases and controls

In case-control studies we can calculate:

- Prevalence of exposure in cases and in controls
  a/(a+c) and b/(b+d)

We cannot calculate prevalence of disease, or risk for exposed and for non-exposed

We cannot calculate the relative risk (RR)

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Odds of exposure

In case-control studies we can calculate:

- The odds ratio to measure association between disease and exposure:

The odds of being exposed for a case is a/c
The odds of being exposed for a control is b/d

The odds ratio of exposure for cases vs controls is

$$OR_{Exp} = (a/c)/(b/d) = (a \times d)/(b \times c)$$

Odds ratio (OR)

	Disease	No disease
Exposed	a	b
Non-exposed	c	d
$Odds_{Exp}$	a/c	b/d

$$OR_{Exp} = a/c / b/d = ad/bc$$

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Odds ratio (OR)

	Disease	No disease
Exposed	a	b
Non-exposed	c	d
$Odds_{Exp}$	a/c	b/d

$$OR_{Exp} = (a/c)/(b/d) = (a \times d)/(b \times c) = (a/b)/(c/d) = OR_{Dis}$$

Interpretation of the odds ratio

- If exposure and disease are not associated, OR=1
- If exposure and disease are positively associated, OR>1
- If exposure and disease are negatively associated, OR<1

The OR is a good estimation of the RR if the disease is rare

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Confidence intervals for the OR

There are several methods:
-Woolf's method: approximate
-Cornfield method: iterative
-Test-based method
-Logistic regression

We usually work in the log scale, ln OR
Woolf's method:

SE ln OR = $\sqrt{(1/a+1/b+1/c+1/d)}$

95% CI for ln OR: ln OR ± $z_{0.025}$ x $\sqrt{(1/a+1/b+1/c+1/d)}$

95% CI for the OR: OR x exp [± $z_{0.025}$ x $\sqrt{(1/a+1/b+1/c+1/d)}$]

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Strategy for data analysis for case-control studies

- Describe study profile: number of cases and controls, identified and analyzed
- Baseline characteristics of cases and controls
- Crude ORs for different categories of use and risk factors
- ORs for different categories of use and risk factors, adjusting for confounders

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Example: Oral contraceptives and breast cancer in young women

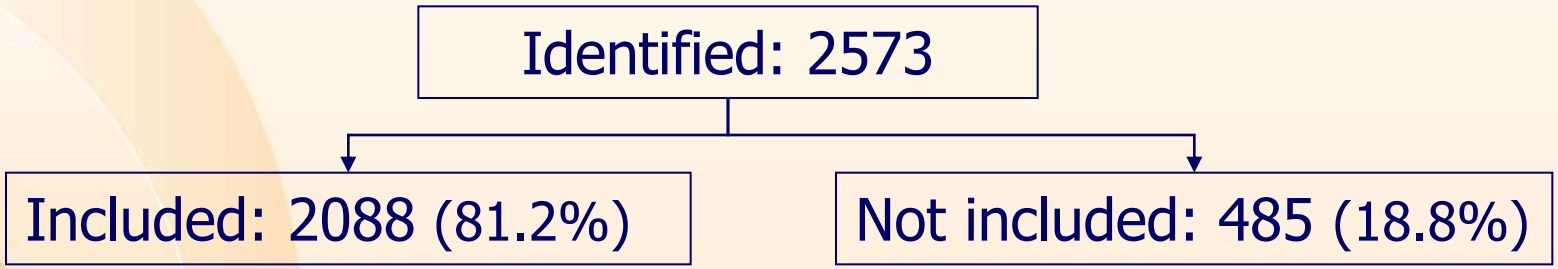
Lancet 1985; 326:970-972

Study aim was to investigate relation between use of oral contraceptives (OCs) by young women and their risk of breast cancer.

Cases: women 20-44 years at initial diagnosis of breast cancer, between Dec 1 1980 and Dec 31 1982, resident in 8 regions of the US, identified from population-based cancer registries.

Controls: women 20-44 years selected during same 25 months as the cases were diagnosed, residents of the 8 regions, selected randomly by telephone calls to households.

Oral contraceptives and breast cancer
Study profile: cases



6.4% refused to participate
3.7% died or were too ill
8.7% miscellaneous reasons

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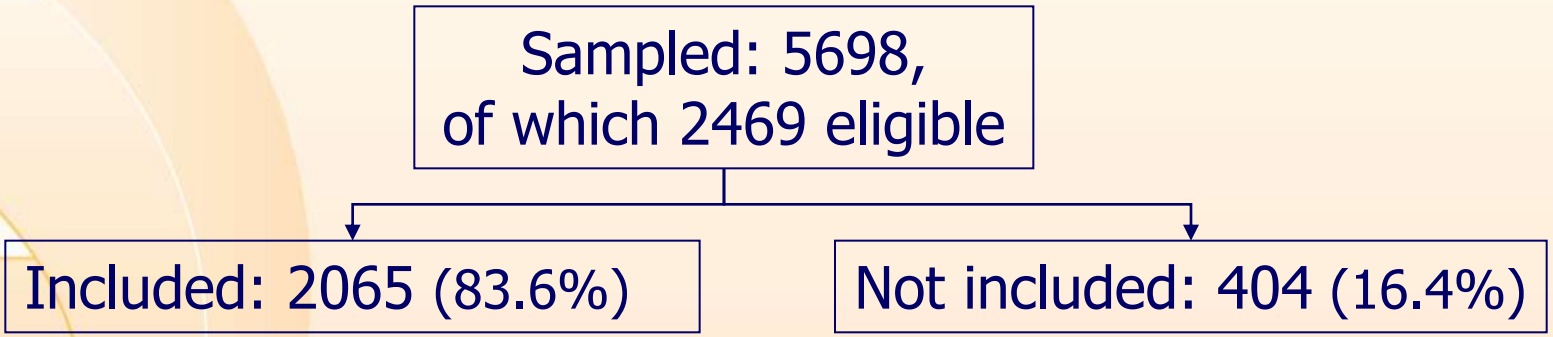
Oral contraceptives and breast cancer
Study profile: controls



11.2% refused to participate
2.2% moved out
3.0% miscellaneous reasons

Oral contraceptives and breast cancer
Baseline characteristics of cases and controls

	Cases(%)	Controls(%)
Age		
20-24	0.7	5.1
25-29	6.0	8.2
30-34	18.3	20.8
35-39	33.5	28.6
40-44	41.4	37.3
Family history of breast cancer		
Yes	29.1	18.7
No	42.3	51.4
Unknown	28.6	29.9

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Oral contraceptives and breast cancer
Baseline characteristics of cases and controls

	Cases(%)	Controls(%)
Age at first term pregnancy		
Nulliparous	18.2	18.4
<20	19.1	22.1
20-22	23.1	24.7
23-26	22.3	21.6
27-29	9.2	7.6
>29	7.0	4.0
Parous, unknown age	1.1	1.6
Benign breast disease surgery		
Yes	4.5	2.3
No	87.2	91.7
Unknown	8.3	6.0

Conclusions about baseline analysis

- Cases were older at diagnosis than controls were at selection
- Larger proportion of cases had family history of breast cancer
- Slightly larger proportion of cases had late age at first pregnancy
- Larger proportion of cases had benign breast disease surgery

Oral contraceptives and breast cancer
Results: crude ORs

	Cases	Controls
Exposed	1701	1662
Non-exposed	387	403
All	2088	2065

OR=1.07

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The odds of being exposed for a case is 1701/387= 4.4

The odds of being exposed for a control is 1662/403 = 4.1

The odds ratio of exposed vs non-exposed is

OR = (1701/387)/(1662/403) =

= (1701 x 403)/(1662 x 387) = 1.07

95% CI: 0.91 to 1.25

Stratification and confounding variables?

- Age: main purpose was stratifying by age

Oral contraceptives and breast cancer
Results: crude ORs

Age at diagnosis or selection	Cases(%)		Controls(%)		OR
	N	% ever users	N	% ever users	
20-24	15	100.0	106	69.8	-
25-29	126	86.5	169	87.6	0.91
30-34	382	89.3	429	88.1	1.13
35-39	700	86.4	590	85.1	1.11
40-44	865	73.0	771	72.6	1.02
Total	2088	81.5	2065	80.5	1.07

Oral contraceptives and breast cancer results: adjusting

We need to adjust for factors associated with the risk of breast cancer or with the likelihood of diagnosis:

- Family history of breast cancer
- Age at first term pregnancy
- History of surgery for benign breast disease
- Frequency of breast examination

Techniques to adjust ORs:

- Logistic regression
- Mantel-Haenszel

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Oral contraceptives and breast cancer
Results: adjusted ORs

Age at diagnosis or selection	Cases(%)		Controls(%)		OR(95% CI) (adjusted)
	N	% ever users	N	% ever users	
20-24	15	100.0	106	69.8	-
25-29	126	86.5	169	87.6	1.0 (0.5-2.1)
30-34	382	89.3	429	88.1	1.2 (0.7-1.8)
35-39	700	86.4	590	85.1	1.1 (0.8-1.6)
40-44	865	73.0	771	72.6	1.1 (0.9-1.4)
Total	2088	81.5	2065	80.5	

Oral contraceptives and breast cancer
Results: adjusted ORs

Use before first term pregnancy	Cases N	Controls N	OR(95% CI) (adjusted)
Never	1143	1174	1 (Reference)
≤12	177	179	1.3 (1.0-1.7)
13-48	323	336	1.1 (0.9-1.5)
>48	231	208	1.2 (0.9-1.6)
Total	1874	1897	

Oral contraceptives and breast cancer
Conclusions

There was no significant increase or decrease in the risk of breast cancer for OC users according to

- Age at diagnosis
- Age at first use
- Duration of use
- Use before first term pregnancy

Use of OCs by young women in the US has no effect on the risk of breast cancer before 45 years of age

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Thank you