Epidemiology Part 6

(Investigation of an Epidemic)

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Investigation of an Epidemic

Investigating an Outbreak

- Deciding whether to investigate a possible outbreak
  - Public health authorities, through various health information systems, get information about the occurrence of diseases of public health importance, and
    - Also occurrence of some unknown disease in the community
  - They must always be on their guard to detect whether the occurrences are more than expected – that is of outbreaks
  - If an outbreak is suspected, prompt action for its control have to be taken

Investigating an Outbreak

- In hospitals, the infection control team routinely monitors certain Hospital associated Infection.
  - Usually, these infections are:
  - Urinary Tract Infection
  - Ventilator Associated Pneumonia, and
  - Surgical Site Infection
- These monitoring usually is done through review of microbiology isolates
- In India, the Centre for Disease Control regularly monitors the IDSP data through its eight regional offices

Investigating an Outbreak

- When the occurrences of any infectious disease exceeds the expected rate, a decision then need to be taken whether the potential outbreak needs to be investigated
- These decisions depend upon various factors some of which may be related to:
  - Health problem
  - Health department
  - External factors

Investigating an Outbreak

- Those that relate to health problem may include:
  - Severity of illness
  - Number of cases
  - The source
  - Mode or ease of transmission, and
  - Availability of prevention and control measures
- Health departments are more likely to investigate an apparent outbreak when
  - Number of affected persons are large

Investigating an Outbreak

- When the disease is severe, i.e., high risks of
  - Hospitalisation
  - Complications, or
  - Death
- When effective control measures exist, and
- When the outbreak has the potential to affect others, unless prompt control measures are taken

- Example
  - A single case of gastroenteritis may not warrant a field investigation but a cluster of cases may

Investigating an Outbreak

- In contrary, even a single case of botulism is likely to be investigated immediately to eliminate the source
  - because it is potentially fatal as well as it can be prevented
- Occurrence of new or rare cases may prompt investigation

- Field investigation is resource intensive
  - Therefore, field investigation will depend upon availability of staff and other priorities
  - Also experience is necessary for conducting investigation

Investigating an Outbreak

- Irrespective of these, field investigations are usually justified for the following reasons:
  - Control or prevention of the health problem
  - Research opportunity
  - Public, political or legal concern
  - Public health programme considerations, and training
- Control and prevention
  - This is the most important public health reason

Investigating an Outbreak

- Opportunity to learn
  - Field investigation provides an opportunity to characterize the natural history
  - This includes agent , mode of transmission, and incubation period and the clinical spectrum of disease
  - Investigation also tries to uncovers those who are at higher risks and the risk factors
- Public, political, or legal concern
  - These can be compelling reasons for investigation
  - Sometimes the public are concerned about the environmental concern for an outbreak, such as toxic waste
  - Health department may alley the apprehension by uncovering that the outbreak is the result of a naturally occurring exposure

Investigating an Outbreak

- Programme considerations
  - There are many vertical health programmes that run in India
  - Many of them are for control and prevention of communicable diseases
  - An outbreak of these programme diseases point to the weakness in the programme planning and implementation
  - The deficiencies uncovered by investigation can be strengthened
- Training
  - Apart from theory knowledge, the field investigation needs various kinds of skills, diplomacy, people skill and communication skills
  - These skills can be acquired by working in the fields with experienced persons

Investigating an Outbreak

- Steps of outbreak investigation
  - Once the decision for field investigation is taken quick action to launch the investigation must be taken
  - This is as essential as obtaining correct data
  - Slipshod method, if employed shall defeat the very purpose of investigation
  - Epidemiological investigation must proceed in a systematic manner
  - It must be conducted in several systematic steps from the beginning to the end so that no important steps are missed

Investigating an Outbreak

- The Epidemiologic steps of outbreak investigation are:
  1. Prepare for field work
  2. Establish the existence of an outbreak
  3. Verify the diagnosis
  4. Construct a working case definition
  5. Find cases systematically and record information
  6. Perform descriptive epidemiology
  7. Develop Hypothesis

Investigating an Outbreak

8. Evaluate hypothesis epidemiologically
9. As necessary, reconsider, refine, and re-evaluate hypothesis
10. Compare and reconcile with laboratory and/or environmental studies
11. Implement control and prevention action
12. Institute or maintain surveillance
13. Communicate findings

- Though these are the sequential steps for epidemic investigation, in actual practice several steps can be done simultaneously
- Sometimes the nature of the epidemic may dictate a different order

Investigating an Outbreak

- Details of the above steps are as under
- Step 1 : Prepare for field work
  - In practice this may not be the first step
  - More commonly, field investigation are not always carried out
  - Already existence of the epidemic is already clear
  - Sometimes enough information is already available in various report that are routinely submitted by the peripheral health facilities
  - Field investigation may only be necessary if there is not enough clarity on the data necessary to arrive at conclusion
  - If it is decided to conduct a field investigation one needs to be well prepared before leaving the office for the field

Investigating an Outbreak

- The preparedness can be grouped into two categories
  - Scientific and investigative issues, and
  - Management and operational issues
- Good preparation in both categories is needed for success of the project
  - Scientific and investigative issues
    - All necessary information regarding the epidemic, types of data required, are to be planned in advance
    - Necessary tools, equipment and materials that will be required should be collected

Investigating an Outbreak

- Laboratory staff should be apprised of the problem being dealt with and they should carry all necessary laboratory materials
  - These will involve proper collection of sample, their storage and transportation techniques
- Necessary supplies of PPE must be arranged and carried to the field
- Before leaving a plan of action should be prepared and communicated to all the team members

- Management and operational issues
  - The investigator besides being a good epidemiologist must also be a good manager and have good capabilities of dealing with people

Investigating an Outbreak

- All team members must know their assigned role and this has to be ensured that know how to carry out their assigned role
- The team may need assistance from various other practitioners from other fields
- These may include as per the need:
  - Laboratorian
  - Veterinarian
  - Translator/interpreter
  - Computer personnel, or
  - Other specialists

Investigating an Outbreak

- In case of suspected bioterrorism, law enforcing agencies also should accompany or should be co-opted locally.
- Necessary instruction from their controlling authority may be got issued

- Necessary communication plan must be established
  - Communication with public health and clinical community should be required
  - The mode and periodicity of communication should be planned and coordinated all those involved
- Operational and logistical aspects also need to be planned
  - Travel, local transportation and lodging must be planned
  - Necessary approval, if required must also be obtained

Investigating an Outbreak

- Step 2 : Establish the existence of an outbreak
  - It is presumed that all cases in the outbreak have a common cause and they are related to each other
  - The observed are to be compared with expected number of cases
  - The expected number is usually the number from the previous few weeks
  - For notifiable diseases, the report received at the National Centre for Disease Control shall form the expected number
  - For other diseases and conditions, hospital discharge records, mortality statistics shall give the expected number

Investigating an Outbreak

- Step 3 : Verify the diagnosis
  - Verifying the disease is important because of:
    a. To ensure that the disease has been properly identified as control measures most often are disease specific
    b. To rule out laboratory error as the basis for the increase in reported cases
  - First clinical findings and laboratory results are to be reviewed
    - If laboratory finding to not conform to clinical and epidemiologic findings, a pathologist may be asked to review the reports
    - For specialised tests, sufficient number of appropriate specimens, isolates and other laboratory material at the earliest

Investigating an Outbreak

- Second, the investigator may like to visit one or more patients with the disease
  - If the investigator does not have clinical background, help of a clinician should be obtained
- Step 4 : Construct a working case definition
  - For case definition a standard set of criteria is used
  - By using the criteria it can be determined whether the individual can be classified as having a disease that fits into the condition the investigator is looking for
  - Case definition includes the clinical criteria within the boundary of time, place and person

Investigating an Outbreak

- The clinical criteria should be based on simple and observable measures
- The criteria must be applied consistently to all persons identified
- The case definition must not include the risk factors or the exposure one is investigating
- The diagnosis, particularly in the early part of the outbreak, may not be certain.
- Therefore cases may be classified as:
  - Confirmed
  - Probable and
  - Possible or suspect

Investigating an Outbreak

- In the outbreak setting, it would be necessary to lay a boundary of time and place for completing the data collection
- A case may be initially classified as probable or possible when the laboratory findings are still not available
- Rarely a case definition is 100% accurate in classifying the cases
  - Some persons may be having a mild illness and may be missed
  - Some may be included with similar symptoms but of a different illness
- Endeavour should be made that no **false positive** cases are included
- For example, in Covid-19, cases with seasonal influenza may be included as they have similar symptoms but have not been tested

Investigating an Outbreak

- Step 5 : Find cases systematically and record information
  - Some cases may be reported by healthcare providers and citizens
  - But they are a small minority of the total affected persons
  - Therefore systematic effort needs to be made to collect information
  - The first place to look for information is healthcare practitioners and healthcare facilities such as clinics, hospitals and laboratories

Investigating an Outbreak

- Investigators may write letters to practitioners and facilities describing the situation and asking for reports that conform to this
  - This is **passive surveillance**
- They can also telephone the facility or physically visit the places to collect information
  - This is **active surveillance**
- Sometimes, the public is alerted directly through media and also media may be pro active and have already spread the news
- If the outbreak has affected a restricted population such as a school or cruise ship or a work site, the entire population may be surveyed to determine the extent of infection

Investigating an Outbreak

- Investigator may also ask the case patients, if they know anybody who may be suffering from similar illness
- Data collection forms need to be developed to collect information
- The form should include:
  - Identifying information
  - Demographic information
  - Clinical information
  - Risk factor information
  - Reporter information

Investigating an Outbreak

- Step 6 : Perform descriptive epidemiology
  - The outbreak needs to be characterised by time, place and person
  - This is descriptive epidemiology
  - This step is critical
  - The reasons are:
    - It provides comprehensive characterization of the outbreak
    - Population at risk can be inferred
    - The characterization may provide clues about aetiology, source, and modes of transmission
      - This can be converted to a probable hypothesis

Investigating an Outbreak

- The descriptive epidemiology may lead to intervention and preventive measures
- Early analysis of descriptive data enables identification of errors and correction of data

- Time
  - A special type of histogram is used to depict the time course of an epidemic
  - This graph is called an **epidemic curve** or **epi curve**
  - It provides a simple visual display of outbreak's magnitude and time trend
  - Epidemic curves are basic investigative tool as they are very informative:

Investigating an Outbreak

- The visual graph provides a simple means of understanding the magnitude of epidemic over time
- It can distinguish between epidemic and endemic disease
- The shape of the epidemic curve provides clues about pattern of spread in the population
  - Point versus intermittent source versus propagated
- The curve shows at point of epidemic we are in
  - Still on the upswing, on the down slope, or after the epidemic has ended
  - This predicts whether more or lesser number of cases will occur in the near future
- The curve can be used for evaluation, answering question like : how long it took to identify a problem?

Investigating an Outbreak

- There are some data that are at the extremes of the curve
- These outliers provide very useful clues
- The incubation period of a disease if known can be used to arrive at a probable exposure time
  - Also it can help in developing questionnaire focused on that time period

- Drawing an epidemic curve
  - To draw the curve the essential information required is the incubation period of the disease for each case
  - For some diseases, date of onset is sufficient to draw the curve
  - For other diseases with short incubation period hour of onset may be more appropriate

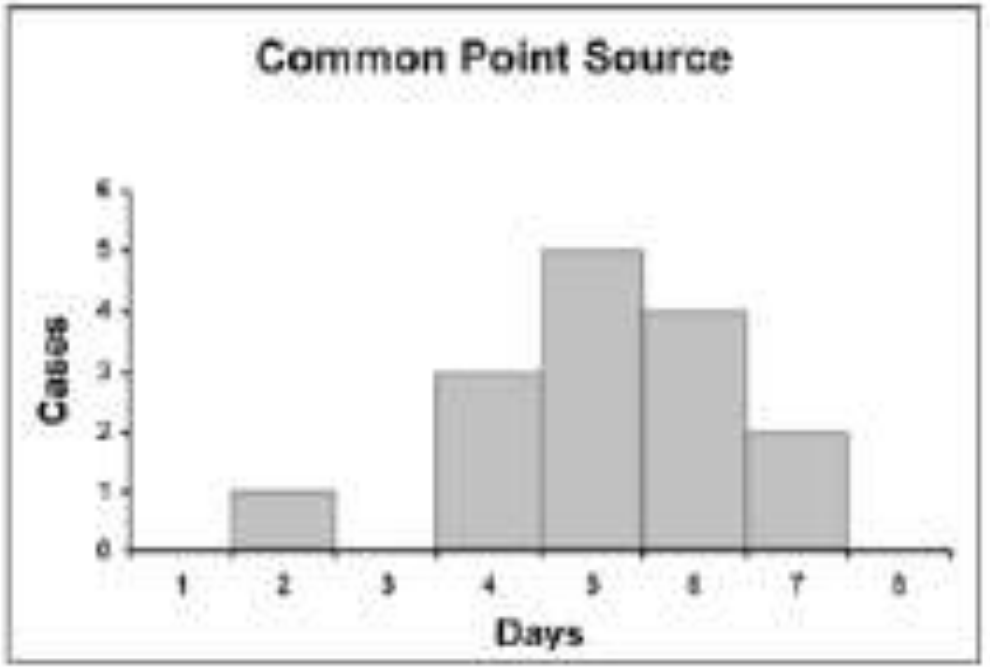
Investigating an Outbreak

- In some outbreaks, neither the disease nor the incubation period may be known
- Under such circumstances, to proceed to draw, several curves should be drawn with different units on the x-axis
- Then the curve which fits the best with the data should be chosen

- Interpretation of an epidemic curve
  - First overall shape of the curve to be studied
    - The shape of the curve is determined by:
      - The pattern of epidemic
      - Periods of time over which susceptible persons are exposed, and
      - Minimum, average, and maximum incubation of the disease

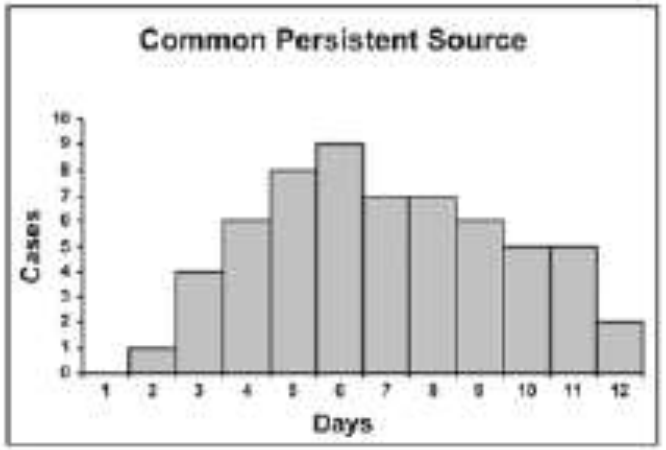
Investigating an Outbreak

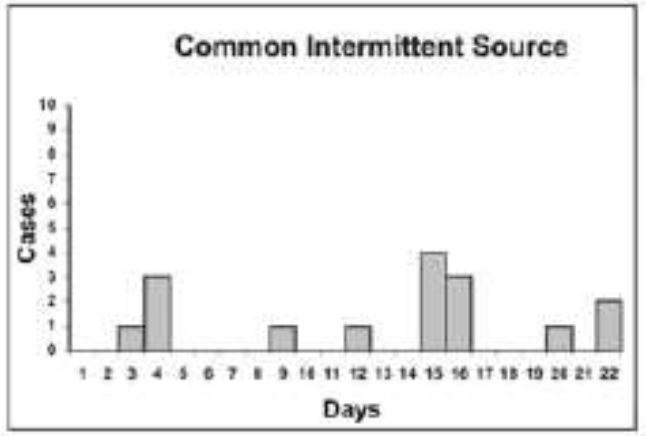
- An epidemic curve with steep upslope and a more gradual down slope is know as a log-normal curve
  - This type of curve is characteristics of a **point-source epidemic**
  - In this type, the persons are exposed to the same source over a relatively short period of time
  - A sudden increase in the number of cases suggests sudden exposure to a common source one incubation period earlier



Investigating an Outbreak

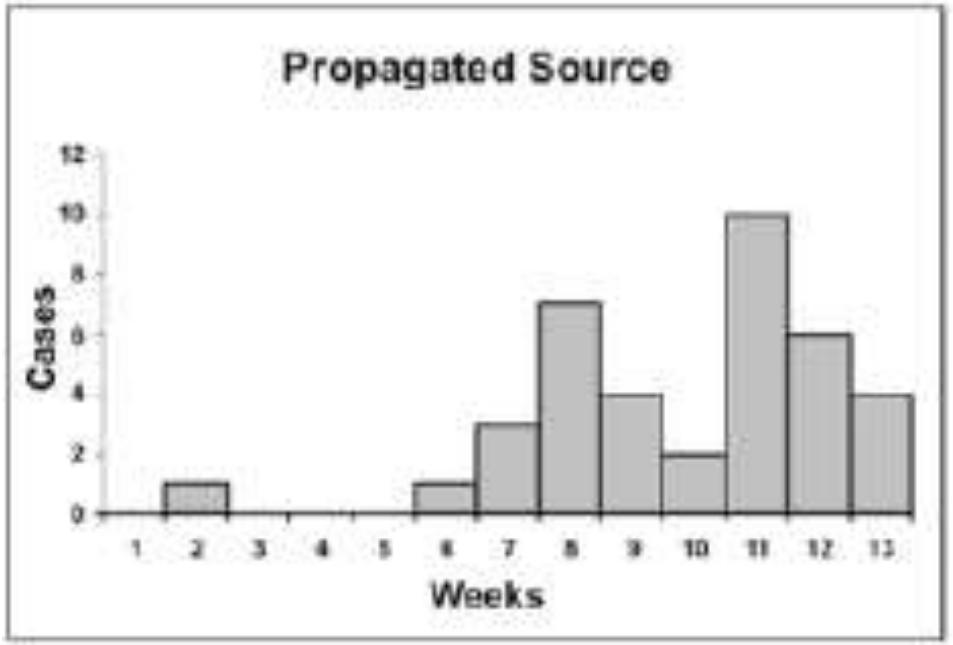
- In a point-source epidemic, all the cases occur within one incubation period
- If the duration of exposure is prolonged, it is called a **continuous common source epidemic**
- In this case, the curve has a plateau instead of a peak
- An **intermittent common source** epidemic usually produce a irregular jagged epidemic curve
    - This reflects intermittence and duration of exposure and the number of persons exposed





Investigating an Outbreak

- In theory, a **propagated epidemic** spreads from person-to-person
- The epi curve should have a series of progressively taller peaks
- The peaks are one incubation period apart
- In reality, such classic pattern is rarely seen



Investigating an Outbreak

- Place
  - Assessment of an epidemic by place provides information on the:
    - Geographic extent of the problem
    - Clusters or patterns that provide important ecological clues
  - A spot map of the affected area is usually used to graphically display the places where the cases live, work, or may have been exposed
  - Some spot maps indicate each patient's residence
  - When a map shows a cluster or other pattern, possible explanation should be attempted

Investigating an Outbreak

- The possible explanation could be perhaps water supplies, wind currents, nearness to a restaurant and so on
- It can give mode of spread
- Example:
  - Clustering of cases in a wing in a hospital points to a focal source or person to person spread.
  - If the cases are scattered all over the facility, then conclusion can be drawn that the spread is from a widely disseminated vehicle
    - It may also be due to a source common to the residents that is not associated with room assignment, such as a common dining hall or water supply

Investigating an Outbreak

- To investigate cluster of surgical site infection, the site map may be plotted by operating room, by recovery room and by ward room
- In a study of “sick building syndrome”, related to airflow patterns in buildings, cases should be plotted by work location

- Spot maps are useful for visualising cases within a geographical area
- Spot maps, however do not take into consideration, the underlying population
  - To compare incidence between different areas with different population densities, an area map showing area specific rates is preferable

Investigating an Outbreak

- Person
  - Outbreak delineation by person provides a description of
    - Whom the case patients are, and
    - Who are at risk
  - Person characteristic included in the description include:
    - Age
    - Race
    - Sex, and
    - Medical status

Investigating an Outbreak

- In the person description besides the demographic characteristics of host, exposure characteristics are also described
- The host characteristics include:
  - Occupation
  - Leisure activities
  - Use of medications
  - Tobacco, and
  - Drugs

Investigating an Outbreak

- Two most common host characteristics included in the person description are Age and Sex
  - Because they can be collected easily
  - They are also often related to exposure and risk of the disease
- Depending on the outbreak characteristics, occupation, race or other personal characteristics specific to the disease may also be important
- Example:
  - In an outbreak of hepatitis B it is important to know if there is any history of intravenous drug use or sexual contact

Investigating an Outbreak

- Step 7 : Develop hypotheses
  - This is the sequential step in the investigation of an outbreak
  - But with the information available from the previous steps, some picture of the epidemic is already emerging
  - Depending on the outbreak, the hypotheses may be formulated as to the source of the infection, the mode of transmission and the exposures that caused the disease
  - The hypothesis should lend itself to testing
- Outbreak hypotheses can be generated in many ways
  - First, it should be considered what is already known about the disease

Investigating an Outbreak

- What is the agent's usual reservoir?
- How it is usually transmitted?
- What vehicle is usually the means of transmission?
- What are the known risk factors?

- This way one can narrow down the possibilities regarding the agent, susceptible host and the environment
- The alternative way is to talk to a few case patients
  - The conversation about possible exposure should be open ended and wide ranging

Investigating an Outbreak

- The conversation need not be only restricted to the known source and vehicles
- It may even be helpful to visit the homes of case patients and look through the refrigerators and shelves for clues for an apparent foodborne outbreak
- Some local health department staff may also provide some important clues
  - They know the people in the community and their habits
  - They might have already framed an hypothesis based on their knowledge
- The descriptive epidemiology may provide important clues that can shape the hypotheses formation

Investigating an Outbreak

- If the epidemic curve points to a narrow period of exposure, what event occurred around that time?
- Why do people living in one particular area have the highest attack rate?
- Why are some groups with particular demographic composition have greater risks than other groups with different person characteristics?

- Answer to such questions may lead to hypotheses
  - These hypotheses can then be tested by appropriate analytic techniques
- There is now growing concern about bioterrorism
  - This should be considered while investigating an epidemic whether there was an intentional dissemination of infectious or chemical agents with criminal intent

Investigating an Outbreak

- The circumstances when an intentional act ether terrorist or criminal intent should be considered are as under:

1. Single case of disease caused by an uncommon agent (e.g., glanders, smallpox, viral haemorrhagic fever, inhalational or cutaneous anthrax) without adequate epidemiologic explanation
2. Unusual, atypical, genetically engineered, or antiquated strain of an agent (or antibiotic-resistance pattern)
3. Higher morbidity and mortality in association with a common disease or syndrome or failure of such patients to respond to usual therapy
4. Unusual disease presentation (e.g., inhalational anthrax or pneumonic plague)

Investigating an Outbreak

5. Disease with an unusual geographic or seasonal distribution (e.g., tularaemia in a non-endemic area, influenza in the summer)
6. Stable endemic disease with an unexplained increase in incidence (e.g., tularaemia, plague)
7. Atypical disease transmission through aerosols, food, or water, in a mode suggesting deliberate sabotage (i.e., no other physical explanation)
8. No illness in persons who are not exposed to common ventilation systems (have separate closed ventilation systems) when illness is seen in persons in close proximity who have a common ventilation system
9. Several unusual or unexplained diseases coexisting in the same patient without any other explanation

Investigating an Outbreak

10. Unusual illness that affects a large, disparate population (e.g., respiratory disease in a large population may suggest exposure to an inhalational pathogen or chemical agent)
11. Illness that is unusual (or atypical) for a given population or age group (e.g., outbreak of measles-like rash in adults)
12. Unusual pattern of death or illness among animals (which may be unexplained or attributed to an agent of bioterrorism) that precedes or accompanies illness or death in humans
13. Unusual pattern of death or illness among humans (which may be unexplained or attributed to an agent of bioterrorism) that precedes or accompanies illness or death in animals

Investigating an Outbreak

15. Similar genetic type among agents isolated from temporally or spatially distinct sources
16. Simultaneous clusters of similar illness in non-contiguous areas, domestic or foreign
17. Large number of cases of unexplained diseases or deaths

- Outliers
  - In an epidemic curve, there may be some cases that do not fit into the body of the curve
  - These cases also may provide some important clues and should be examined carefully
    - They may have an easily identifiable exposure that may point directly to the source

Treadwell TA, Koo D, Kuker K, Khan AS. Epidemiologic clues to bioterrorism. Public Health Reports 2003; 118:92–8. (In CDC Principles of Epidemiology in Public health, pp 447

Investigating an Outbreak

- Step 8 : Evaluate hypotheses epidemiologically
  - There are two methods of epidemiologically evaluating a hypothesis
    1. Comparing the hypothesis with the established facts, or
    2. By using analytic epidemiology to quantify relationships and assess the role of chance
  - The first method is likely to be used when there is an obvious support of clinical, laboratory, environmental, and/or environmental evidence
  - When the supporting evidences are very glaring, there is no need of formally testing the hypothesis
  - An example as quoted by the CDC

Investigating an Outbreak

- There was an outbreak of hypervitaminosis D in one city
- Investigation found that all case-patients were drinking milk delivered by a local diary
- The hypothesis developed was that milk was the cause
- The investigating team visited the diary supplying milk
- They found that the dairy was fortifying milk with more dose of vitamin D than was recommended
- In this case no analytic to evaluate the hypothesis
- Investigators, of course, did conduct additional studies to identify additional risk factors

Investigating an Outbreak

- In some circumstances, the situation may not be as straight forward as this
  - In such circumstances investigators resort to analytic epidemiology to test the hypothesis
    - The key feature of analytic epidemiology is a comparison group
  - In this, a comparison is made between the case-patients or exposed group (Observed pattern) with non-cases or unexposed persons (Expected pattern)
    - By comparing, it can be determined whether observed pattern differs substantially from the expected pattern
  - This comparison can quantify relationship between the two groups and to test causal relationships
    - Two most common types of analytic epidemiology studies used in field investigations are retrospective cohort studies and case-control studies

Investigating an Outbreak

- Retrospective cohort studies
  - This type of study is suitable for a small well defined population, such as, an outbreak of gastroenteritis among wedding guests
    - In this a complete list of wedding guests is available – a well defined population
  - In a cohort study, the investigator contacts each guest to determine each person's exposure to determine possible sources and vehicles
    - i.e., what food and drink each person consumed and notes whether the person later became sick (gastroenteritis)
  - After collecting similar information from each attendee, the attack rate of those exposed to a particular item and attack rate for those who wee not exposed are calculated

Investigating an Outbreak

- Generally, an exposure that has the following three characteristics are a strong suspect
  1. The attack rate is high among those exposed to the item
  2. The attack rate is low among those not exposed, So the difference or ratio between the attack rates is high
  3. Most of the case-patients were exposed to the item, so that the exposure could explain or account for most, if not all, of the cases
- Relative and attributable risk
  - Commonly, a comparison of the attack rates between the two groups is made
  - This measures the association between the exposure and disease
  - This is called the **risk ratio** or the **relative risk**

Investigating an Outbreak

- When the attack rates of the two groups are equal, the relative risk is equal to 1.0
  - In this case the exposure is not associated with the disease
- The greater the difference between the attack rates between the exposed and unexposed groups, the larger the relative risk, and
  - The stronger the association between exposure and disease

- Statistical significance testing
  - When the relative risk is different from 1.0, a chi-square or other tests of statistical significance is carried out to find out the likelihood of finding an association as large or larger on the basis of chance alone

Investigating an Outbreak

- To test an association for statistical significance an assumption needs to be made
  - The assumption is that the exposure is not related to the disease
  - This means that the relative risk equals 1.0
  - This assumption is known as **null hypothesis**
  - Another hypothesis that will be adopted if null hypothesis is proved wrong is called **alternative hypothesis**
    - This means that indeed the exposure is associated with the disease
  - Next a measure of association, such as risk ratio or odds ratio to be calculated

Investigating an Outbreak

- After that a chi-square or other statistical tests to be carried out
- The test indicates the probability of finding an association as strong as or stronger than the observed value if the null hypothesis were really true
  - This means that the exposure was not related to the disease
- This probability is called the **p-value**
- A very small p-value means that the observed association occurs only rarely if the null-hypothesis is true
- If the p-value is smaller than some cut-off then null hypothesis is rejected
  - The cut-off value is specified in advance and is commonly 0.05 or 5%, and in that case the alternative hypothesis is accepted

Investigating an Outbreak

- The most common statistical test for data in a 2 X 2 table from an outbreak is the chi-square test
- To calculate,
  - The chi-square statistic is calculated then its corresponding p-value is looked up in a chi-square table

Standard notation of a Two-by-two Table

	Ill	Well	Total
Exposed	a	b	$a+b = H_1$
Unexposed	c	d	$c+d = H_0$
Total	$a+c=V_1$	$b+d=V_2$	T

One Formula chi-square

$$\frac{T(ad-bc)^2}{H_1 \times H_0 \times V_1 \times V_2}$$

Investigating an Outbreak

- Table of chi square

Degrees of Freedom	Probability .50	.20	.10	.05	.02	.01	.001
1	.455	1.642	2.706	3.841	5.412	6.635	10.827
2	1.386	3.219	4.605	5.991	7.824	9.210	13.815
3	2.366	4.642	6.251	7.815	9.837	11.345	16.268
4	3.357	5.989	7.779	9.488	11.668	13.277	18.465
5	4.351	7.289	9.236	11.070	13.388	15.086	20.517
10	9.342	13.442	15.987	18.307	21.161	23.209	29.588
15	14.339	19.311	22.307	24.996	28.259	30.578	37.697
20	19.337	25.038	28.412	31.410	35.020	37.566	43.315
25	24.337	30.675	34.382	37.652	41.566	44.314	52.620
30	29.336	36.250	40.256	43.773	47.962	50.892	59.703

- A 2 X 2 table has 1 degree of freedom
  - A chi-square larger than 3.84 corresponds to a p-value smaller than 0.05

Investigating an Outbreak

- Since a 2 X 2 has 1 degree freedom, a chi-square larger than 3.84 corresponds to p-value smaller than 0.05
  - It means, to reject a null hypothesis if the p-value is less than 0.05, the chi-square value should be larger than 3.84
- It may be understood that the chi-square or similar other tests are guide to make decision about a hypothesis
  - Decision taken may be either right or wrong
  - A p-value may be calculated that is not less than 0.05 then null hypothesis may not be rejected and this decision may come out to be true
  - This frequently happen when in the study there are only a few people
    - (χ works better with population $\approx$ 30)
  - The opposite may also be true – a p-value less than 0.05 may be a chance finding rather than true explanation of the outbreak

Investigating an Outbreak

- Confidence Interval
  - An alternative to calculating a p-value is calculating a confidence interval
    - Most commonly a confidence interval of 95% is used in epidemiologic calculations
    - The interval corresponds to p = 0.05 cut off
    - Simply, it means confidence interval for a risk ratio is the range of values of the risk ratio consistent with the data in a study
    - A wide confidence interval indicates that the study is consistent with a wide range of values
      - It means the study is not very precise in describing the strength of association (risk ratio) between exposure and disease

Investigating an Outbreak

- A narrow confidence interval indicates that the risk ratio is fairly precise
- A confidence interval provides more information than a p-value does
  - Many medical and epidemiologic journals now prefer confidence intervals to p-values
- However, in the outbreak investigation setting the difference is not relevant
  - The objective of an outbreak investigation is to identify the implicated source of exposure
- In this situation a relative risk and p-value is by and large equivalent to relative risk and confidence interval

Investigating an Outbreak

- Case-control studies
  - A cohort study can only be done when the population is well defined and the cohorts can be followed over a period of timed
  - In many outbreak setting, the population is not well defined
    - And also speed of information is important for controlling the outbreak
  - In such situation a case control study is more suitable
    - Two groups are chosen – one group with disease and the other group without disease
  - Exposure history of both the groups is obtained
  - The **odds ratio** is then calculated to quantify the relationship between exposure and disease
    - Finally, a p-value or confidence interval is calculated to assess statistical significance

Investigating an Outbreak

- Choosing controls
  - Controls are group of individuals without disease being studied
  - The control should be representative of population in which cases have occurred
    - They are similar to the cases but don't have the disease
  - The controls will have the same levels of exposure, if the null hypothesis is true
  - If the exposure is much more in the case-group than among the controls then exposure is considered to be associated with the illness

Investigating an Outbreak

- In the outbreak investigation, the number of case-patients that can be enrolled is limited by the size of the outbreak
  - In a small outbreak, number of individual for control is plenty
  - In an outbreak of 50 to 60, one control per case may be sufficient
  - In a small outbreak 2 to 4 controls may be recruited
  - Including more than 4 controls per cases is not useful as the increase of statistical power may not contribute additional benefit
- There could be some practical difficulties in choosing appropriate controls
  - There could be logistical issues, such as,
    - How to contact potential controls

Investigating an Outbreak

- Gain their cooperation
- Ensure that they are disease free, and
- Obtain appropriate exposure data from them

- In a community outbreak, a random sample of the healthy population may be the best control group
- But choosing such controls also may not be problem free
- Other common control groups could be:
  - Neighbours of case patients
  - Patients from the same physician practice, or hospital
  - Friends of case patients
- They would be more cooperative but may not be representative of the population

Investigating an Outbreak

- Odds ratios
  - In most case control studies, population is not well defined
  - Also, the total number of people exposed to a suspected vehicle or source is not known
  - Without a proper denominator attack rates cannot be arrived at
  - For a case control study, the measure of association of choice is the **odds ratio**

Method for calculating the odds ratio:

$$\frac{\left(\begin{array}{c}\textit{Number of exposed cases}\\ X\\ \textit{Number of unexposed controls}\end{array}\right)}{\left(\begin{array}{c}\textit{Number of exposed controls}\\ X\\ \textit{Number of unexposed cases}\end{array}\right)}$$

OR

$$\frac{ad}{bc}$$

Investigating an Outbreak

- Step 9 : Reconsider, refine, and re-evaluate hypotheses
  - Analytic study may not always be revealing
  - Unless good hypotheses are formed at the beginning, doing analytic epidemiologic study is not helpful
  - When analytic epidemiology is unrevealing, then a rethinking about the hypotheses should be done
  - Re-Consider then about the possible agent, the vehicle, the mode of transmission etc. to refine or rehash the hypotheses
  - Even when an association between the exposure and disease is found, the hypotheses may need to be refined to come to the exact agent or vehicle that was the cause of spread

Investigating an Outbreak

- Step 10 : Compare and reconcile with laboratory and environmental studies
  - Epidemiologic studies may pin point the agent, the source, the vehicle and the mode of transmission
  - These conclusion is by way of logical deductions from the data and statistical analysis
  - Still these are not the hard and irrefutable evidence
  - For these purposes, confirmatory laboratory findings will provide the required evidence
  - The investigation may not be considered complete until the implicated organism has been isolated

Investigating an Outbreak

- Environmental studies are also equally important
  - They can explain often why an outbreak occurred
- For example:
  - In an outbreak of *E.coli* among visitors in a fair, it was possible to identify one very strong risk factor
  - Consumption of beverages with ice
  - Environmental inspection found lack of chlorination of water source to that area. It was also found that the water source was contaminated from a nearby septic tank
- Thus laboratory, epidemiologic environmental examination complement one another

Investigating an Outbreak

- Step 11 : Implement Control and preventive measure
  - The primary goal of outbreak investigation is control of the outbreak, and to prevent additional cases
  - Control and prevention of the disease should be started as soon as possible and need not wait till all the action of of previous steps are completed
  - If appropriate control measures re known and available they should be initiated even before the investigation is launched
  - For example,
    - A child in a community with measles with other susceptible children may prompt a vaccination campaign before an investigation of how the child became infected

Investigating an Outbreak

- Step 12 : Initiate or maintain surveillance
  - Once control and prevention measures have been implemented, they must be monitored on a continuing basis
  - If surveillance has not been ongoing, it should be initiated now
  - If active surveillance was initiated as part of case finding efforts, it should be continued
  - There are two reasons for active surveillance now:
    - Firstly, To determine that the control and prevention measures are working
      - Whether new cases are declining
    - Secondly, to know whether the outbreak has spread outside its original area
      - In that cases, effective measures to be implanted in the new area(s)

Investigating an Outbreak

- Step 13 : Communicate findings
  - Findings must be communicated on need to know basis expeditiously
  - This is critical for initiating control and prevention measures by the public health authorities
  - The communication usually takes two forms:
    - An oral briefing for local authorities
    - A written report
      - Investigators should also prepare a written report in a scientific format
      - It forms a blue print for action
      - It serves as a document for potential legal issues
      - It serves as a reference document for the health department for future

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Thank you

End of the Final Part