

EPIDEMIOLOGY AND BIostatISTICS

Outbreak Investigation

University of Zambia
School of Health Sciences
Course: BMS4430 / RAD4620

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Objectives

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Introduce students to:

1. Definitions of disease occurrence in a population
2. Types of disease outbreaks
3. General steps in an outbreak investigation
4. Role of laboratory in outbreak investigation
5. Case studies

Definitions

Occurrence of infectious diseases?

Infectious diseases may occur in a population as

- 1) Cluster
- 2) Sporadic
- 3) Epidemic
- 4) Endemic disease
- 5) Pandemic

Definitions

CLUSTER.

- **Definition:** Is an aggregation of cases of a disease which are closely grouped in time and place and the number of cases may or may not exceed the expected number.
- Mostly the expected number is not known.
- Cases are more likely to represent a cluster if they involve (1) a specific disease or condition, (2) a rare type of disease or condition, or (3) a disease or condition in a group of people not usually affected by that particular disease or condition.

Definitions

SPORADIC.

Definition: A disease that occurs infrequently and irregularly. occurring at irregular intervals or only in a few places; scattered or isolated and the cases seem not to be related.

E.G Tetanus, Rabies, Plague

Definitions

EPIDEMIC.

Definition: The occurrence of more cases of disease than expected in a given area or among a specific group of people over a particular period of time.

OUTBREAK.

Definition: Technically it is synonymous with epidemic. It is usually used to refer to a localized as opposed to generalized epidemic. (Still this term is used more flexibly than others)

Definitions

ENDEMIC DISEASE.

Definition: The constant presence of a disease or infectious agent within a given geographic area or population.

E.G Malaria in Zambia.

Definitions

PANDEMIC.

- **Definition:** this is an epidemic occurring over a very wide area (several countries or continents) and usually affecting a large proportion of the population.
- Examples are the 1918 Spanish Influenza pandemic, HIV pandemic, COVID-19 pandemic.

ROLE OF DISEASE MONITORING & SURVEILLANCE

- **Disease Monitoring and Surveillance**
 - This is the ongoing systematic collection, analysis, and interpretation of health data for action
 - All types of common diseases and their manageable frequencies known in the population.
 - Helps us determine when any particular disease “goes out of control” or when a novel disease emerges.

CRITERIA FOR DECIDING IF IT IS AN EPIDEMIC

- When a disease appears in the population, its frequency is compared to the expected level for that disease in that **specified area or population** in that **specified time period** using **disease monitoring and surveillance information**.
- A disease is **epidemic (sometimes called an outbreak)** when its frequency within the population during a given time interval is clearly in **excess** of its expected frequency.
- Once we have a “**suspected outbreak**” an **outbreak investigation is conducted**.

CONDUCTING AN OUTBREAK INVESTIGATION

10 steps in conducting an outbreak investigation

- 1) Constitute an outbreak investigation team.**
- 2) Verify the diagnosis**
- 3) Create a Case definition, find cases systematically and record epidemiologic information for each case.**
- 4) Perform descriptive epidemiological analyses**
- 5) Develop hypotheses and evaluate (test) hypotheses**

CONDUCTING AN OUTBREAK INVESTIGATION

10 steps in conducting an outbreak investigation cont...

- 6) Perform supplemental laboratory or environmental investigations
- 7) As necessary reconsider, refine, and / or re-evaluate hypotheses
- 8) Implement control and prevention measures
- 9) Initiate or maintain monitoring and surveillance
- 10) Communicate findings

I) CONSTITUTE AN OUTBREAK INVESTIGATION TEAM.

- Constitute a team of experts from various sectors to constitute your outbreak investigation team.
- May include experts from medical, vet, laboratory services, social sciences, environmental health etc. (multidisciplinary team).

2) VERIFY THE DIAGNOSIS

- The diagnosis of the infectious agent found in the reported cases should be verified using a gold standard confirmatory test.
- When diagnosis has already been done using inferior test, the investigator “upon arrival” can send a sample or samples to verify the diagnosis e.g to a higher reference laboratory.
- This can be done in a small sample of the current total suspected cases or all of them.

3) CREATE A CASE DEFINITION, FIND CASES SYSTEMATICALLY AND RECORD EPIDEMIOLOGIC INFORMATION

- **Case definition** is a standard set of criteria for deciding whether an individual should be classified as having the outbreak health condition of interest or not.
- Includes a clinical criteria and an epidemiological restriction criteria by place, time, and person.
- Clinical criteria involves a combination of signs and symptoms and/or with a laboratory confirmation. Confirmed case are those who match all the criteria plus with a positive laboratory diagnosis.

3) CREATE A CASE DEFINITION, FIND CASES SYSTEMATICALLY AND RECORD EPIDEMIOLOGIC INFORMATION

- Various categories of case definition i.e **confirmed case, probable case, suspected case** etc. Also primary cases and secondary cases.
- Case definition should be flexible at start and can be modified during outbreak as more information is obtained.
- A highly sensitive case definition may be used initially to capture as many cases but a highly specific one (i.e confirmed cases) is used for the data analysis.
- Case definition will help to begin to identify and count the outbreak cases and to begin to determine the extent of the outbreak in a systematic way.

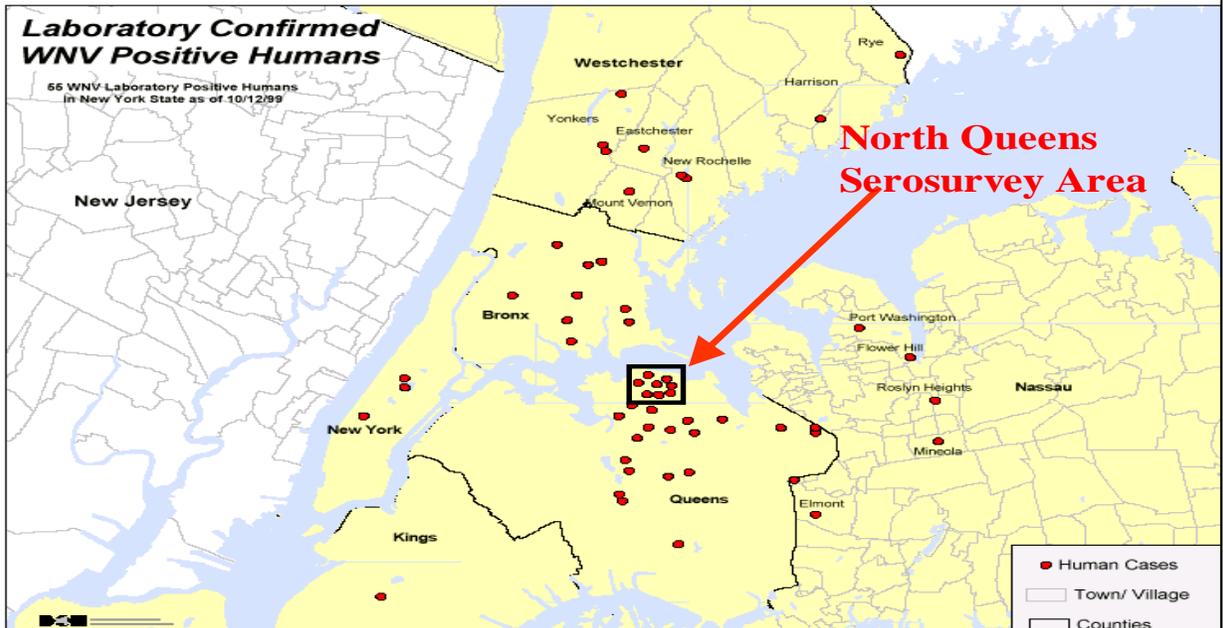
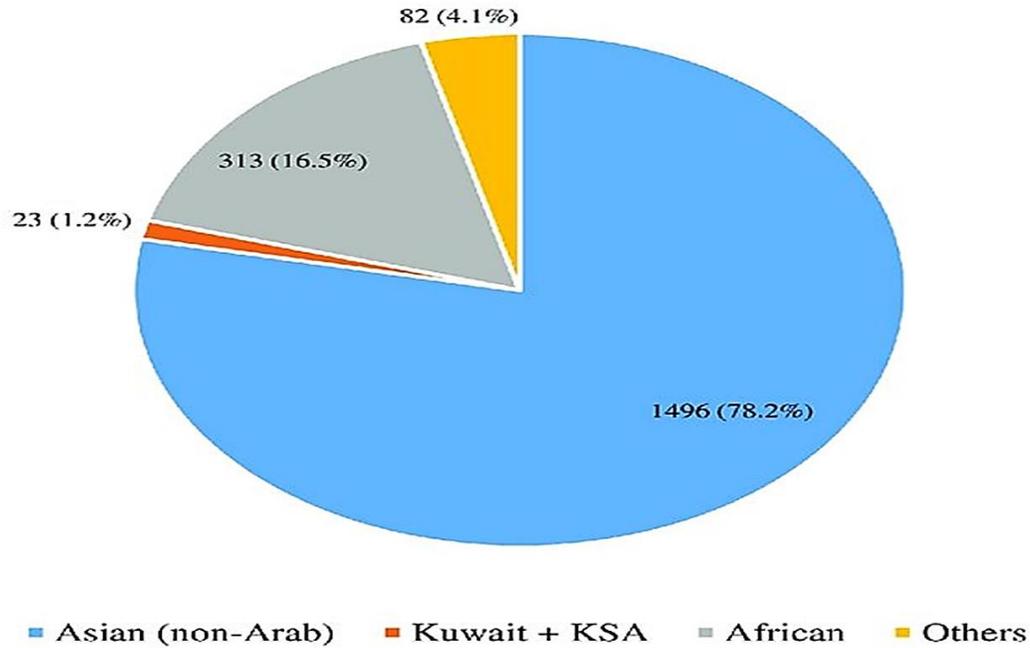
3) CREATE A CASE DEFINITION, FIND CASES SYSTEMATICALLY AND RECORD EPIDEMIOLOGIC INFORMATION

- Using case definition, actively look for cases as the outbreak is in progress.
- Record as much epidemiological data (**e.g demographics and other possible risk factors**) from the cases which will be used to perform both descriptive and analytical epidemiology (hypothesis testing) to assess the patterns and determinants of disease.
- Conduct case counts and **create line list**

4) PERFORM DESCRIPTIVE EPIDEMIOLOGICAL ANALYSES

- Summarize epidemiological data collected from **CONFIRMED** cases.
- Maps, distribution by person, place, and time etc.
- i.e create frequencies distribution for qualitative variables and numeric summary measures for the quantitative variables using various descriptive statistics tools.
- Graphical summaries
- This will reveal basic patterns that will lead to a **hypothesis**

Malaria Cases (n, %) by Ethnic Groups in Kuwait (2013-2018)



Characteristic	No. of Patients (%)	Population at Risk	Rate of Infection per Million Population
Age (years)			
0-19	2 (3)	2,324,081	0.9
20-29	1 (2)	1,553,981	0.6
30-39	3 (5)	1,549,111	1.9
40-49	1 (2)	1,177,190	0.8
50-59	9 (15)	867,331	10.4
60-69	12 (22)	814,838	16.0
70-79	18 (31)	534,785	33.7
≥80	12 (20)	281,054	42.7
Age category (years)			
≥50	52 (88)	2,498,008	20.8
<50	7 (12)	6,604,363	1.1
Sex			
Male	31 (53)	4,289,988	7.2
Female	28 (47)	4,812,383	5.8
Race			
White	41 (69)	5,983,901	6.9
Nonwhite	9 (15)	3,118,470	2.9
Unknown	9 (15)	--	--
Borough or county of residence			
New York City			
Brooklyn (Kings)	3 (5)	2,300,664	1.3
Bronx	9 (15)	1,203,789	7.5
Manhattan	1 (2)	1,487,536	0.7
Queens	32 (54)	1,951,599	16.4
Staten Island (Richmond)	0	379,999	0.0
New York State			
Nassau	6 (10)	1,287,348	4.7
Westchester	8 (14)	847,811	9.4

4) PERFORM DESCRIPTIVE EPIDEMIOLOGICAL ANALYSES

- Also create an **Epidemic curve (Epi curv)**.
- An epidemic curve is a graphic depiction of the number of outbreak cases by date of illness onset (time).
- Epidemic Curve to reveal the following information:
 - A) **Pattern of spread (Type of outbreak)**
 - B) **Magnitude of outbreak**
 - C) **Time trend of outbreak**
 - D) **Most likely period of exposure for point source epidemic**

4) PERFORM DESCRIPTIVE EPIDEMIOLOGICAL ANALYSES

Pattern of spread

1) Epi curve for Common Source epidemics (**intermittent** OR **continuous** exposure).

- If exposure is **intermittent**, it can result in an epidemic curve with irregular peaks (**Fig 1 next slide**)
- If exposure is **continues**, it can result in epidemic curve with gradual rise and a possible plateau e.g contaminated river (**Fig 2 next slide**)

Figure 1. Example of an epidemic curve from a common intermittent exposure source

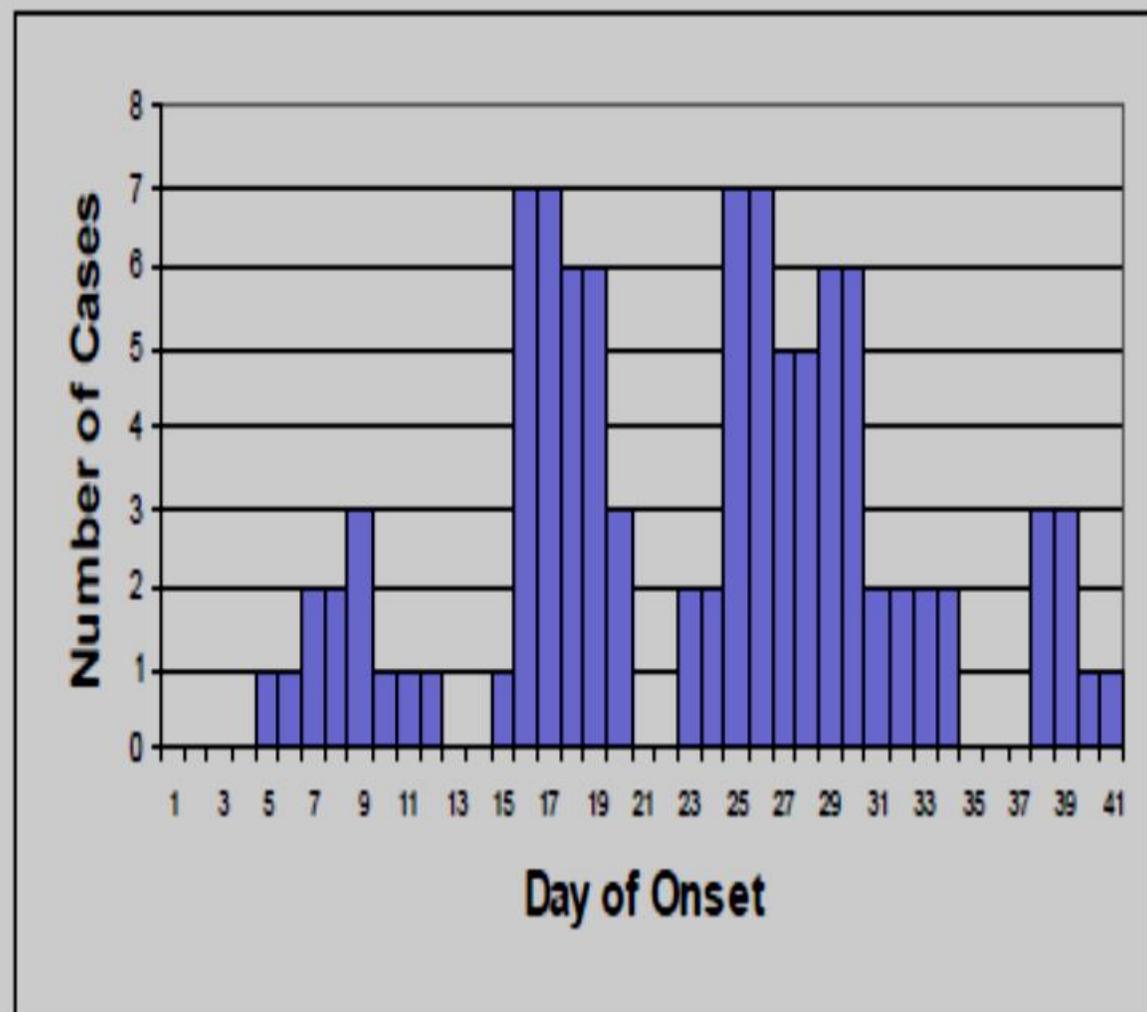
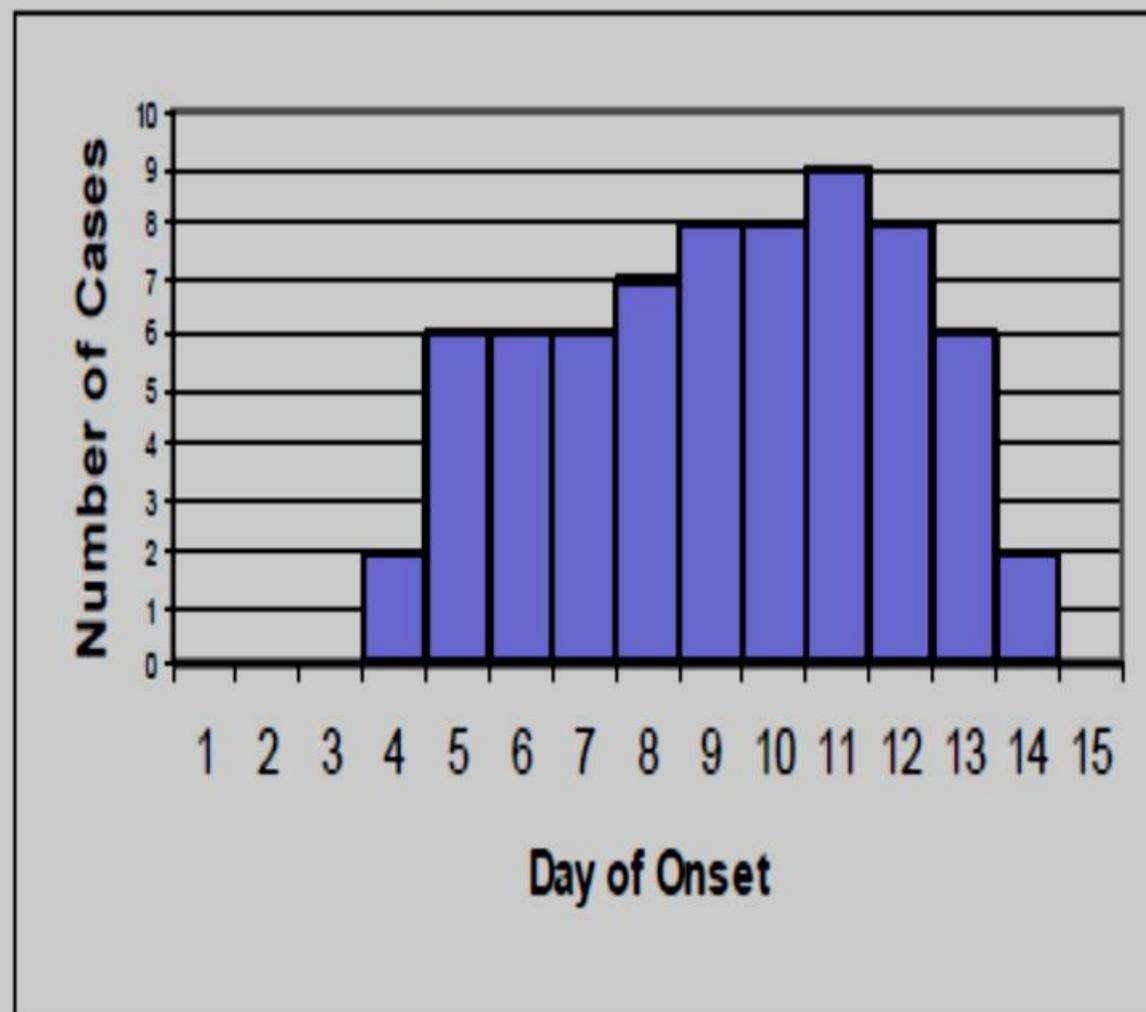


Figure 2. Example of an epidemic curve from a common continuous exposure source

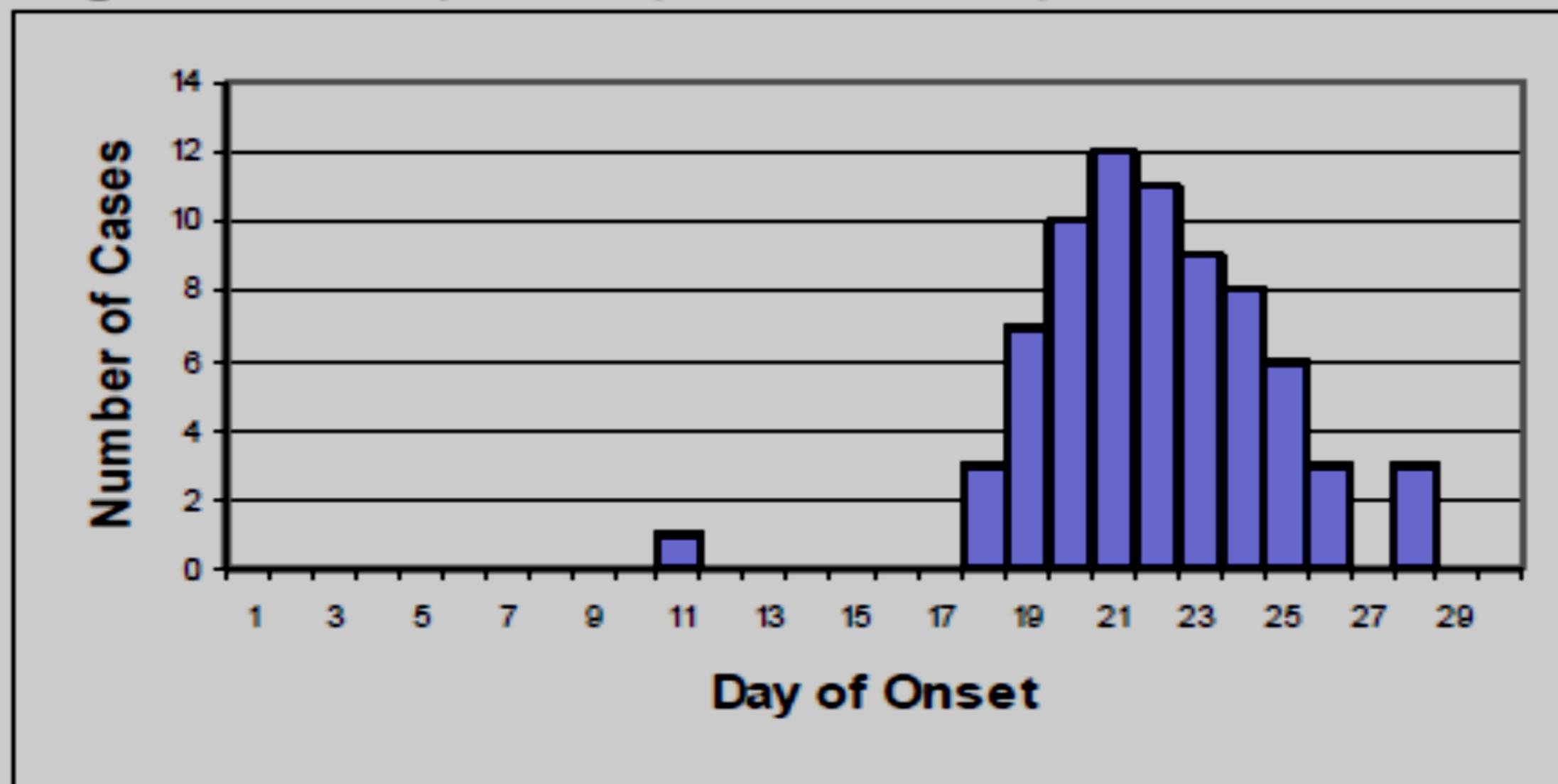


4) PERFORM DESCRIPTIVE EPIDEMIOLOGICAL ANALYSES

2) Point Source epidemic.

- This is a common source outbreak in which the exposure period is relatively brief and all cases occur within one incubation period.
- Has a sharp upward slope and a gradual downward slope. e.g salmonella infection after a party

Figure 3. Example of a point source epidemic curve



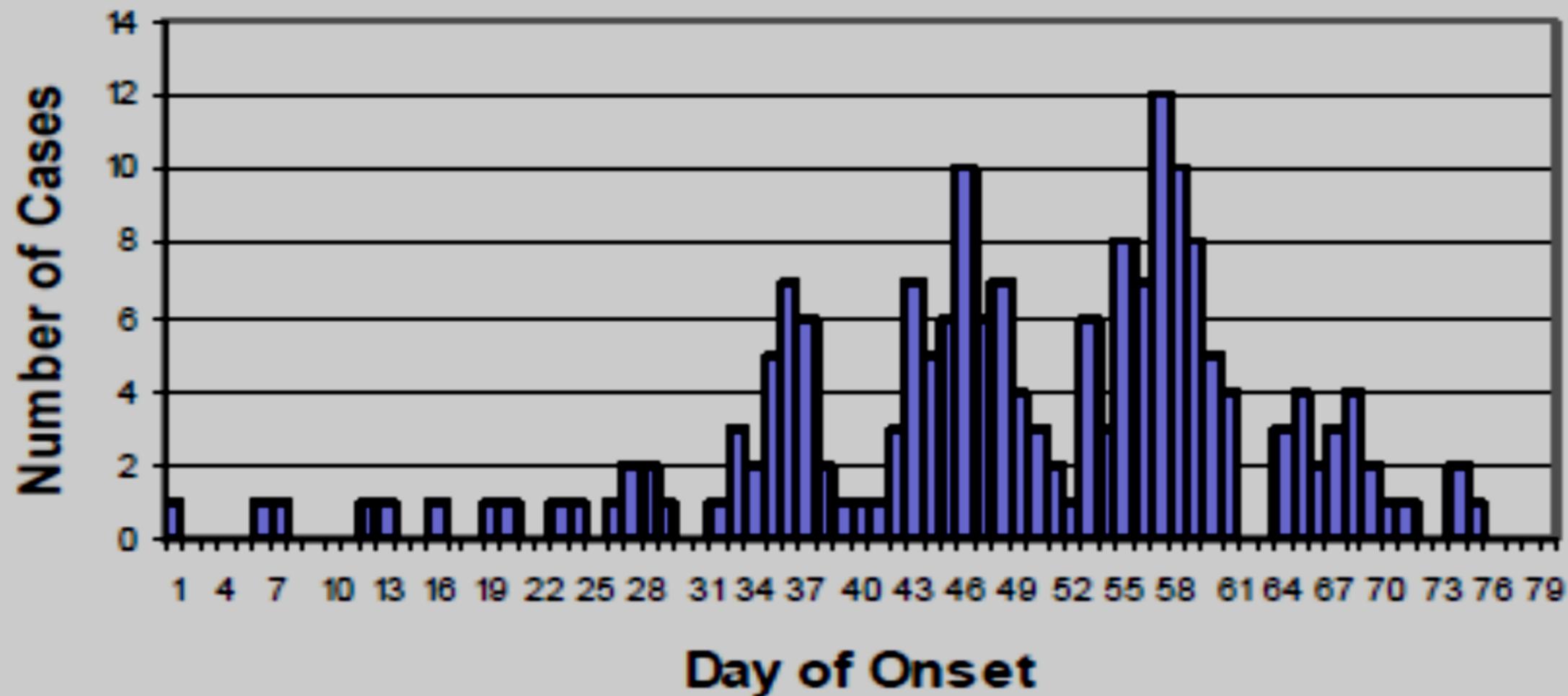
4) PERFORM DESCRIPTIVE EPIDEMIOLOGICAL ANALYSES

Pattern of spread

3) Propagated epidemic.

- This is an outbreak that is spread from one person to another.
- Therefore, normally lasts longer than common source epidemics
- May have multiple waves of infection leading to multiple progressively taller peaks each an incubation period apart.

Figure 4. Example of a propagated epidemic curve



5) DEVELOP HYPOTHESIS AND EVALUATE HYPOTHESIS

- A hypothesis is an attempt to explain the cause of the disease or epidemic.
- It is a tentative declarative explanation about the cause of the outbreak (that is the **determinant** OR causing **risk factor**)
- Hypothesis is built based on your analysis of the descriptive epidemiology in the previous steps as well as previous experience and other basic knowledge by the investigator.

5) DEVELOP HYPOTHESIS AND EVALUATE HYPOTHESIS

- Something is considered a **risk factor** OR **determinant** when: (a) the number of disease cases who were exposed to it are many, (2) the number of disease cases who were not exposed to it are few.
- Statistical association between the disease and suspected risk factor in your hypothesis can be tested using e.g **relative risk (RR)** or **Odds ratio, Chi-squared test, correlation, logistic regression etc**
- This statistical association can be assessed using a simple study design such as a **case control** study or retrospective **cohort study** for small populations.

Table 1: Data from an investigation of an outbreak of *Salmonella typhimurium* gastroenteritis following a company's holiday banquet in December 2003

Food Items Served	Number of Persons who ATE Specified Food				Number of Persons who DID NOT EAT Specified Food				Risk Ratio
	Ill	Not Ill	Total	Attack Rate	Ill	Not Ill	Total	Attack Rate	
Beef	53	28	81	65%	4	31	35	11%	5.7
Ravioli	43	35	78	55%	14	24	38	37%	1.5
Cajun sauce*	19	11	30	63%	37	48	85	44%	1.5
Pesto cream*	37	29	66	56%	19	30	49	39%	1.4
California rolls*	21	14	35	60%	34	44	78	44%	1.4
Mushrooms*	32	26	58	55%	24	31	55	44%	1.3
Broccoli*	34	30	64	53%	22	29	51	43%	1.2
Carrots*	34	30	64	53%	23	28	51	43%	1.2
Potatoes*	39	41	80	49%	17	17	34	50%	1.0

*Excludes 1 or more persons with indefinite history of consumption of that food.

6) PERFORM SUPPLEMENTAL LABORATORY OR ENVIRONMENTAL INVESTIGATIONS

- If a site e.g a food place is implicated in the majority of cases, an inspection of the site can be conducted/food samples can be collected and tested in the lab
- If an environmental site is implicated environmental samples can be collected e.g Water samples tested etc
- To **correlate** with findings in patients
- This can give further support for your hypothesis about the cause (risk factor or determinant) and spread of the outbreak.
- **preliminary** control measures can be implemented here if positive outcome!!

7) AS NECESSARY, RECONSIDER, REFINE, AND / OR RE-EVALUATE HYPOTHESES

- After the above data Analysis and other evidences, reconsider any other alternative factors or hypotheses to explain the disease pattern seen. See to it that your data analysis results make sense at almost all levels of explaining the outbreak situation.
- Assess alternative explanations if possible

8) IMPLEMENT CONTROL AND PREVENTION MEASURES

- At this point, implement **definitive** control measures based on all final investigation and statistical analysis results.
- The established determinants or sources of infection simply provide the **control points** to control the outbreak.
- This involves eliminating the source or the risk factor, breaking the chain of transmission, and preventing any further infection through these channels.
- This is done in a **multi-disciplinary approach** and also involving all stake holders in the community and necessary mobilization of resources.

9) INITIATE OR MAINTAIN SURVEILLANCE

- Set up a specific surveillance and monitoring system for the disease of the outbreak to closely monitor the disease data.
- Or intensify the existing disease monitoring and surveillance system in the area.
- This is done in order to also see if the control measures implemented to control the outbreak are really working etc.

10) COMMUNICATE FINDINGS

- A job is complete when all paper work is done.
- The outbreak should be reported accurately and timely to all relevant stake holders and policy makers.
- Reporting conclusions beyond the scope of the investigation findings should be avoided.
- The Established channel of reporting and reporting style should be followed.

NOTE

- The above steps are just the general standard outlined steps for an outbreak investigation.
- Sometimes during an outbreak investigation, the steps may not always follow that order. Sometimes some steps may even be done concurrently while some steps may even be omitted depending on how obvious the cause is or the nature of the outbreak and environment setting.

ROLE OF LABORATORY IN OUTBREAK INVESTIGATION

Laboratory services are critical at steps:

Step 2. Verify the diagnosis

Step 3. Create a Case definition, find cases systematically and record epidemiologic information for each case.

Step 6. Perform supplemental laboratory or environmental investigations

Step 9. Initiate or maintain monitoring and surveillance

CASE STUDIES

- The book (**Dworkin, M.S., 2009. Outbreak Investigations Around the World: case studies in infectious disease field epidemiology. Jones & Bartlett Publishers**) contains reports of real world examples of outbreak investigations conducted from various places around the world. The book can be found at this link:

https://scholar.google.com/scholar?hl=en&as_sdt=0%2C5&q=Dworkin%2C+M.S.%2C+2009.+Outbreak+Investigations+Around+the+World%3A+case+studies+in+infectious+disease+field+epidemiology.+Jones+%26+Bartlett+Publishers.&btnG