Epidemic Investigation

Definitions

- **Outbreak**: Sudden occurrence of an epidemic in relatively limited geographic area.

  An outbreak is usually limited to a small focal area, an epidemic covers larger geographical areas & has more than one focal point.

- **Outbreak Epidemiology**:

  Study of a disease cluster or epidemic in order to control or prevent further spread of the disease in the population.

Outbreak In Field Epidemiology

A definition has been proposed by Goodman.
The essential elements are:

1. The problem is unexpected
2. An immediate response may be necessary
3. Epidemiologists must travel to & work on location in the field
4. The extent of investigation is likely to be limited because of imperative for timely intervention

What is the need for field investigation during out break?

Objectives

1. Primary- to control the spread of disease
2. To define the magnitude of the epidemic outbreak in terms of time, place & person.
3. To determine factors responsible for its occurrence
4. To identify cause, source (s) of infection, modes of transmission to determine control measures
5. To make recommendation to prevent recurrence.

Objectives continued….

6. To identify new agent
7. To determine the effectiveness of control measures
8. To identify methods for present & future prevention & control
9. Research & training opportunities
10. Public, Political and legal concerns

Unique aspects of OI

1. Data sources are often incomplete & less accurate.
2. There is a pressure & urgency to conclude the investigations quickly which may lead to hasty decisions.
3. Decreased statistical power due to analysis of small numbers.
4. Publicity surrounding the investigation – community members may have preconceived ideas.

Trigger events & Warning Signals

1. Clustering of cases/deaths in time/place
2. Unusual increase in cases/deaths
3. Shift in age distribution of cases
4. High vector density
5. Acute hemorrhagic fever or acute fever with renal involvement/altered sensorium
6. Severe dehydration following diarrhea in patients above 5 years age
7. Unusual isolate

Diseases requiring investigations

1. Endemic diseases with epidemic potential – malaria, cholera, measles, hepatitis, meningococcal meningitis
2. Even a single case of diseases for which eradication/elimination goals have been set – polio, guineaworm and yaws
3. Rare but internationally important diseases with high case fatality rates – yellow fever
4. Outbreaks of unknown etiology

Steps

1. Verification of diagnosis
2. Confirmation of the existence of an epidemic
3. Defining population at risk
4. Rapid search for all cases & its characteristics
5. Data analysis
6. Hypothesis formulation
7. Testing of hypothesis
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Verification of diagnosis

- The initial report may be spurious & arise from misinterpretation of the clinical features.

Verify the diagnosis

- This involves a review of available clinical & lab findings that supports the diagnosis.
- **Do not apply newly introduced, experimental or otherwise not broadly recognized confirmatory tests at this stage.**
- 15-20% of the suspected cases may be lab confirmed.

Verification of diagnosis

- It is the first step in epidemic investigation
- A clinical examination of a sample of cases
- Laboratory investigation if applicable

Epidemic investigation should not be delayed until the laboratory result are available.

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Confirm the existence

- Are there cases in excess of the baseline rate for that disease?

- AIM-

To find the disease under investigation is far excess of usual or normal expectation?

Confirm the existence

- The excess frequency should be found out with **Epidemic Threshold Curve**. The periodic frequency for previous 3 years is plotted on a graph. Another graph at mean + 2SD level is superimposed on it. Any fluctuations beyond these 2 graphs should be treated as epidemic fluctuations (method of moving averages).

Confirmation of the existence of an epidemic

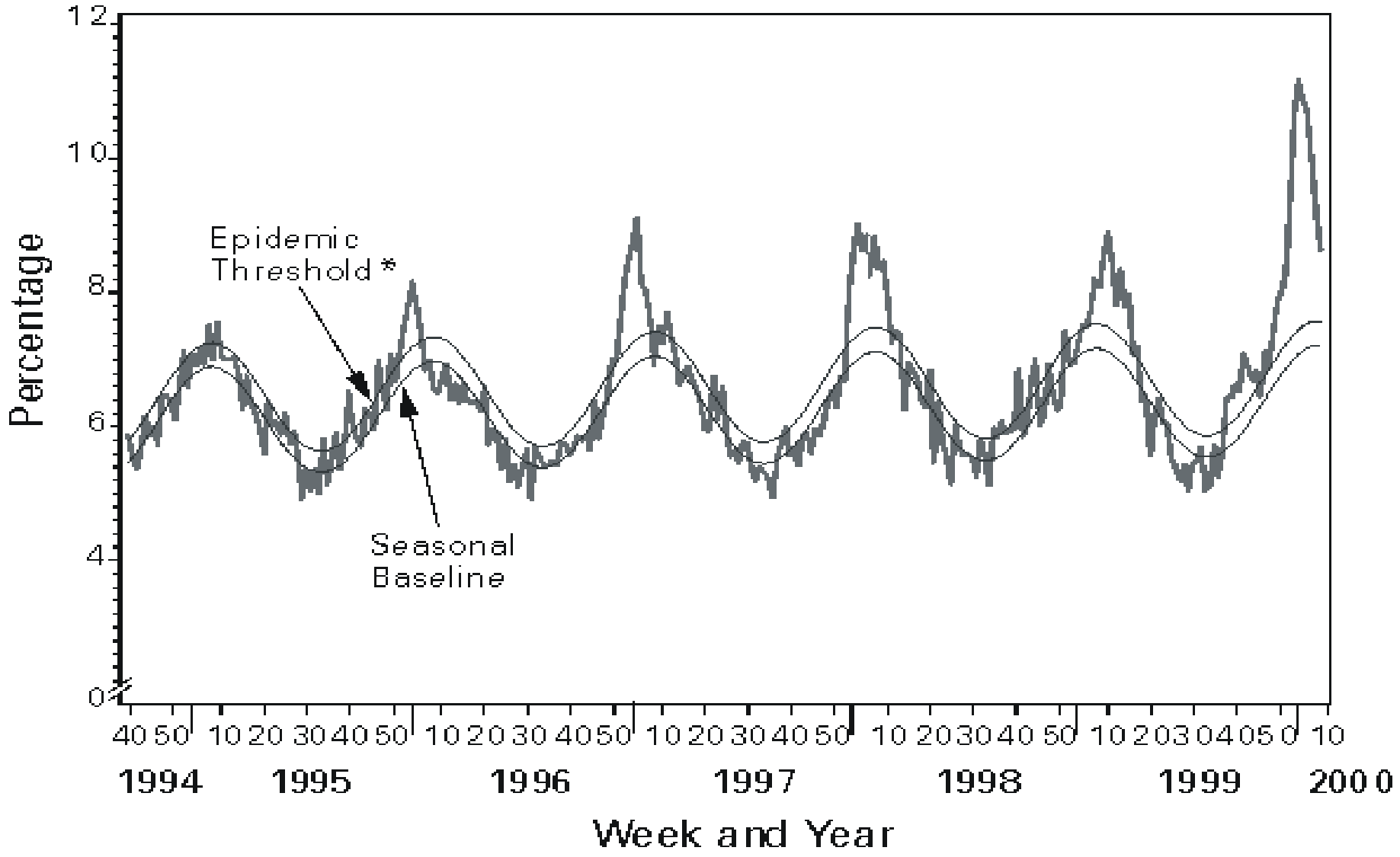
- Usual or normal expectation must be known.

- Any fluctuations beyond

  Mean of previous 3 years + 2SE

  (Epidemic threshold)

FIGURE 1. Percentage of mortality attributable to pneumonia and influenza (P&I) in 122 cities, by week of report — United States, 1994–2000



*The epidemic threshold is 1.645 standard deviations above the seasonal baseline. The expected seasonal baseline is projected using a robust regression procedure in which a periodic regression model is applied to observed percentages of deaths from P&I since 1983.

Confirmation of the existence of an epidemic

- If data is not available
- Hospital records- OPD, IPD..
- Other systems of medicine…

Confirmation of the existence of an epidemic

Precaution—

- Seasonal variation
- Population migration of susceptible
- Multiple reporting of the same case by different workers
- Exaggerated reports-

  e.g. Deaths of children

- Improve reporting– Awareness & publicity>> More reporting from private practitioner & public…

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3-Defining population at risk

A- By obtaining the map of an area

B- Counting the population

Defining population at risk

Counting the population

- Identify additional cases not known or reported initially.
- Persons who meet the case definition should be “line-listed”.

Defining population at risk

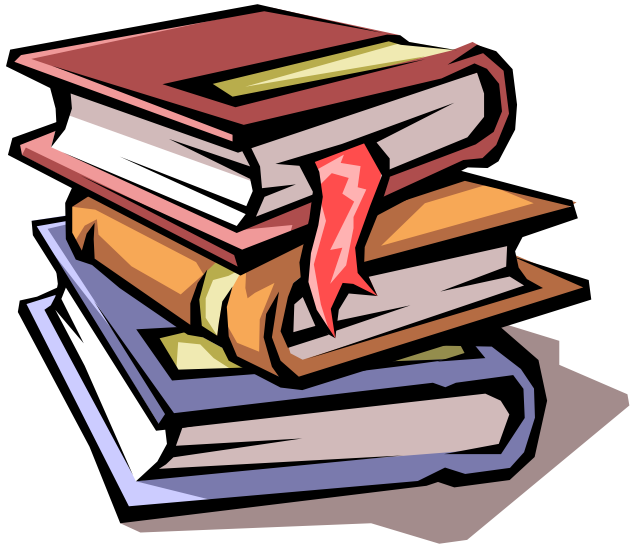
Counting the population

- Identify the population at risk or the exposed persons

  places where the cases live, work & have traveled to, & the possible exposures that might have lead to the disease.

Case Definition

- Standard set of criteria
- Clinical and lab
- Allows for comparison
- Sensitive vs. Specific



Case Definition Gradient

The case definition must be **precise** but **not too exclusive.**.

Suspected C/O of DF

- Acute onset
- High grade fever <7 days duration
- Severe headache, backache
- Joint , post orbital & muscle pain
- With or without rash

Probable C/O of DF

- Suspected case
- High vector velocity
- Presence of confirmed cases in area
- Bd. –ve for Mp, No response to anti- malarials

Confirmed case of DF

- Isolation of virus from the blood in early phase
- IgM abs. in single serum samples or

- 4 fold rise of Abs. in paired serum samples.

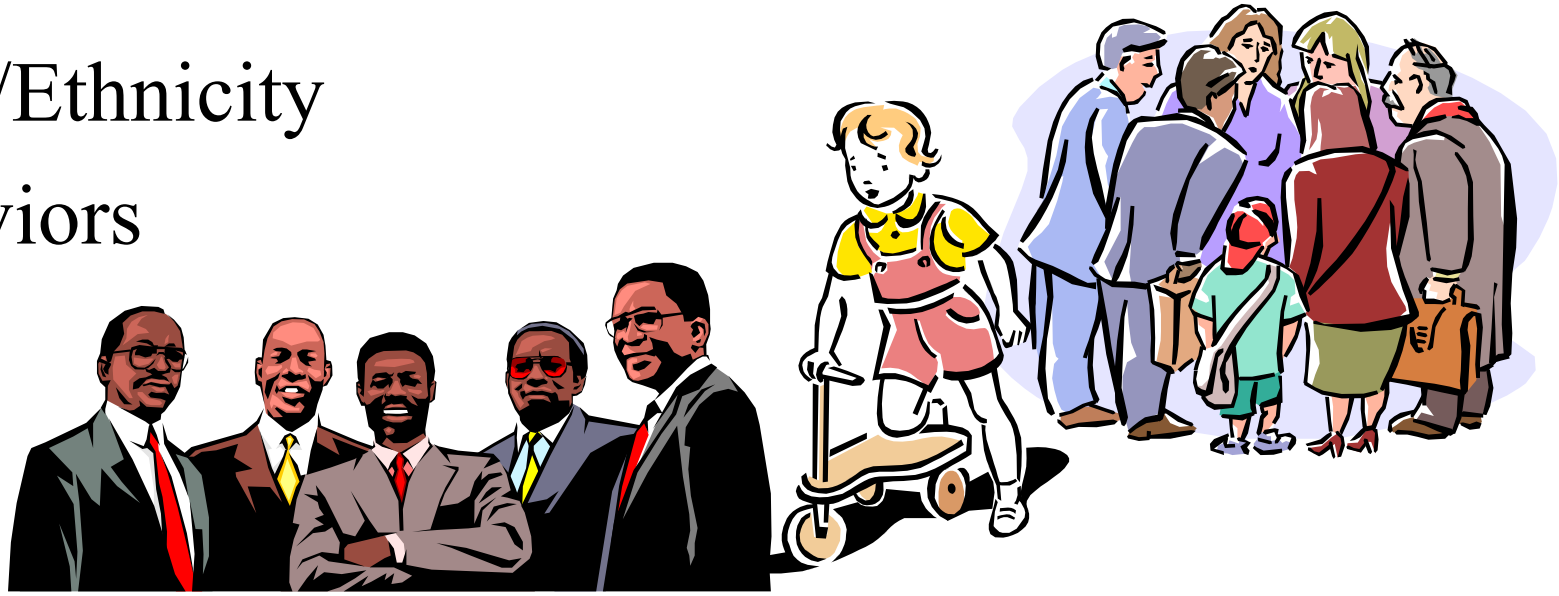
3-Defining population at risk

Epidemiologic Information

- Case definition
- Person
- Place
- Time

Person

- Name
- Age
- Sex
- Socio-Economic Status
- Race/Ethnicity
- Behaviors



Person

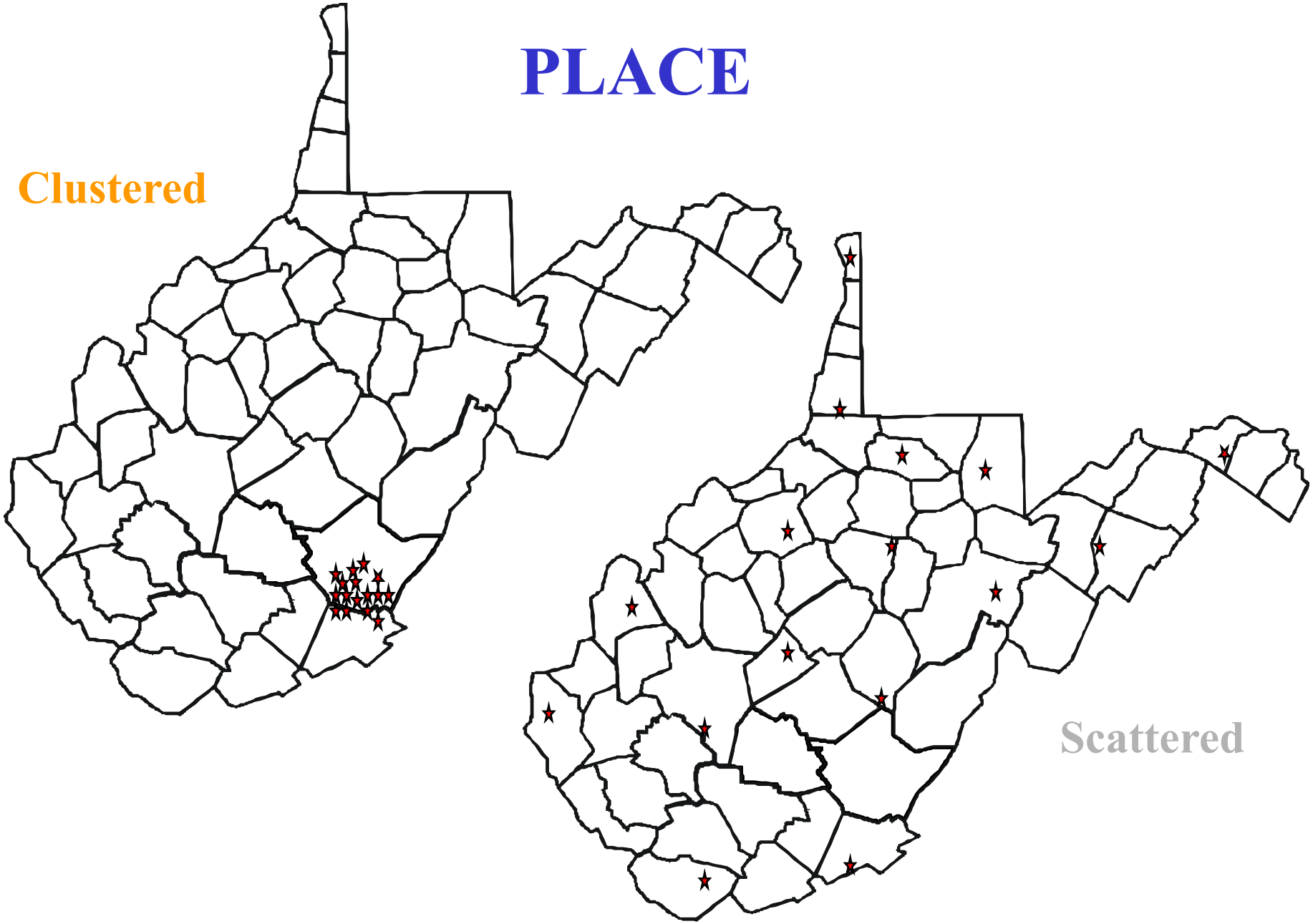
- Parties attended last wk
- Food eaten
- Water, food ,milk source…

Place

- Geographic Distribution
  - Natural
  - Clustering vs. uniform
- Home
- Work
- School
- Hospital room

PLACE

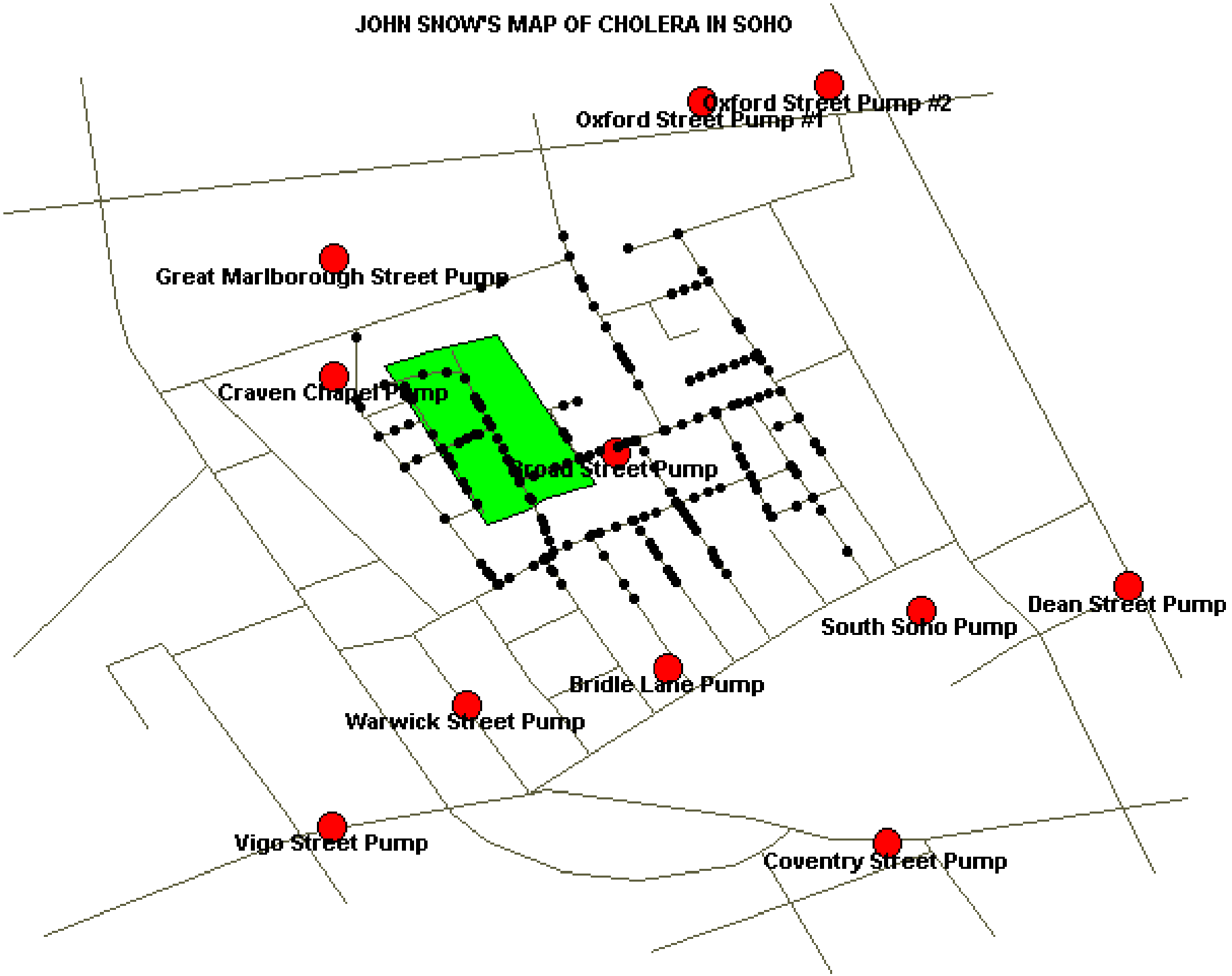
Clustered



Scattered

“Place”

- Neighborhood
- Home visits
- Mosquito Breeding Sites
  - Tires
  - Pots
  - Standing Water


JOHN SNOW'S MAP OF CHOLERA IN SOHO
Oxford Street Pump #2
Oxford Street Pump #1
Great Marlborough Street Pump
Craven Chapel Pump
Broad Street Pump
Dean Street Pump
South Soho Pump
Bridle Lane Pump
Warwick Street Pump
Vigo Street Pump
Coventry Street Pump

Time

- Onset of symptoms
- Incubation Period
- Infectious Period
- Seasonality
- Baseline vs. epidemic
- Interval
    - Long-term trends
    - Shorter for environmental exposure

Steps

1. Verification of diagnosis
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4-Rapid search for all cases & its characteristics

A) Medical survey

B) Epidemiological case sheet

C) Searching for more case

4-Rapid search for all cases & its characteristics

Medical survey

- To identify all cases including those who have not sought medical cure & including those possibly exposed to risk.
- Screening of each member of the population for the disease in question
- Health worker should be trained to administer “epidemiological case sheet” or questionnaire to collect relevant data.

4-Rapid search for all cases & its characteristics

B) Epidemiological case sheet

- Interview form made based on the findings of rapid preliminary inquiry.
- Used for collecting the data from cases & from apparently exposed but unaffected.

4-Rapid search for all cases & its characteristics

C) Searching for more case

-By asking the patient if he knew any cases in the home, family, neighborhood, work place…within the incubation period of an Index case.

-Search of secondary cases

Twice the incubation period of the disease.

Step 7 - Identify & count cases

Identify additional cases not known or reported initially.

Persons who meet the case definition should be “line-listed”.

Identify the population at risk or the exposed persons, places where the cases live, work & have traveled to, & the possible exposures that might have lead to the disease.

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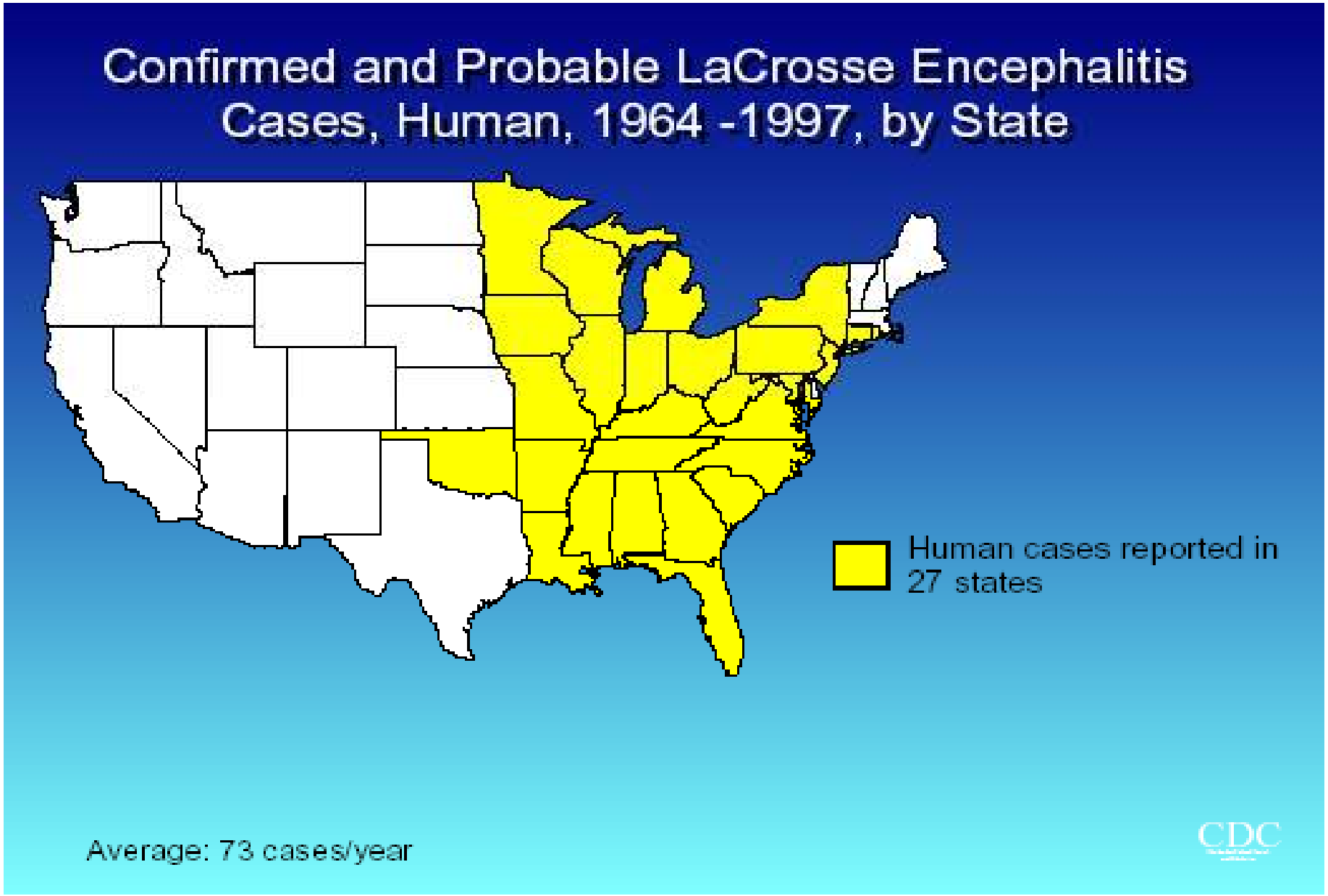
Geographic Distribution of LaCrosse



Data analysis

a) Time—Epidemic curve

   Time trend– Single/Multiple source, Cyclic, seasonal

b) Place– Spot map (geographical distribution)

c) Person

Incidence of the disease in women by marital status and age

Age Group (years)	Married Women			Single Women		
	Population	#Cases	Rate per 1,000	Population	# Cases	Rate per 1,000
16-29	1,905	89	46.7	1,487	16	10.7
30-49	1,684	98	58.2	141	4	28.4
≥50	387	4	10.3	26	0	0
Total	**3,976**	**191**	**48.0**	**1,654**	**20**	**12.1**

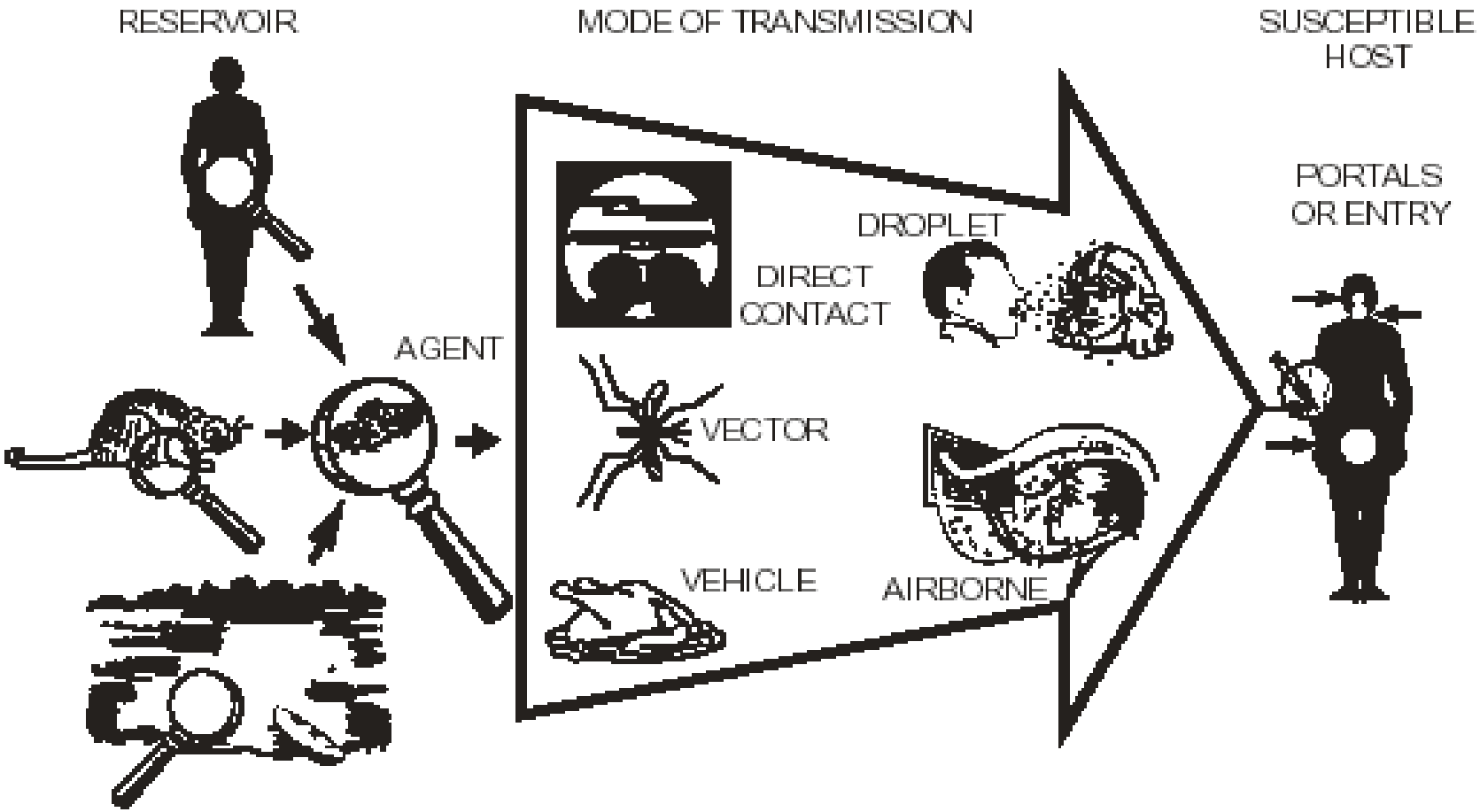
Information for any outbreak

- Symptom onset date
- Symptoms present and agent if known
- Suspected exposure date if known
- Residence
- Age
- Gender
- Laboratory testing
- Outbreak Case Definition
- Organized case information in a line list

Exposure

- Possible Cause of illness
- Know your agent/disease
  - Clinical picture
  - Pathogenesis
  - Mode of transmission
  - Natural Reservoir
  - Common Vehicle or Vector

Chain of Infection



Transmission

- Direct
  - Contact
  - Droplet
- Indirect
  - Airborne
  - Vehicle
  - Vector
    - Mechanical vs. biologic
- Portal of Exit
- Portal of Entry

Types of Outbreaks

- Propagated
  - Indicative of person to person transmission
- Point-source
  - Indicative of a common exposure to a contaminated vehicle or reservoir

Use of Two-By-Two Tables

- Calculate association between disease and exposure

	Ill	**Well**	**Total**
Exposed	a	b	
Unexposed	c	d	
Total			N

ad/bc = Odd Ratio ☞ Relative Risk

Interpreting Measures of Association

- Odds ratios and risk ratios measure the degree of relatedness of an exposure and a health event (an outcome)
- The farther away the OR/RR is from 1, the more we would say the exposure and outcome are associated
- Confidence intervals and p-values help to determine if association is due to chance

Occurrence of diarrhea by exposure to menu A, residents of Nursing Home A, 1989

		Diarrhea		
		Yes	No	Total
Menu A	Yes	12	5	17
	No	2	17	19
	Total	14	22	36

OR = 12 x 17/2 x 5

= 204/10

OR = 20.4

People who ate from menu A were about 20 times more likely to have diarrhea than those that did not eat from menu A.

More OR interpretation

- OR = $\frac{\text{odds of exposure among ill}}{\text{odds of exposure among well}}$
- If OR(RR) > 1, then the exposure is a risk factor for being ill
- If OR < 1, then the exposure is protective of illness
- If OR = 1, then there is no association between exposure and illness
- OR can NEVER be negative!

P-value

- Used in LOTS of statistical tests
- A guide to tell us that a result is “significant”
- Generally at the 95% level
- $p \leq 0.05$ = Significant at the 95% level = there is a 95% probability that the result is accurate (not by chance)
- Example: OR=4, p-value=0.01
- Example: OR=15, p-value=0.36

95% Confidence Intervals

- Used with risk ratios and odds ratios
- Tell us about both precision and accuracy
- With an OR or RR we have estimated the magnitude of the association – 95% confidence intervals tell us that we can be 95% sure that the true association is somewhere in that interval
- Example: OR = 7 95%CI= (5.2, 8.8)
- Example: OR = 7 95%CI= (0.4, 18.7)

Strength of Association

- Magnitude of Odd Ratio
- 95% Confidence Interval or P-value
- Be careful
  - Plausibility
  - Confounding

Attack Rate

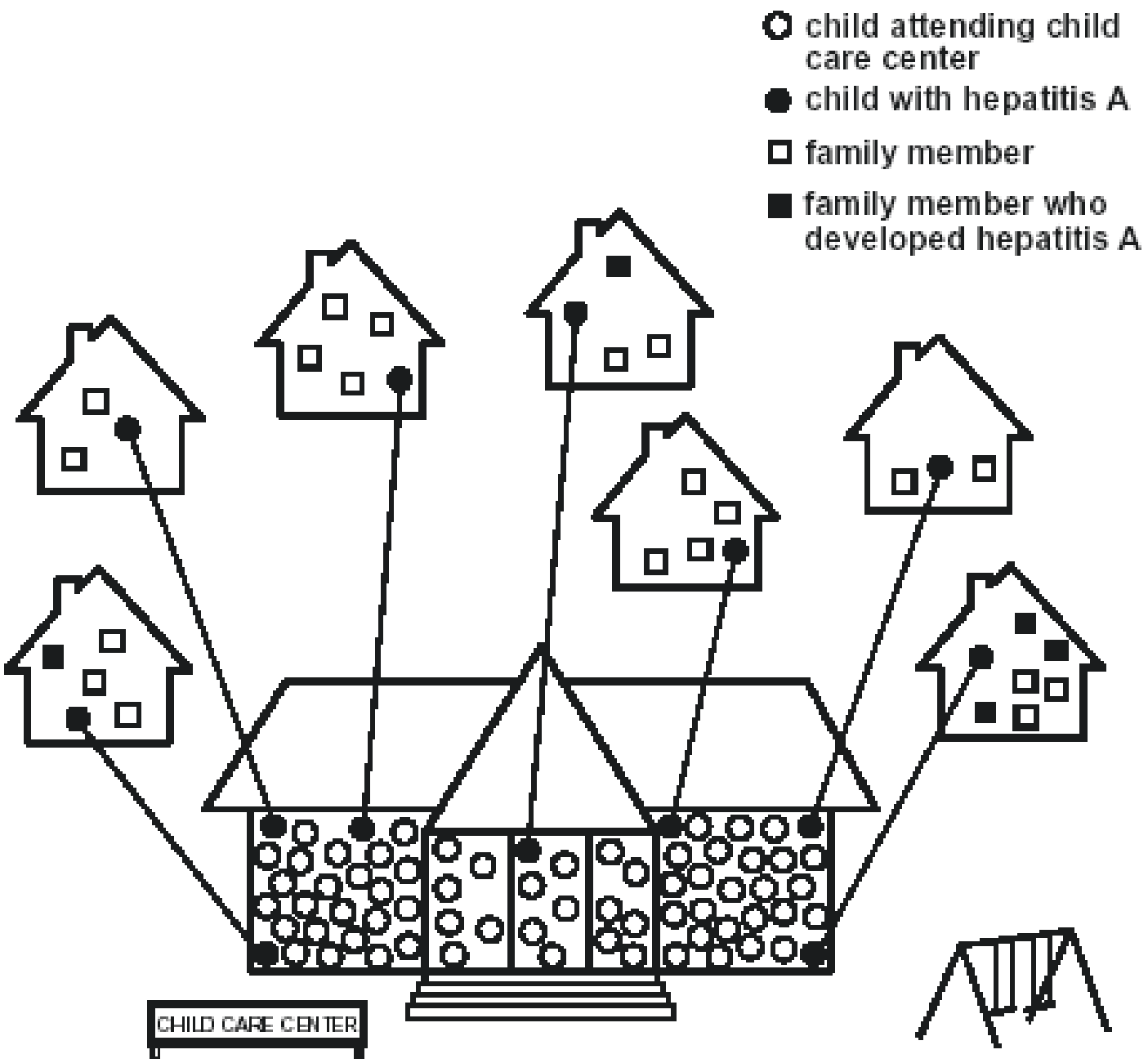
$$AR = \frac{\text{\# of people who became ill}}{\text{\# of people at risk}} \times 10^{n}$$

- People at risk could be those at a party, in a class, on a cruise ship…
- Usually express AR as a %, so n = 2

Secondary Attack Rate

- Measure of frequency of new cases among contacts of known cases

$$\text{SAR} = \frac{\text{\# cases among contacts of primary cases during the period}}{\text{total \# of contacts}}$$


child attending child care center
child with hepatitis A
family member
family member who developed hepatitis A
CHILD CARE CENTER

The calculations

- # of children in day care center = 70
- # of ill children at day care center = 7
- # of contacts (of those 7) at home = 25
- # of ill contacts = 5

- AR = 7/70 = 0.1 x 100 = 10% AR
- SAR = 5/25 = 0.2 x100 = 20% SAR

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Analytic Epi Studies

- Associations between exposure and disease
- Experimental
- Observational
  - Cohort
  - Case Control
  - Cross-sectional

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Summary

- Case definition, person, time, place
- Know disease/agent
- Recognize Point-Source vs. Propagated
- Set up analytic epi study
- Measures of association

Search for the source of infection

The main purpose here is to eliminate, terminate or isolate the source. The steps involved are – identify the time of disease onset, ascertain the range of incubation periods & look for the source in time interval between the maximum & the minimum IPs. In outbreaks with person-to-person transmission, all the contacts of the ***index case*** are to be searched (contact tracing).

Step 8 – Compile & Orient data

Identify when patients became ill (time), where patients became ill (place) & what characteristics the patients possess (person). The earlier one can develop such ideas, the more pertinent & accurate data one can collect.

(a) **Time**: The ***epi-curve*** gives the magnitude of outbreak, its mode of spread & the possible duration of the epidemic. The unit of time on X-axis are smaller than the expected incubation period of the disease.

(b) **Place**: It provides major clues regarding the source of agent and/or nature of exposure. ***Spot maps*** show a pattern of distribution of cases.

(c) **Person**: Examine characters such as age, sex, race, occupation or virtually any other character that may be useful in portraying the uniqueness of case population.

Step 9 – Choose a Study Design

The design (Case-control, Cohort & Case-cohort) is chosen based on size & availability of the exposed population, the speed with which the results are needed & the available resources. The study design that is chosen will then dictate the appropriate analysis & hypothesis testing.

Step 10 – Perform Lab analysis

It consists of collecting & testing appropriate specimens. To identify the etiologic agent, the collection need to be properly timed. Examples of specimens include - food & water, other environmental samples (air settling plates), and clinical (blood, stool, sputum or wound) samples from cases & controls.

Step 11 – Environmental Investigation

A study of environmental conditions & the dynamics of its interaction with the population & etiologic agents will help to formulate the hypothesis on the genesis of the epidemic. Such actions assist in answering How? And Why? questions.

Step 12 – Formulate & Test Hypothesis

As soon as the preliminary data indicate the magnitude & severity of the outbreak, a hypothesis should be made regarding time, place and person; the suspected etiological agent & the mode of transmission. Risk specific attack rates are calculated & compared & relative risk/odds ratio is calculated.

Important points

1. **Rare disease assumption**: The OR & RR approximate each other if the attack rates is less than 5% but the attack rates are much higher in outbreaks.
2. To correct for multiple comparisons, the most effective approach is to lower the *p-value* according to the number of comparisons made.

Step 13 – Control measures

Simultaneous to data collection & hypothesis formation, steps should be taken to contain the epidemic. These measures depend upon knowledge of etiologic agent, mode of transmission & other contributing factors. Protective measures are necessary for patients (isolation & disinfection), their contacts (quarantine) and the community (immunization, etc).

3- Defining Population At Risk

a) Obtaining the map of an area
b) Counting the population

>H-H visit--- defining the population by age, sex

> Population census

Employing sufficient number of health worker

Epidemiologic Information

- AIM

To find out how the transmission of pathogen could have occurred from the case or carrier of the susceptible

Hypothesis formulation

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