Study Design and Analytic Epidemiology for Outbreak Investigations

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Objectives

- Define analytic epidemiology
- Describe types of studies to investigate outbreaks
- Discuss control group selection
- Prepare 2 x 2 table
- Calculate and interpret measures of association

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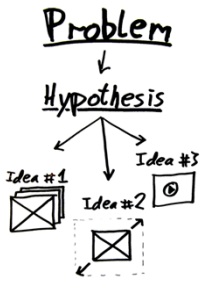
Analytic Epidemiology

- Differs from descriptive epi (person, place, time)
- Develop then test hypothesis
- Examine **exposures** and **outcomes**
- Use **comparison group** (controls)



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Exposure and Outcome

- Exposure= potential risk factor
  - Food item
  - Occupational
  - Behavioral (e.g., smoking)
- Outcome= Disease
  - Cancer
  - Diarrhea
  - Injury

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Common Types of Studies

- Cohort
- Case-Control
- Case-case

- These are **observational** studies, as compared with experimental studies

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Cohort Design

- Start with defined group, classified by exposure status
  - Exposed group
  - Non-exposed group

- Assess who developed disease

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Cohort Studies examples

- Nurse's Health Study- 1970's
  120,000 female nurses – risk factors for cancer and cardiovascular disease

www.nhs3.org

- Outbreak following a wedding reception
- Illness in a school classroom
- Outbreak after church potluck

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Why use a cohort?

- Known denominator: # at **risk** of disease
- Compare exposed and unexposed groups
- However, not always possible to define cohort

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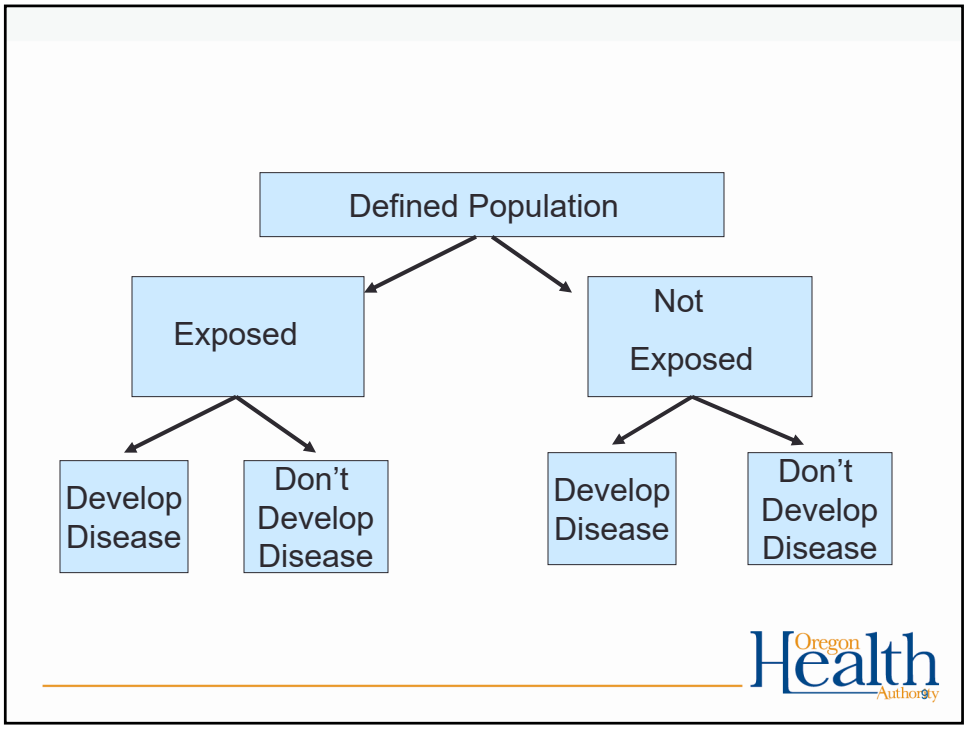
Defined Population
Exposed
Not Exposed
Develop Disease
Don't Develop Disease
Develop Disease
Don't Develop Disease
Oregon Health Authority

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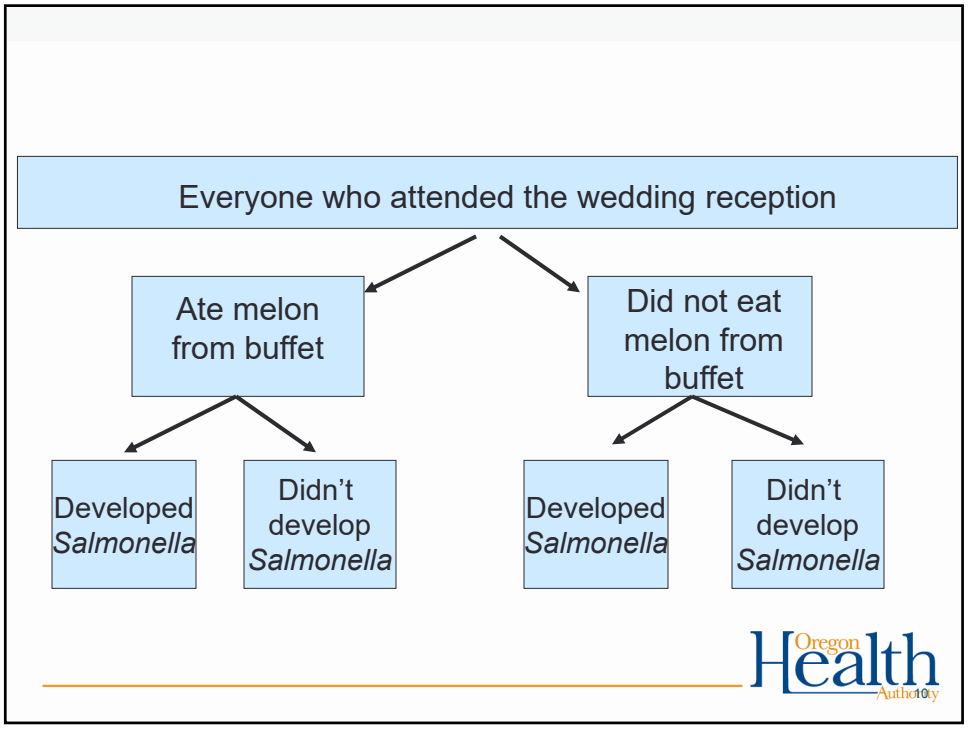
Everyone who attended the wedding reception
Ate melon from buffet
Did not eat melon from buffet
Developed *Salmonella*
Didn't develop *Salmonella*
Developed *Salmonella*
Didn't develop *Salmonella*
Oregon Health Authority
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Case-Control Design

- Classify people by outcome
  - Cases: have disease
  - Controls: do not have disease
- Assess past exposure

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Case-control study examples

- Smoking and lung cancer, 1950s
- *Salmonella* outbreak associated with nationally distributed product
- Restaurant outbreak of norovirus

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Selecting Controls

- Do not have the disease
- At risk of disease: had potential for exposure
- Should be representative of cases

- Key: **If they developed the disease, could they be identified as case?**

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Potential control groups

- Others who ate at same restaurant
- Neighborhood residents
- Family members
- Friends
- Coworkers
- Random digit dialing
- Classmates
- Medical clinic patients

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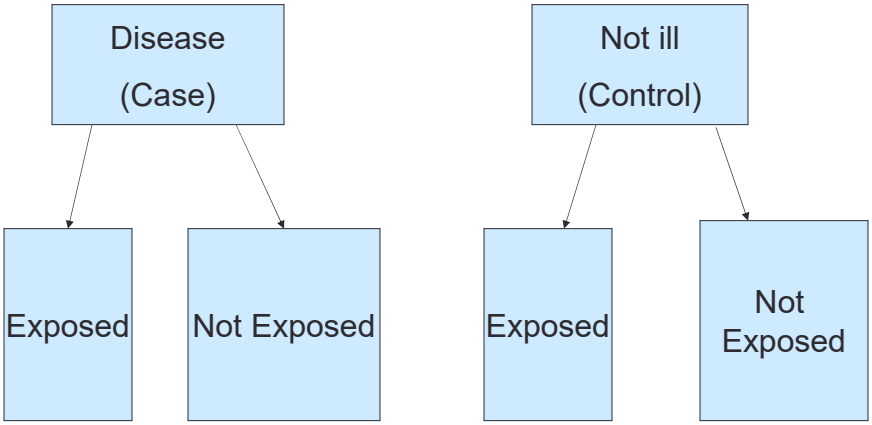
Case-control Study



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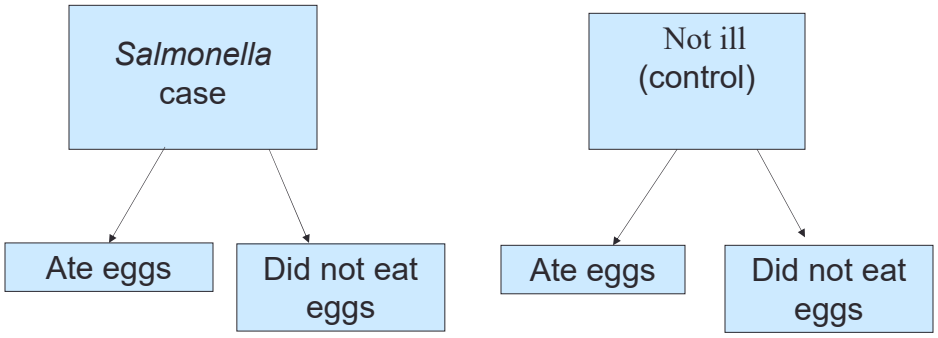
Case-control Study Example



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Advantages & Disadvantages

	Cohort	Case-control
Advantages	Can evaluate rare exposures Can calculate risk	Quick Smaller size Cost effective Can evaluate rare disease
Disadvantages	Inefficient if incubation is long Potential expense Loss to follow up	Recall bias Selection bias

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Measures of Association

- Quantifies magnitude of association between exposure and disease
  - Cohort study: relative risk (RR)
  - Case-control study: odds ratio (OR)

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2 X 2 table

	Diseased	Not diseased	Row total
Exposed	a	b	a+b
Not exposed	c	d	c+d
Column total	a+c	b+d	a+b+c+d= Grand total

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Cohort Study: Relative Risk (RR)

- Risk of disease in exposed ÷ risk of disease in unexposed
- RR= a/(a+b) ÷ c/(c+d)

		Disease: Yes	Disease: No
Exposure	Yes	a	b
	No	c	d

How to interpret If RR = 1?

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Calculate RR for Cohort Study

- *Salmonella* Enteritidis outbreak among group of coworkers that had catered lunch with taco bar
- 40 workers ate fresh salsa; 30 developed *Salmonella* Enteritidis and 10 did not
- Another 40 workers did not eat fresh salsa; 2 developed *Salmonella* Enteritidis and 38 did not

Fill in 2X2 table and calculate RR
Put your answer in chat

Exposure	Disease: Yes	Disease: No
Yes	a	b
No	c	d

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Relative Risk conclusion:

Those who ate salsa had higher risk (15X) of developing *Salmonella* Enteritidis than those who didn't eat salsa

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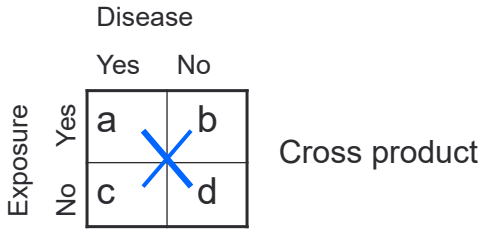
Case-Control Study: Odds Ratio (OR)

- Compare odds of exposure for cases and controls
- **Odds Ratio (OR) =**
  - a/c ÷ b/d
  - **ad/bc**



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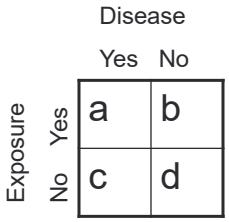
Case-Control Study: Calculate OR

- Cases: 40 restaurant patrons with *Salmonella* Enteritidis; 30 ate eggs and 10 did not
- Controls: 40 restaurant patrons without *Salmonella* Enteritidis; 2 ate eggs and 38 did not

Fill in table and calculate OR
Put your answer in chat



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Odds ratio 2X2 table results

- **Odds Ratio (OR) = (a*d)/(b*c)**
- **OR=**
- Conclusion:
  Cases were ___ times
  more likely than controls to
  have eaten eggs

Complete with your table group.

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Case-case study example

- Compare Shotgun exposures between 2 groups of cases
  - Cluster cases versus other cases with shotgun interview
- Cluster of STEC 4 cases: compare exposure frequencies with background exposure frequencies in Shotgun database
- Shotgun report with background exposure frequencies

Exposure	Code	YES	%	Backgrnd	Binomial
331	CarrotsLoose	2 / 4	50	18%	0.1547
336	PepperBell	2 / 4	50	26%	0.2813
338	PepperRed	2 / 4	50	16%	0.1180
339	PepperYellow	2 / 4	50	9%	0.0456

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Is this a true association?

- P-value <0.05)
  https://tidsskriftet.no/en/2015/09/why-p-value-significant

- Case control study example
  OR=57 (95% CI, 12—280) P<0.0001
  https://www.medcalc.org/calc/index.php

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Study Design and Analytic Epidemiology

Questions?

Stand up and stretch break

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Exercise

- Handout: CD 303 Exercises (Study Design and Analytic Epidemiology: questions 1-4)
- Complete each question before proceeding to next question
- Review questions together at end

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Review of Opening Scenario

On **August 10,** the Oregon County Health Department received a report of a child with *E. coli* O157 (O157) diarrhea. This was their first O157 report in over a year. Within 24 hours Oregon County had received 3 more reports of O157 infection in children.

All 4 ill children that were reported to Oregon County Health Department over 24-hour period had attended the Oregon County Fair and had bloody diarrhea. The fair had been held **August 1 – 6**. Over ~120,000 people had attended this fair. However, the fair ended 3 days earlier. The fairground facilities are used for activities throughout the year.

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Additional Information:

The Oregon County Fair is a major annual event in Oregon each August. It is a large agricultural fair with hundreds of animal exhibits, food vendors, and amusement rides. More than 170,000 visits were recorded this year.

The fairgrounds are supplied by shallow wells approximately 20-feet deep. Since the fairgrounds are only in operation 42 days of year, the fairground water supply is not considered a community water system but is considered an alternative water source and is regulated under the food code. This type of well must be tested within 60 days of an event. Testing for coliforms was performed on June 20th and was negative.

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Question 1: What hypotheses do you want to evaluate?

- *E. coli* was obtained at the fair but exactly where is unknown.
- The usual suspects would be food, water and animals. More specifically, unpasteurized milk, cheese, juice, alfalfa sprouts, uncooked beef and farm animals, (cow, sheep, goats).
- Need to further investigate the water source (wells) as possible source.

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Additional information

An environmental investigation of the fairground revealed that much of the fair was supplied by chlorinated water. However, in one area of the fairground, a shallow well (well #6) provided unchlorinated water to several vendors who used the water to make beverages and ice. This area was close to the large animal barn.

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Question 2: Do we need a study, if so what type of study?

- Oregon County health department Investigators decided to conduct a case-control study.
- Initial evidence is usually not enough to conclude a point source and investigators look at several possible hypotheses.

Why might case control study be used in this investigation?

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Additional information

Cases eligible for inclusion in case control study were people who had attended the Fair and who had stool culture positive for *E. coli* O157 and were the first case in a household (primary cases).

Why limit to first case in household?

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Question 3: Whom might you get for controls? How do you find them?

- Family members
- Friends of cases
- Neighbors of case household
- Random digit telephone dialing

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Additional information

For the Oregon County Fair, controls were obtained from credit card receipts of attendees and from persons entered in photography exhibit and children's art exhibit. Controls were selected who had a similar age distribution as the cases.

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Results

Investigators identified 46 primary cases and 84 controls. All primary cases had attended the fair during the last 4 days. Analysis included only controls who attended the fair at least once during the final 4 days and cases and controls with available exposure data (32 cases and 57 controls).

Hypothesis 1: Water from well #6

Among cases, 26 were exposed to well #6 and 6 were not exposed. Among controls, 9 were exposed to well #6 and 48 were not exposed.

Hypothesis 2: Vendor A chicken

Among cases, 14 were exposed to Vendor A chicken and 18 were not exposed. Among controls, 5 were exposed to Vendor A chicken and 52 were not exposed.

Complete 2X2 tables for each exposure.

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Question 4: What is an appropriate measure of association for a case-control study? (put in chat)

- Odds ratio
- $\frac{a/c}{b/d} = \frac{ad}{bc}$

- Measure of association for water from well #6? (put in chat)
  - OR=?

- Measure of association for Vendor A chicken? (put in chat)
  - OR=?