

A Brief Introduction to Epidemiology

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The purpose of this lecture is
to provide an overview of
the fundamentals of epidemiology
as the basis for the science of
public health.

Why Teach Epidemiology?

Epidemiology is an objective, scientific method of problem solving based on quantitative analysis.

Teaching epidemiology

- improves students' **reasoning and research skills**,
- enhances their ability to analyze and solve **complex problems**, and
- sensitizes them to good health practices.

Outline

1. Define epidemiology and explain its role as the foundation for public health
2. Describe common measures of disease frequency
3. Descriptive and analytic epidemiology
 - John Snow and cholera in London 1854,
 - Case – control study, cohort study, clinical trials
4. Disease / Public health surveillance
 - Influenza surveillance
5. Outbreak investigations
 - Emerging Infectious Diseases
 - SARS Health Communication
6. Screening Test
7. OR and RR
8. Four types of causal relation
9. Guidelines for assessing causation
10. Summary

1. Define epidemiology
and explain its role
as the foundation for
public health

Medicine



Clinical
medicine

Preventive
medicine

Clinical Medicine

The study and practice of medicine
by direct examination of the patient.

Webster's Online Dictionary

Preventive Medicine

The branch of medicine concerned with preventing disease; "the medical establishment doesn't profit from preventive medicine".

Webster's Online Dictionary

Public Health

The science and act of
preventing diseases,
prolonging life, and
promoting health and efficiency
through organised **community efforts.**

Specialty Definition: Webster's Online Dictionary

Public health

- The approach to medicine that is concerned with **the health of the community as a whole**.
- Public health is **community health**.
- It has been said that:

**"Health care is vital to all of us
some of the time,
but public health is vital to all of us
all of the time."**

Core Public Health Functions

1. Assessment
2. Policy development
3. Assurance

The three core public health functions

1. The assessment and monitoring of the health of communities and populations at risk to identify health problems and priorities;
2. The formulation of public policies designed to solve identified local and national health problems and priorities;
3. To assure that all populations have access to appropriate and cost-effective care, including health promotion and disease prevention services, and evaluation of the effectiveness of that care.

Notable public health achievements in the 20th century

- Vaccination
- Control of infectious diseases
- Safe and healthier foods
- Fluoridation of drinking water
- Decline in deaths from coronary heart disease and stroke
- Recognition of tobacco as a health hazard
- Motor vehicle safety
- Healthier mothers and babies
- Family planning
- Safer workplaces

Epidemiology

The study of the **distribution** and **determinants** of health-related states or events in **specified populations**, and the application of this study to **control** of health problems.

Epidemiology

- The study of the distribution and determinants of health-related states or events (including disease), and the application of this study to the control of diseases and other health problems.
- Various methods can be used to carry out epidemiological investigations:
 - surveillance and descriptive studies can be used to study distribution;
 - analytical studies are used to study determinants.

<http://www.who.int/topics/epidemiology/en/>

Epidemiology

The study of the **distribution** and **determinants** of health problems in **specified populations** and applying the learned information to **control** the health problems.

<http://www.cdc.gov/excite/about.htm>

Epidemiology

Study

- Epidemiology is the basic science of public health.
- It's a highly quantitative discipline based on principles of statistics and research methodologies.

Epidemiology

Distribution

- Epidemiologists study the distribution of frequencies and patterns of health events within groups in a population.
- To do this, they use **descriptive epidemiology**, which characterizes health events in terms of person, place and, time.

Epidemiology

Determinants

- Epidemiologists also attempt to search for causes or factors that are associated with increased risk or probability of disease.
- This type of epidemiology, where we move from questions of "who," "what," "where," and "when" and start trying to answer "how" and "why," is referred to as *analytical epidemiology*.

Epidemiology

Health-related states

- Although **infectious diseases** were clearly the focus of much of the early epidemiological work, this is no longer true.
- Epidemiology as it is practiced today is applied to the **whole spectrum of health-related events**, which includes
 - chronic disease, environmental problems, behavioral problems, and injuriesin addition to infectious disease.

Epidemiology

Populations

One of the most important distinguishing characteristics of epidemiology is that it deals with **groups of people** rather than with individual patients.

Epidemiology

Control

- Finally, although epidemiology can be used simply as an analytical tool for studying diseases and their determinants, it serves a more active role.
- Epidemiological data steers public health decision making and aids in developing and evaluating interventions to control and prevent health problems.
- This is the primary function of applied, or field, epidemiology.

What is Epidemiology?

- Like investigators at the **scene of a crime**, disease detectives begin by **looking for clues**.
- They systematically **gather** information about what happened—
Who is sick?
What are their symptoms?
When did they get sick?
Where could they have been exposed to the illness?
- Using statistical analysis, investigators study the **answers** to these questions to find out **how** a particular health problem was introduced into a community.

What is Epidemiology?

Disease **detectives** then use what they have learned to prevent further illness.

For example,

when in 1993 more than 200 people in Washington State developed **similar gastrointestinal symptoms**, investigators **traced** the illnesses to undercooked **hamburgers** from a fast-food chain.

Warnings to **cook beef until it is no longer pink** halted the outbreak and prevented further transmission.

What is Epidemiology?

It is the **scientific method** of problem solving
used by "**disease detectives**"—

epidemiologists, laboratory scientists,
statisticians, physicians,
other health care providers, and
public health professionals—

to get to the root of health problems in a community,

whether the problem is

a measles outbreak on a small college campus or
a global influenza pandemic,
an increase in homicide in a single community,
a national surge in violence, or
a localized or widespread rise in cancer.

Epidemiology

- Epidemiology has been defined as the study of the distribution and determinants of disease and injury in human populations.
- Epidemiologist study the variation of disease in relation to age, sex, race, occupational and social characteristics, place of residence, susceptibility, exposure to specific agents or other pertinent characteristics.
- Also of concern are the temporal distribution of disease, the examination of trends, cyclical patterns and intervals between exposure to causative factors and onset of disease.

Epidemiology

Epidemiology advances the field of knowledge of disease causation, transmission and prevention through studies of the distribution of diseases in human populations, through laboratory studies and through incorporation of techniques derived from other disciplines; and provides a technical base for development of the optimal use and distribution of health resources for the promotion of community health.

Epidemiology

- The scope of the field ranges from **study** of the **causes** of disease to the **control** of prevention of **disease** and distribution of **health resources**.
- It should be emphasized that epidemiology **focuses** on **health problems** in population groups rather than on an individual.
- Epidemiology is a relatively young field with constantly **expanding boundaries**.

Epidemiology

The range of **activities** which may be at least partly epidemiologic **includes**

- Investigation and control of **disease outbreaks**
- Study of **environmental** and **industrial hazards**
- Evaluation of **new**, **preventive** or **curative clinical treatment** and **intervention**
- Determination of the **health needs** of the **populations**
- Evaluation of **effectiveness of health services**

Epidemiology

- Many of the tools of epidemiology are borrowed from other fields such as microbiology, immunology, medicine, statistics, demography and medical geography.
- There is a growing core of purely epidemiologic methodology.
- This methodologic core includes not only statistical methodology and principles of study design but a unique way of thinking which is beyond the rote memorization of rules

Epidemiology

- The contribution of epidemiology to any study involving groups of people is increasingly being recognized and demanded.
- An epidemiologist may work in a wide variety of settings, including
 - international health agencies,
 - state and local health departments,
 - federal government agencies and health programs,
 - health maintenance organizations, colleges and universities, and
 - numerous research institutions, both privately and publicly sponsored.

Three essential components

1. Disease distribution:

how are cases of the condition of interest spread across a population differently by gender, age, geographic location, socio-economic status, other features?

2. Disease determinants:

what risk factors or antecedent events are associated with the appearance of a disease or condition?

3. Disease frequency:

how many cases of the condition occur over a given time period?

Epidemiology in Action

- Outbreak and cluster investigations
- Public health surveillance and
- Community screening programs

Represent key areas
of public health practice
in which systematic application
of epidemiologic methods
have a large and positive impact.

Outbreaks and Clusters

Outbreaks

- Generally involve infectious disease
- The problem is unexpected
- An immediate response may be demanded
- Public health epidemiologists must travel to and work in the field to solve the problem
- The extent of the investigation is likely to be limited because of the need for timely intervention

Outbreaks and Clusters

Clusters

- Usually refer to an aggregation of relatively uncommon events / diseases of noninfectious origin (e.g., leukemia, spontaneous abortions, suicides) in space and/or time in amounts believed or perceived to be greater than expected by chance.
- These events are often perceived to be due to environmental exposures.

Cluster investigators

Clustering of disease is intriguing and some cluster investigations have led to important scientific discoveries.

For example,

investigation of the spatial clustering of enamel discoloration led to the discovery of the relation between fluoride levels in drinking water and dental caries

Most cluster investigations focus on cancer.

Many carcinogens have been discovered through occupational or medical cluster investigations

Cluster investigators

Studies of disease clusters often are **challenging** because of the constraints of information available to investigators.

Some of the biggest issues include:

- Rare health events
- Vague definition and/or heterogeneity of cases
- Lack of a population base for rate calculation
- Weak association and multiple risk factors
- Long induction periods
- Multiple comparisons
- Low-level, long-term, heterogeneous exposures
- Intense publicity
- Resource intensiveness of full investigations

The Objective of Epidemiology

- To identify the etiology or the cause of a disease and the risk factors
- To determine the extent of disease found in the community and set up priorities for interventions
- To study the natural history and prognosis of disease
- To evaluate public health intervention, policies and modes of health care delivery
- To provide the foundation for developing public policy and regulatory decisions relating to environmental problems
- To communicate the findings to health professionals and the public

Field Epidemiology

by Michael B. Gregg

- “The constellation of problems faced by epidemiologists who are called upon to investigate **urgent public health problems...**”
- “Public health epidemiologists must travel to and work **in the field to solve the problem.**”
- Thus, for those practicing in this arena, the motivation is **not primarily research oriented** but rather geared to those problems for which **government agencies** usually are given the **primary mandates and responsibilities.**
- Perhaps the title of
“**The Field of Acute Public Health Epidemiology,**” although awkward, is a better description of the content of this book.

Field Epidemiology

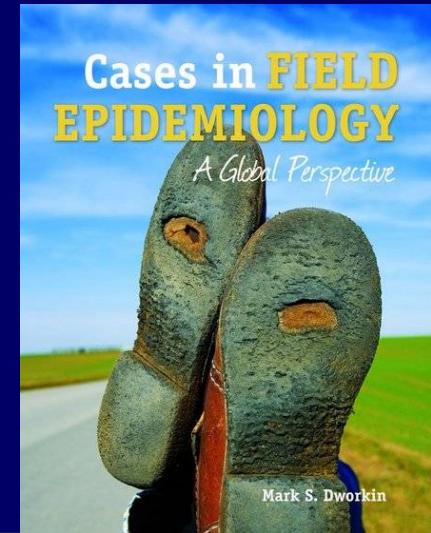
by Michael B. Gregg

We can define field epidemiology as the application of epidemiology under the following set of general conditions:

- The problem is unexpected.
- A timely response may be demanded.
- Public health epidemiologists must travel to and work in the field to solve the problem.
- The extent of the investigation is likely to be limited because of the imperative for timely intervention.

Field Epidemiology Training Programs

- “CDC has re-emphasized the priority it places on responding effectively and efficiently to health threats—domestic or global—and
- Reaffirmed its traditional focus on science and evidence-based public health practice.
- Key to this has been the strengthening of surveillance and epidemiology—historically among the organization’s greatest assets.”



Thomas Frieden, CDC Director
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Global Disease Detection Program



Global Disease Detection Program

2010 Monitoring and Evaluation Report

Center for Global Health
Division of Global Disease Detection and Emergency Response



JUNE 2011

Global Disease Detection Program, 2010 Monitoring and Evaluation Report

Global Early Warning System for Major Animal Diseases, including Zoonoses (GLEWS)

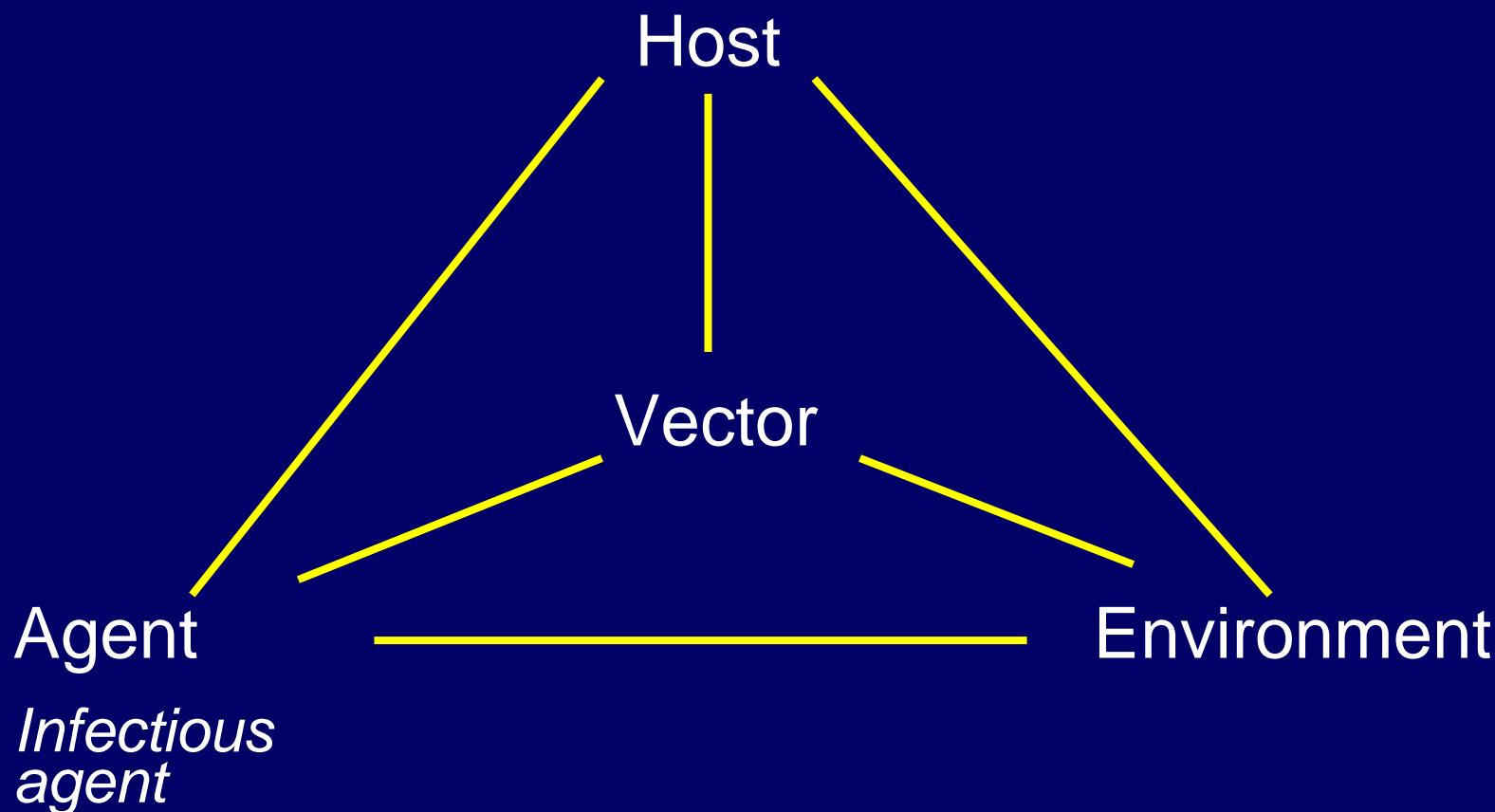
- Disease emergence and spread do not respect geographical boundaries, and animals are often implicated as the source of human infection.
- Zoonotic disease management therefore requires an integrated approach that involves different sectors; mainly human, animal and food.
- Efficient early warning and forecasting of zoonotic disease trends through functional surveillance systems is key to effective containment and control.
- Early intervention during a disease epidemic often leads to better outcomes with reduced disease burden and associated economic impact.

Global Health - Global Disease Detection and Emergency Response Health Systems Reconstruction

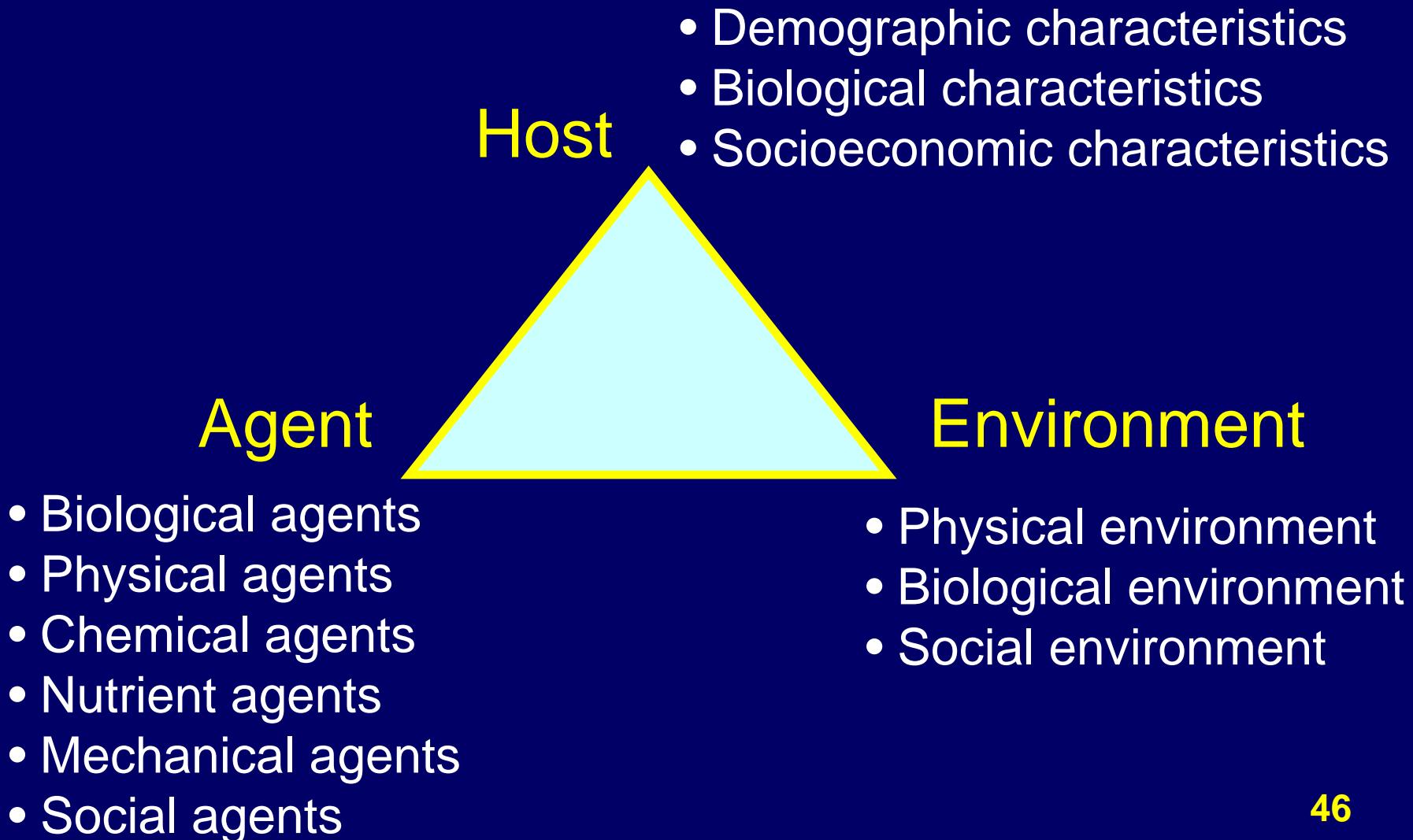
- National **laboratory** systems
- National **surveillance** systems
- Field Epidemiology and Laboratory **Training** Program (FELTP)
- Vector Control Program
- Water Sanitation and hygiene interventions
- National nutrition surveys
- Childhood immunizations
- HIV and TB control
- Reproductive health and emergency obstetrical care



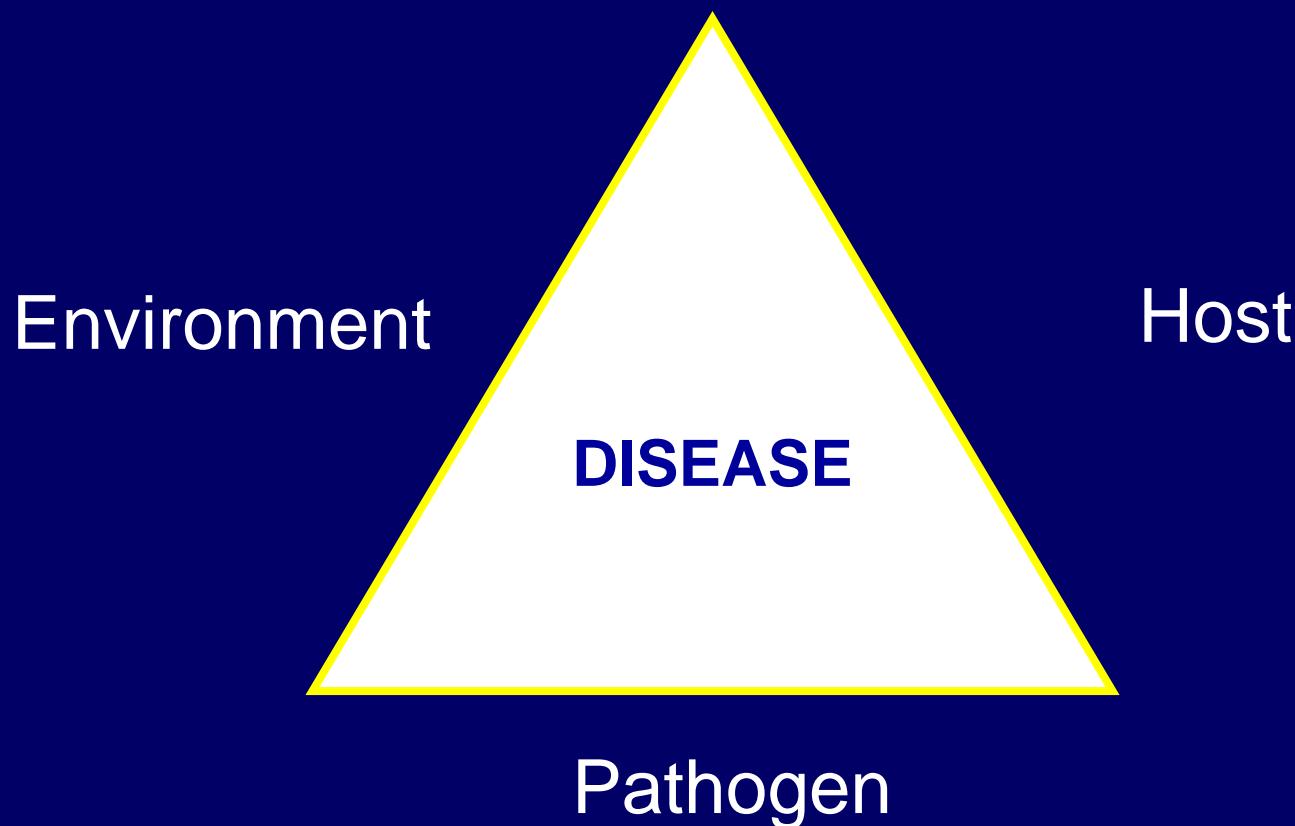
The epidemiologic triad of a disease



Epidemiologic triad



Disease Triangle

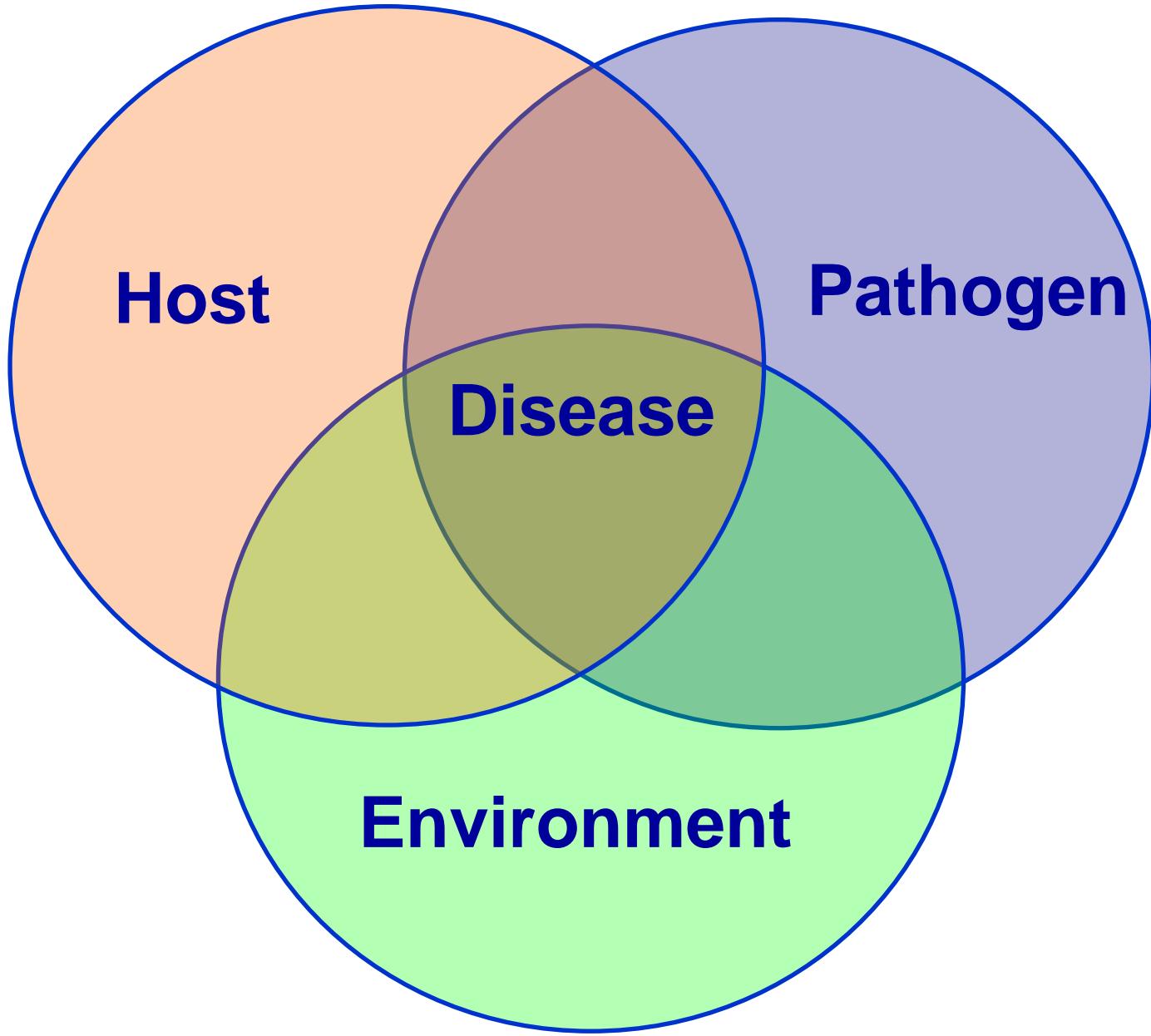


Disease is the result of forces within a dynamic system consisting of:

Agent

Host

Environment



Agent

The **entity necessary** to cause disease in a susceptible host.

- Biological - bacterium, parasite, or virus
- Physical force - motor vehicle crashes
- Chemical - environmental problem
- Nutritional imbalance - rickets

Several characteristics are important to consider:

- **Infectivity** - the capacity to cause infection in a susceptible host
- **Pathogenicity** - the capacity to cause disease in a host
- **Virulence** - the severity of disease that the agent causes in the host

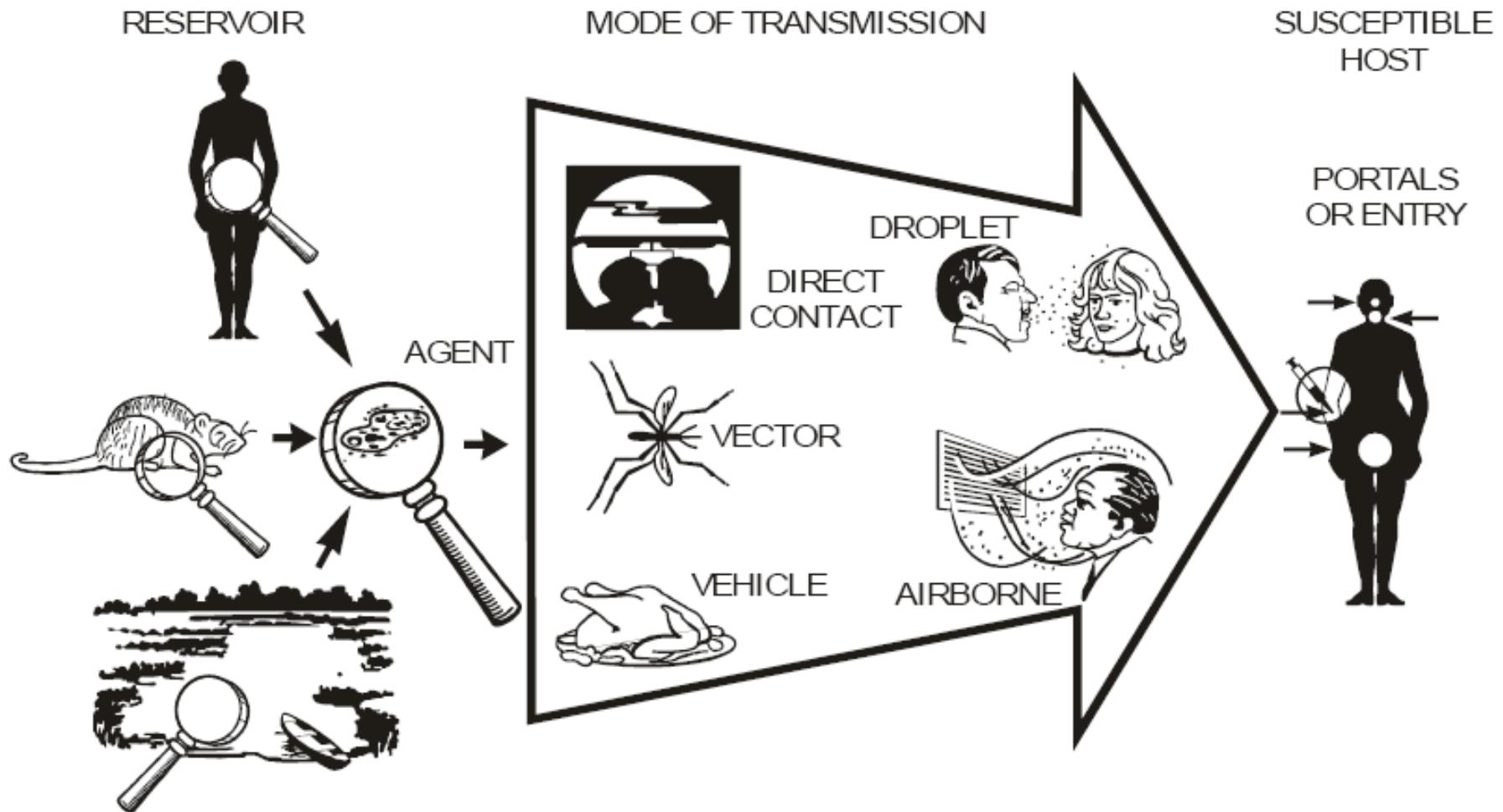
Host

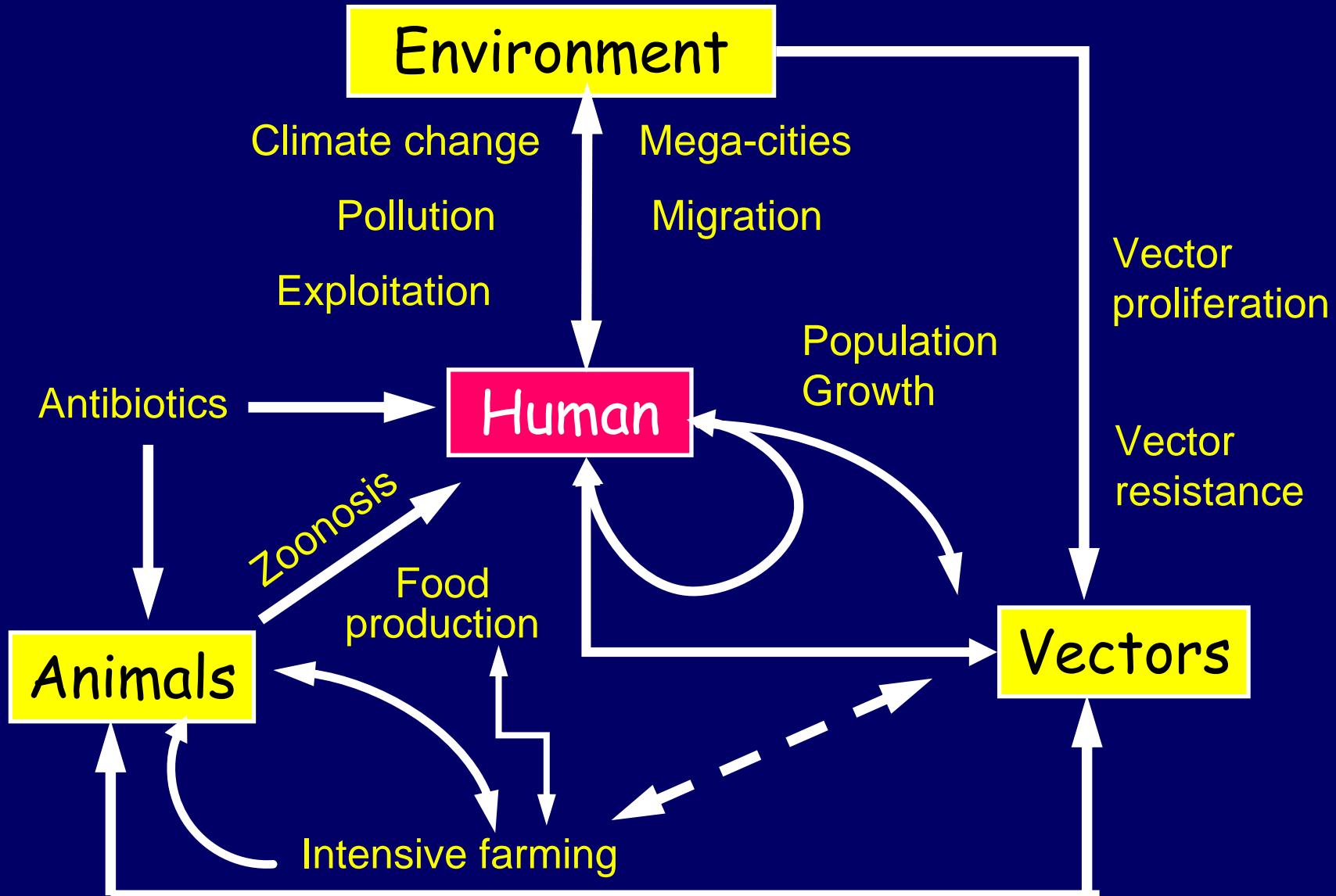
- Person, or in a more generic definition, the organism, that is susceptible to the effect of the agent.
- The status of the host is quite important and is generally classifiable as susceptible, immune, or infected.
- Finally, and also quite important, is that the host's response to exposure can vary widely, from showing no effect to manifesting subclinical disease, atypical symptoms, straightforward illness, or severe illness.

Environment

- The **conditions** or influences that are not part of either the agent or the host, but that **influence their interaction**.
- A wide variety of **factors**, including **physical, climatologic, biologic, social**, and **economic conditions**, can come into play.
- For instance, in a study of **motor vehicle injuries**, the agent (mechanical energy) and the host (driver) could be affected by the topography, the weather, and the actions of other drivers.
- In many infectious disease outbreaks, **social and economic conditions** cause **overcrowding** and lead to high levels of exposure.

Chain of infection





Transmission

Reservoir (of infectious agents)

Any person, animal, arthropod, plant, soil or substance (or combination of these)

in which an infectious agent normally lives and multiplies,

on which it depends primarily for survival, and where it reproduces itself

in such manner that it can be transmitted to a susceptible host.

- **Descriptive Epidemiology**
provides the
 - Who
 - What
 - When and
 - Whereof health-related events in a population
- **Analytic Epidemiology**
attempts to provide the
 - Why and
 - How (To react and control)of health-related events in a population

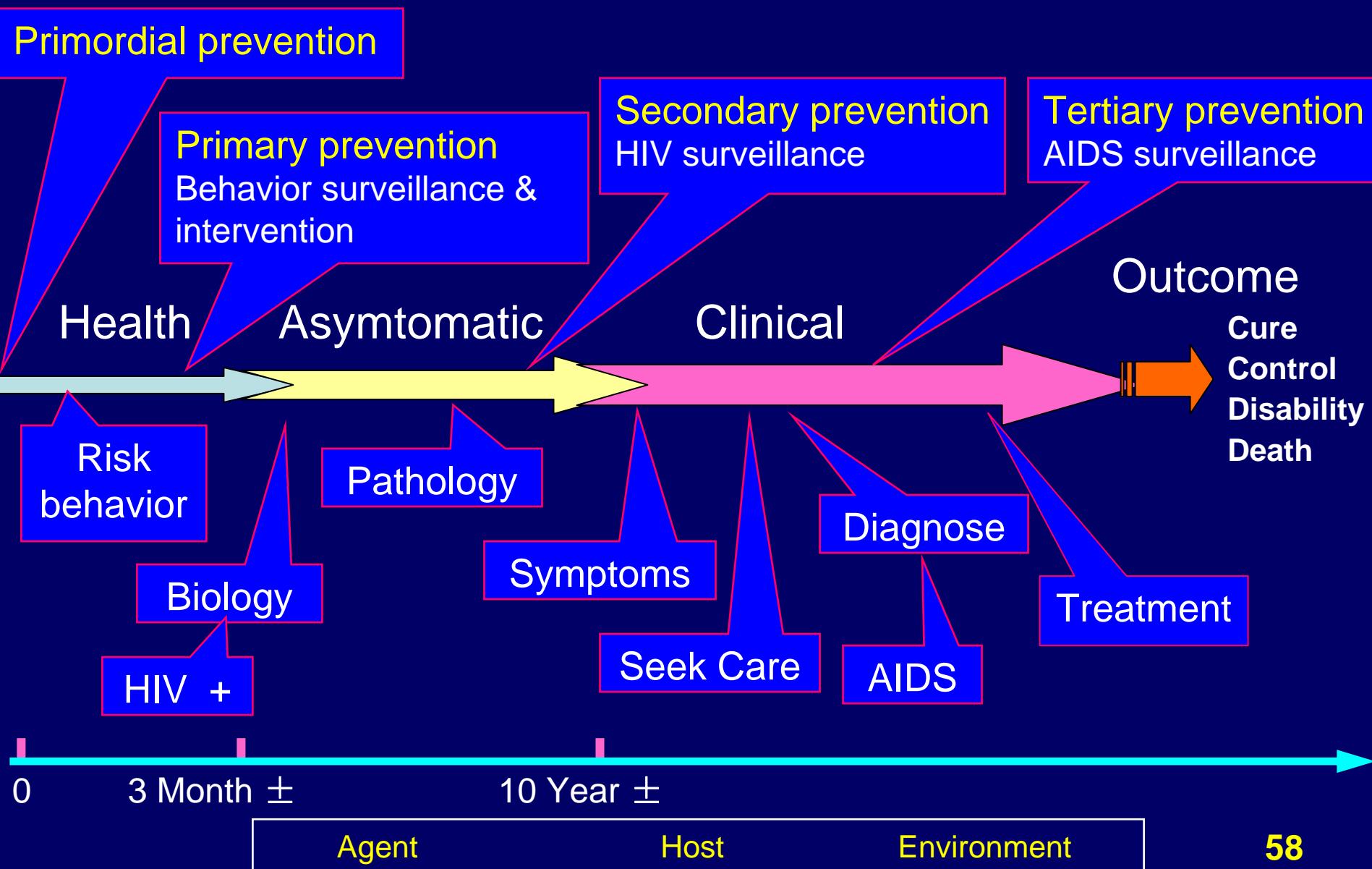
Descriptive Studies

- Collecting information that characterizes and summarizes a health event or health problem.
- Routinely collected data from such sources as death certificates, hospital discharge records, health surveys (e.g., cross-sectional surveys) and disease surveillance programs are used for most descriptive studies.
- Characteristics related to person may include age, gender, race, ethnicity, marital status, socioeconomic class and occupation.
- Descriptive studies on occurrence of conditions according to place might involve examining their frequency within or between natural or political boundaries, urban versus rural localities, or latitude.
- Examination of time relationships can both identify and evaluate possible causes for changes in health conditions.

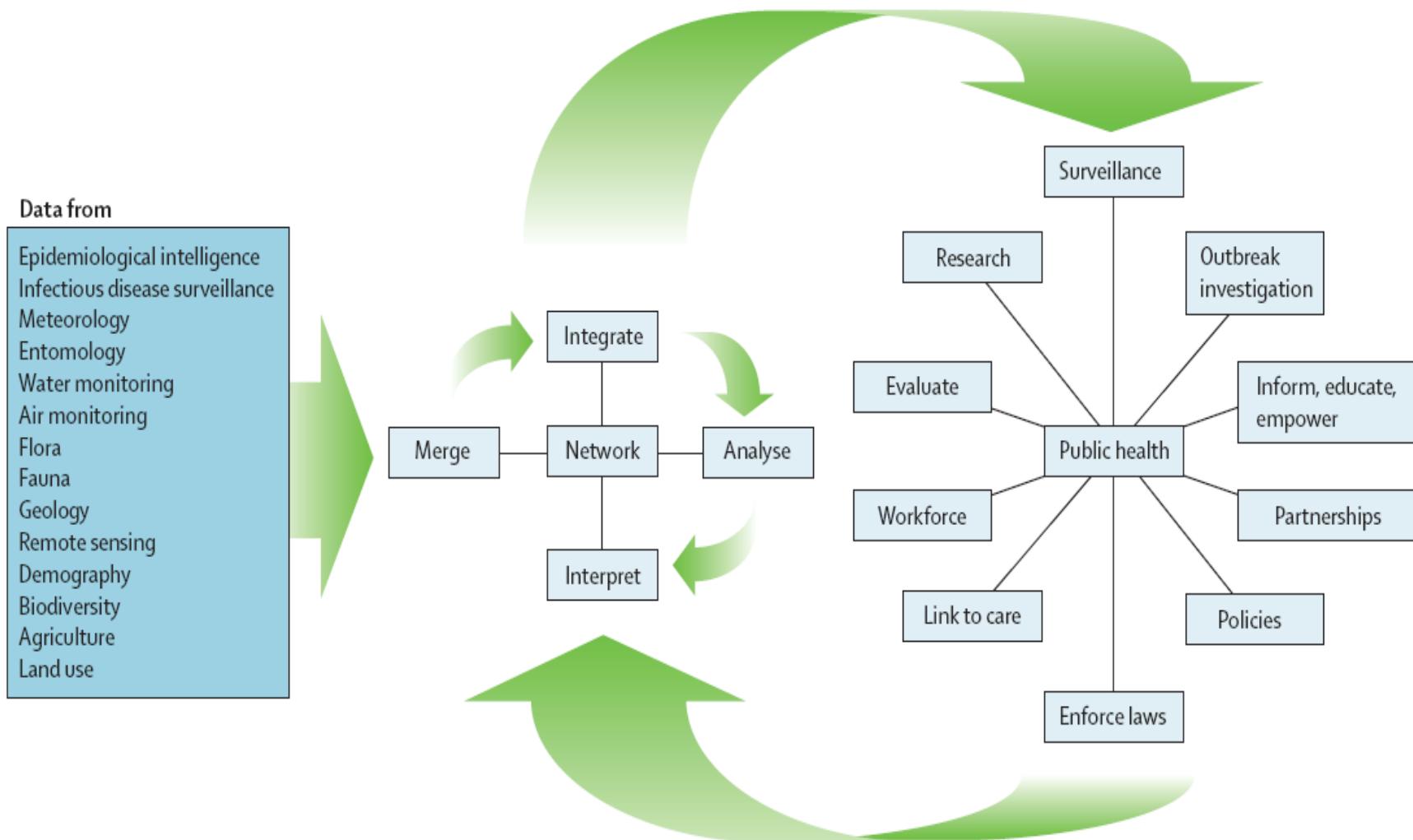
Causal Pathway of Disease or Disability

- Environment (pre-exposure)
- Hazard / agent
- Behavior/risk factor
- Exposure
- Pre-symptomatic phase
- Apparent disease
- Death

Disease natural history & HIV/AIDS intervention



Proposed diagram of an environment and epidemiology network



2. describe common
measures of
disease frequency

Disease frequency

Expected level

baseline level of observed occurrence of a particular disease

Endemic

persistent occurrence at a low to moderate level, sometimes referred to as a high background rate

Sporadic

irregular pattern with occasional cases occurring at irregular levels

Epidemic

occurrence of a disease within an area exceeds expected level for a given time. Also called an outbreak.

Note that these mean basically the same thing, but public perspective is that epidemic is much more serious than an outbreak.

Pandemic

epidemic that has spread over several countries or continents, affecting large numbers of people

Measures of Disease Frequency

Prevalence and incidence
are commonly confused.

They are similar,
but differ in the number of cases
included in the numerator:

- Prevalence includes all cases (new and old) during a given time period.
- Incidence includes only the number of new cases during a given time period.

Prevalence

Prevalence = number of *existing cases* divided by total population

The numerator for prevalence includes all persons during a specified interval or point in time,
regardless of when the condition began.

For example, a visual examination survey of 2477 persons between the ages of 52 and 85 years showed that 310 had cataracts.

The prevalence of the condition was
 $310 / 2477 \times 100 = 12.5 \%$

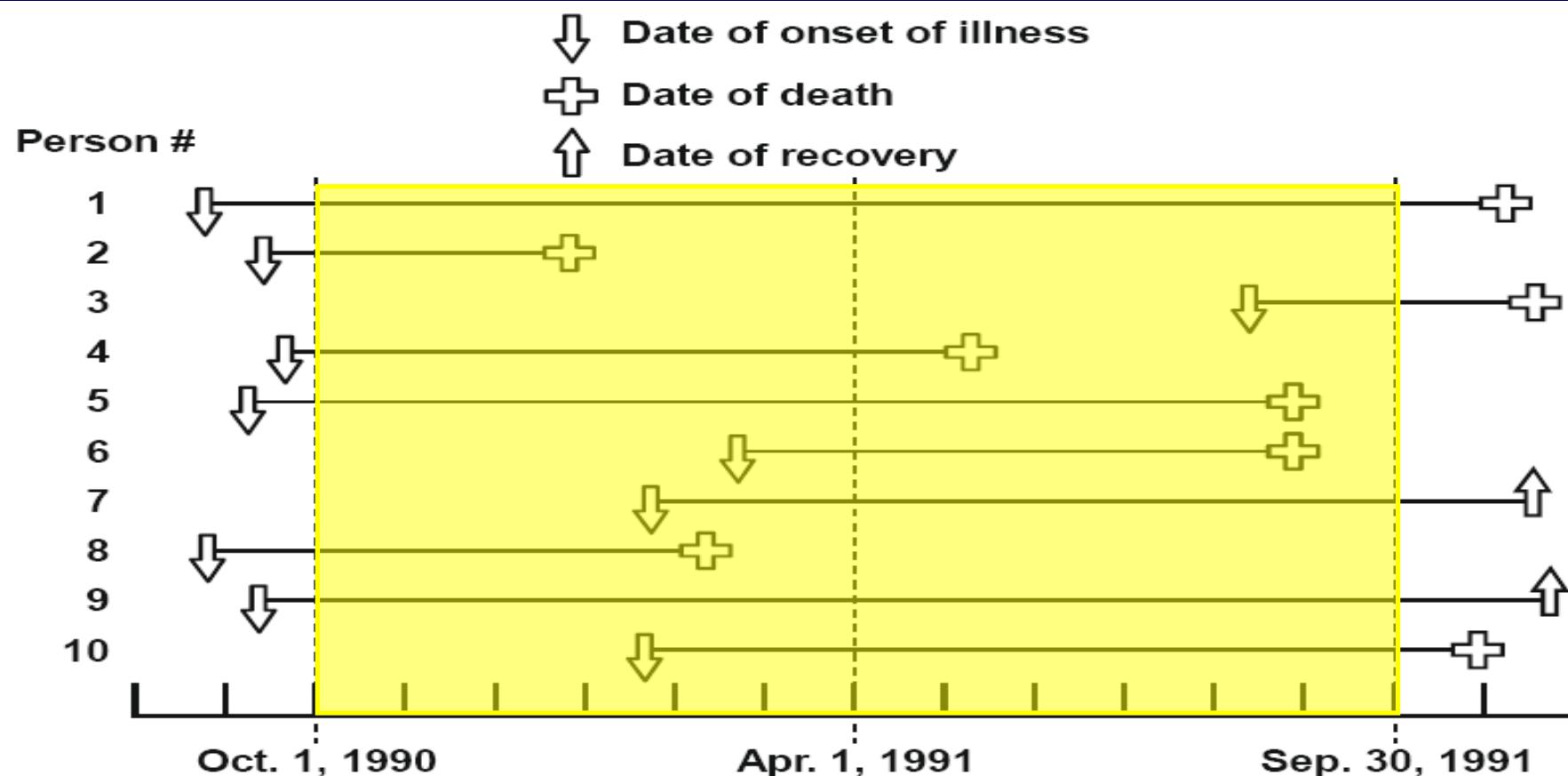
Prevalence

Several types of prevalence rates

Rate	Numerator	Denominator
Disease rate at autopsy	Number of cases disease	Number of persons autopsied
Birth defect rate	Number of babies with a given abnormality	Number of live births
Smoking rate	Number of people who smoke	Total population

All have in common a numerator that includes all cases
(new and old) of the condition under study.

Ten episodes of an illness in a population of 20



x = cases present between 10/1/90 and 9/30/91 = 10

y = population = 20

$x / y \times 100 = 10 / 20 \times 100 = 50 / 100$

So Period prevalence 10/1/90~9/30/91 was 22 cases per 100 population 65

Incidence

Incidence = number of **new cases** in a given period of time divided by the total population at risk

The numerator for incidence includes **only those persons who develop the condition during the specified time period.**

For example, in a study of 2390 women between 16 and 49 years of age, it was found that 482 used oral contraceptives. 27 of the oral contraceptive users developed bacteremia.

The incidence was therefore:

$$27 / 482 \times 100 = 5.6 \%$$

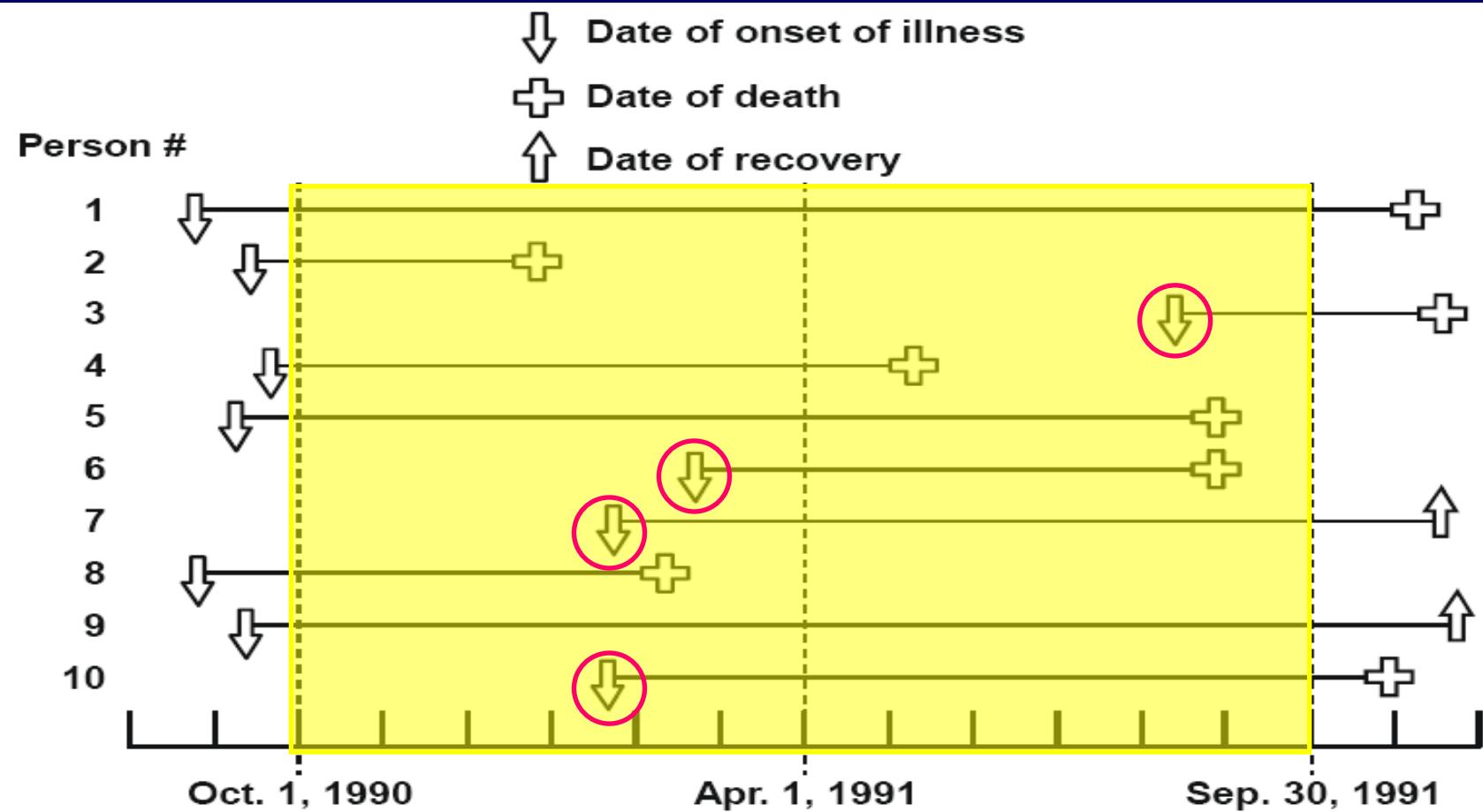
Incidence

Several types of incidence rates

Rate	Numerator	Denominator
Morbidity	New cases of a disease	Total population
Mortality	Number of deaths from a disease	Total population
Case-fatality	Number of deaths from a disease	Number of cases of that disease
Attack	Number of cases of a disease	Total population at risk during a epidemic period

All have in common a numerator that includes only **new cases** of the condition under study.

Ten episodes of an illness in a population of 20



x = new cases occurring $10/1/90 \sim 9/30/91 = 4$

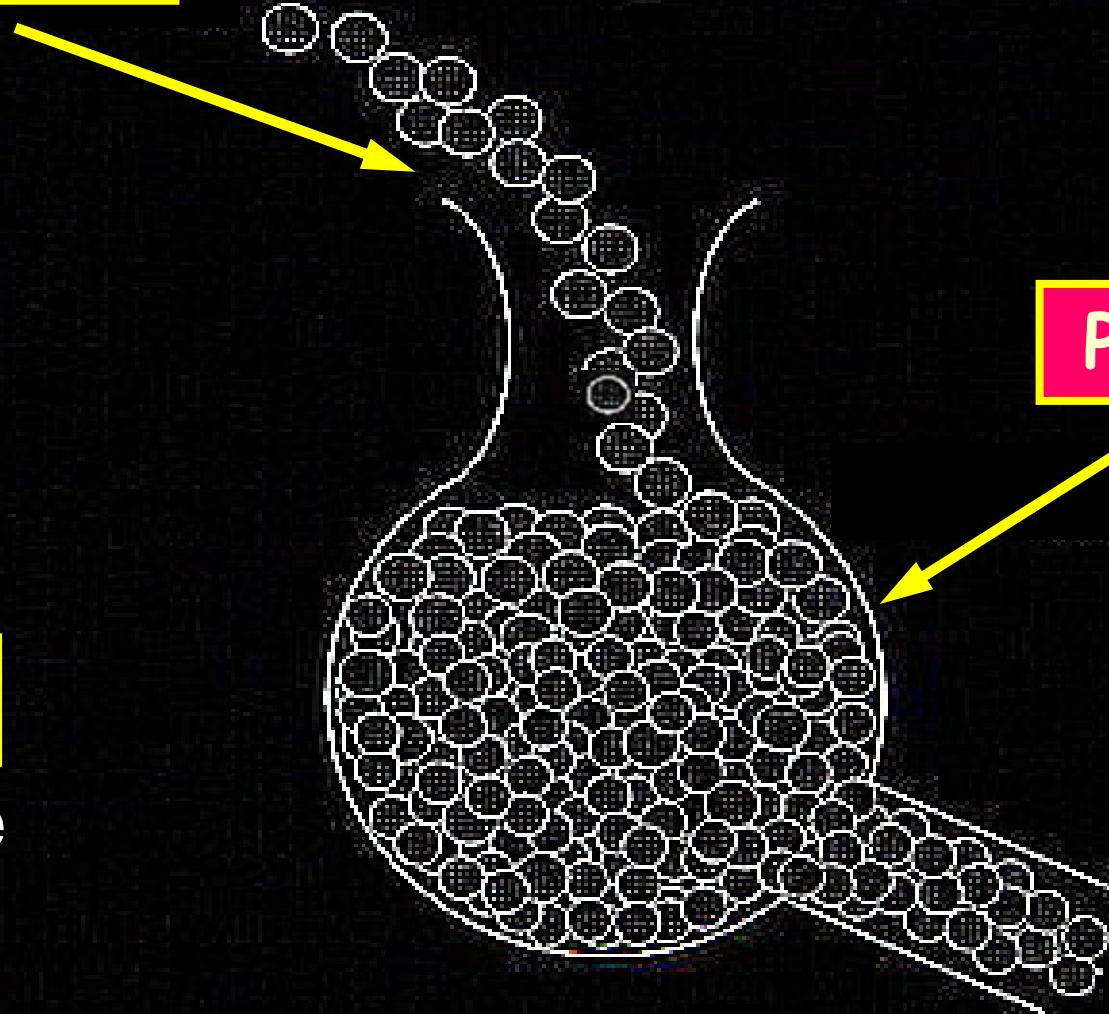
y = total population at midpoint = $20 - 2 = 18$

$x / y \times 100 = 4 / 18 \times 100 = 22 / 100$

So the one-year **incidence** was 22 cases per 100 population. 68

Relationship between incidence and prevalence

Incidence



Prevalence

Deaths
Cures

3. Descriptive and analytic epidemiology

John Snow and cholera
in London 1854

Case – control study

Cohort study

Clinical trials

JOHN SNOW



This site is devoted to the life and times of Dr. John Snow (1813-1858), a legendary figure in the history of public health, epidemiology and anesthesiology.

Click with your left mouse key to see and hear the material or and to see the material. The maps and narrations present the Snow story in place and time.

WHAT IS THIS SITE ALL ABOUT?

The following articles describe the intent of the John Snow site and comment about his life.

- "Pioneer..." *Chronicle of Higher Education*
- "Cyber Sleuths" *UCLA Magazine*
- "History, maps..." *SoC Bulletin* (PDF)
- "When Cholera Met its Match" *Science*
- "John Snow" *BBC Online*
- "The Handle" *UAB School of Public Health Magazine*
- "Popularity of Epi site grows" *UCLA School of Public Health Magazine*
- "Beyond Google. The great internet search engine is still no match for the expertise of a wise human being." *Discover* (PDF)
- "Own your Own Words" *New York Times*

WHO IS JOHN SNOW?

ENCYCLOPEDIA ENTRY ON JOHN SNOW

Providing a summary of John Snow's life in *Encyclopedia Britannica* is UCLA Professor Emeritus Ralph R. Frerichs, author of this site. Frerichs' description is a good starting point for exploring the extensive material on the life and times of John Snow that are here presented.

SIGHT AND SOUND

Sight and sound animation describing the life and accomplishments of John Snow.

- Instructions and test of system
- Part 1: The Early Years
- Part 2: Broad Street Pump Outbreak
 - The U North Carolina Version
- Part 3: The Grand Experiment (in process)

THE FATHER OF MODERN EPIDEMIOLOGY

In an article in *Old News*, David Vachon writes of John Snow's life and achievements, and concludes: "For his persistent efforts to determine how cholera was spread and for the statistical mapping methods he initiated, John Snow is widely considered to be the father of [modern] epidemiology."

Search

Ralph R. Frerichs

John Snow site

1818 London map

1846 London map

1856 Water map

1856 E&W map

1859 London map

1872 L region map

"Drummer" Book

Current Cholera

Bioterrorism

Contemporary history of bioterrorism

Disease detectives

HIV controversies

Personal screening

Rapid Surveys

Winners and losers

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Count, Past Year

Visits (hits): 2,034,070

Count, Sept., 2012

Visitors: *12,888

Total visits: **145,585

Visits per visitor: 11.3

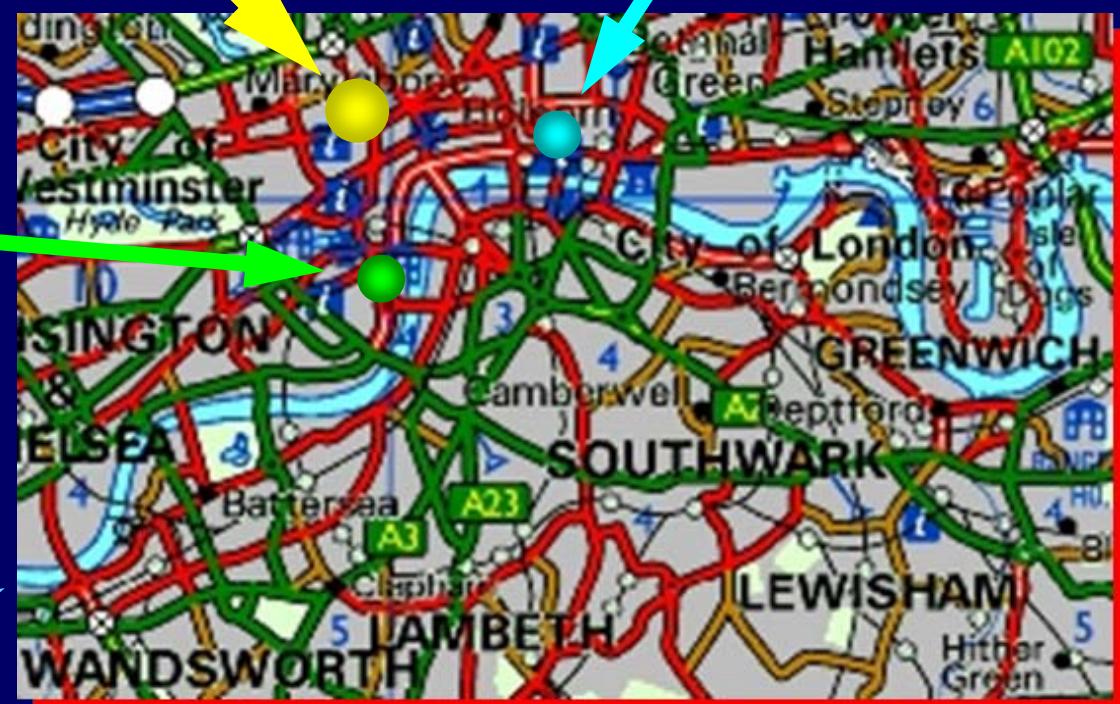
Location of the Broad Street Pump Epidemic

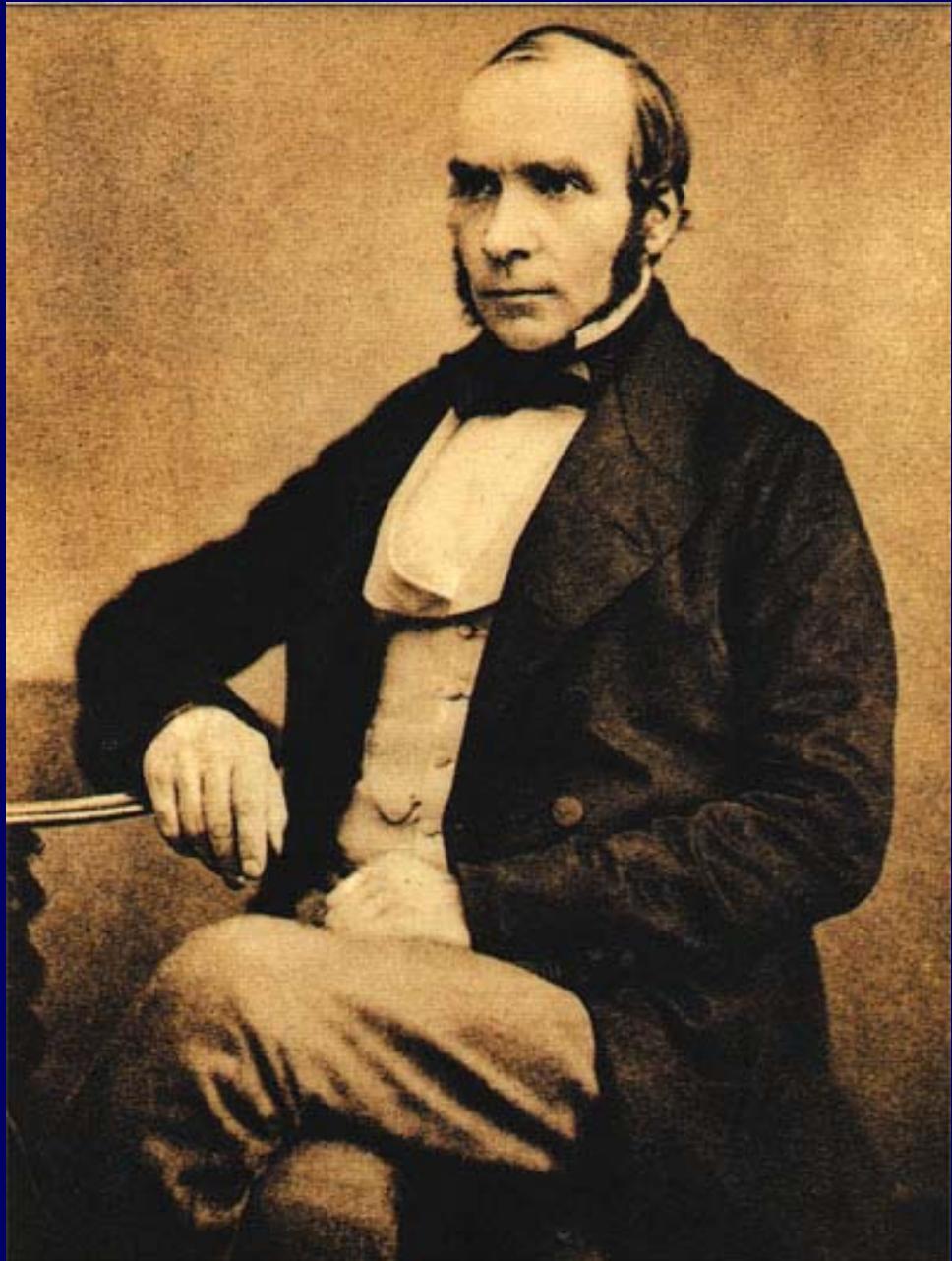


Houses of Parliament

Thames River

Saint Paul's Cathedral





Dr John Snow (1813-1858)

The most common image of Dr. Snow which appears in most textbooks or references.

It was photographed by an anonymous person some time during 1857 when Dr. Snow was 44 years old, one year before his death.

John Snow and cholera in London

- John Snow and cholera in London, which provide a dramatic illustration of epidemiologic analysis
- When a wave of Asiatic cholera first hit England in late 1831, it was thought to be spread by "miasma in the atmosphere." By the time of the Soho outbreak 23 years later, medical knowledge about the disease had barely changed,
- In August 1854, the most terrible outbreak of cholera which ever occurred in this kingdom, is probably that which took place in Broad Street, Golden Square, and the adjoining streets
- in 1883 , 29 years later, Robert Koch finally identified Vibrio cholerae as the causative agent

Deaths from Cholera in 10,000 Inhabitants by Elevation of Residence Above Sea level, London, 1848 ~ 1849

Elevation Above Sea Level (Ft)	Death in 10,0000 Inhabitants
< 20	120
20 ~	Miasma
40 ~	34
60 ~	27
80 ~	22
100 ~ 120	17
340 ~ 360	8

Spurious
Association !

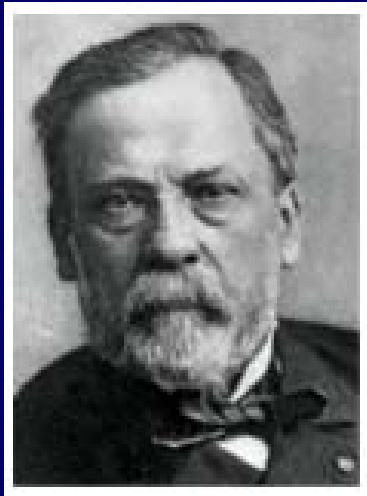
Deaths from Cholera per 10,000 Houses, by Source of Water Supply, London, 1854

Water Supply	No. of Houses	Death from cholera	Deaths /10,000 Houses
Southwark & Vauxhall Co.	40,046	1,263	315
Lambeth Co.	26,107	98	38
Other districts In London	256,423	1,422	56

Real Association !

Data adapted from Snow J: On the mode of communication of cholera ,1936
76

1859

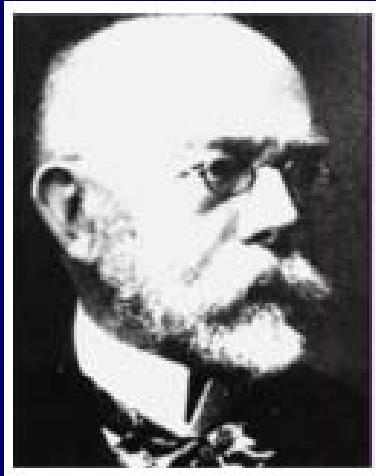


Louis Pasteur (1822-1895)
French chemist who founded
modern microbiology.

He provided strong evidence
against the miasma theory with
a prize winning study
in France in 1859.

1 year after the death of John Snow

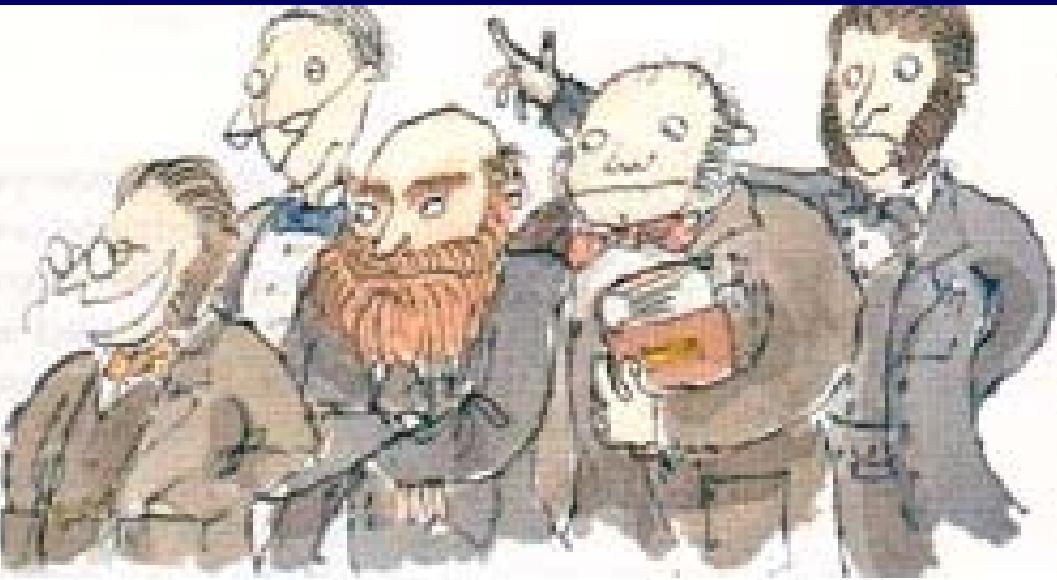
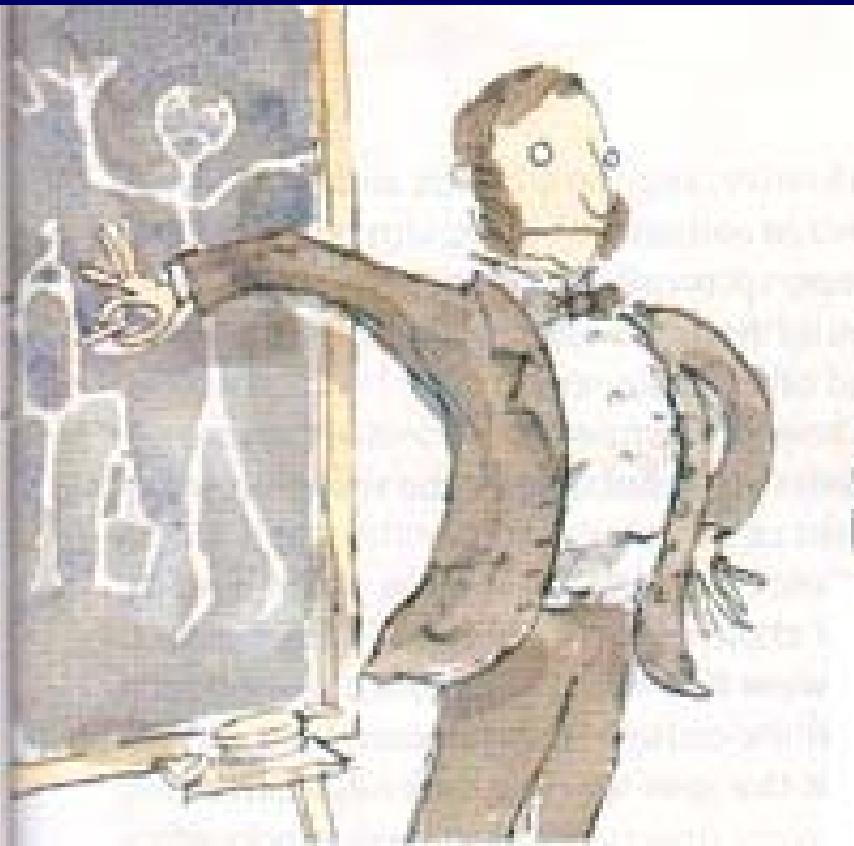
1884



Robert Koch (1843-1910)
German bacteriologist who
rediscovered, isolated, and
first cultured *Vibrio cholerae* –
the cholera-causing microbe
in early 1884.

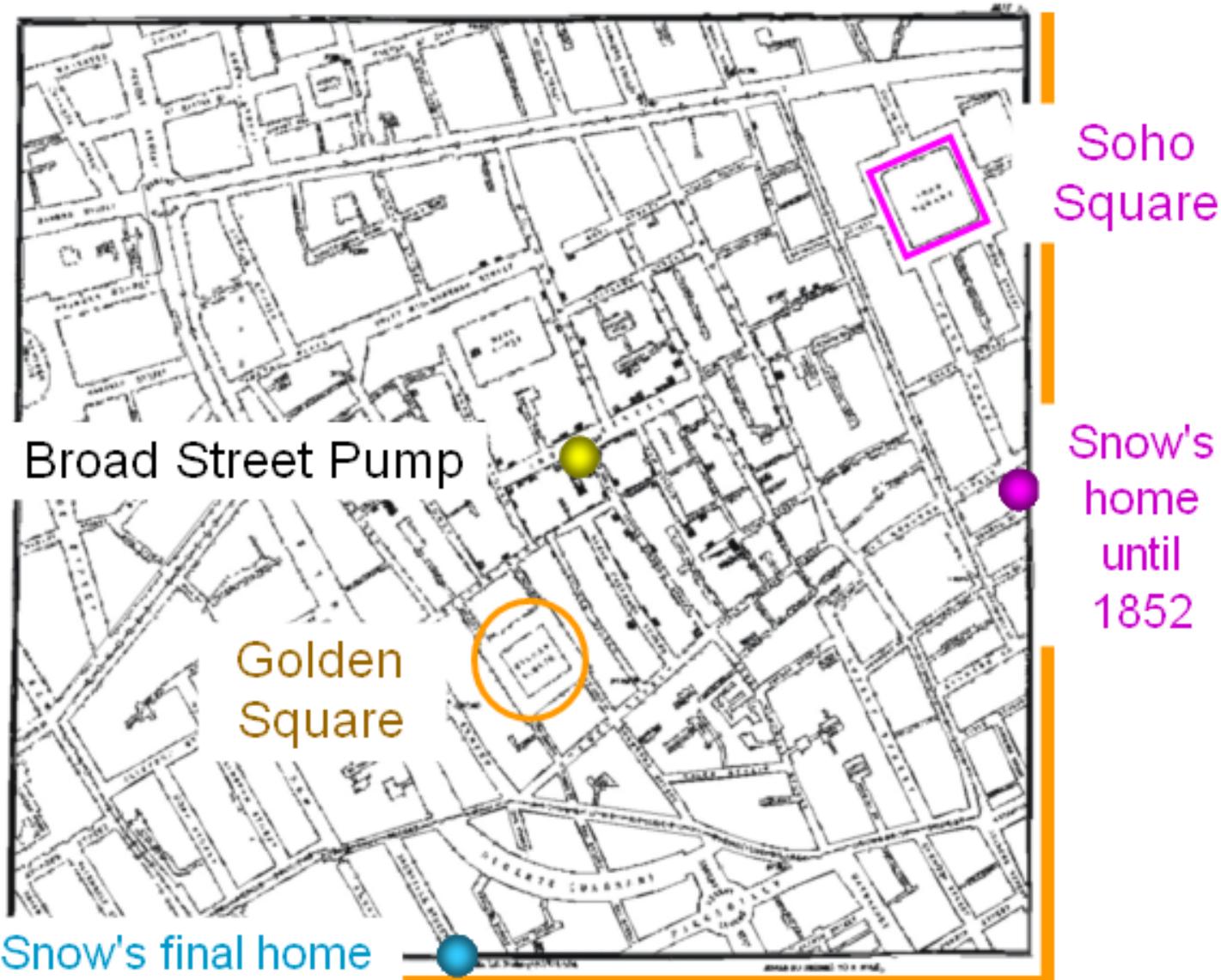
26 years after the death of John Snow

Snow was able to use careful logic and quantitative epidemiological methods to identify the germ origin of cholera, with no recognition during his lifetime of ***Vibrio cholerae***, the organism that causes cholera.



In 1849 Snow published a small pamphlet “On the Mode of Communication of Cholera” where he proposed that the “*Cholera Poison*” reproduced in the human body and was spread through the contamination of food or water.

C.F. Cheffins Map modified by Dr. John Snow 1850-54



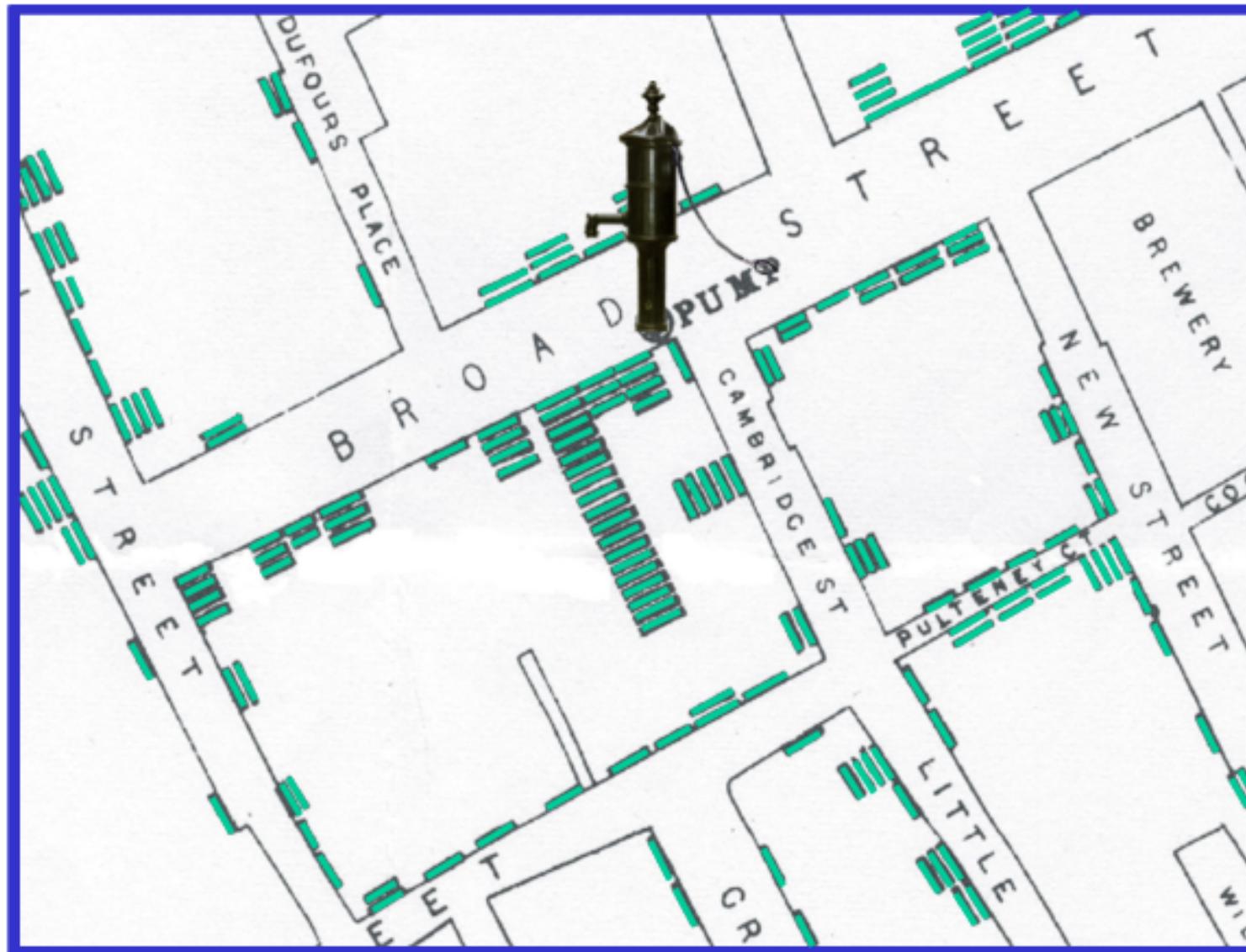
JOHN SNOW'S MAP

Broad Street
Pump Outbreak,
1854



A short line
to represent
each death
in the
household

Assembling Data

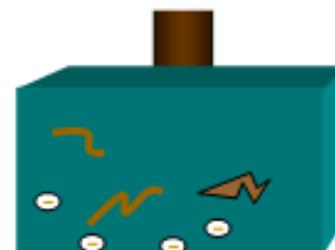


...a short
line to
represent
each death
in the
household



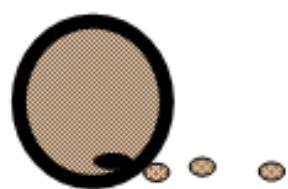
"... quantity of morbid matter which is sufficient to produce cholera is inconceivably small..."

"...shallow pump-wells in a town cannot be looked on with too much suspicion..."

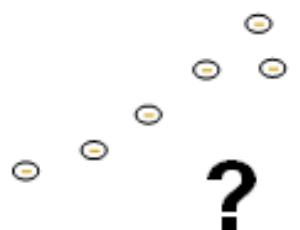


Cesspool

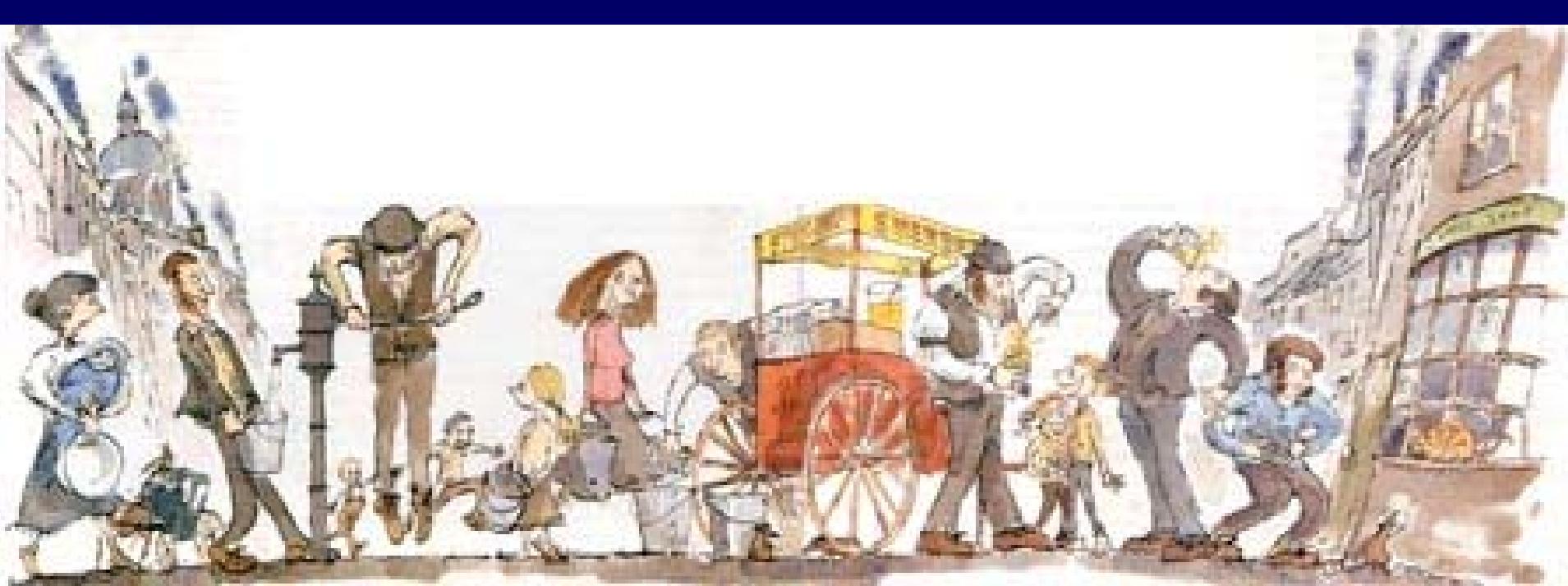
Sewer pipe



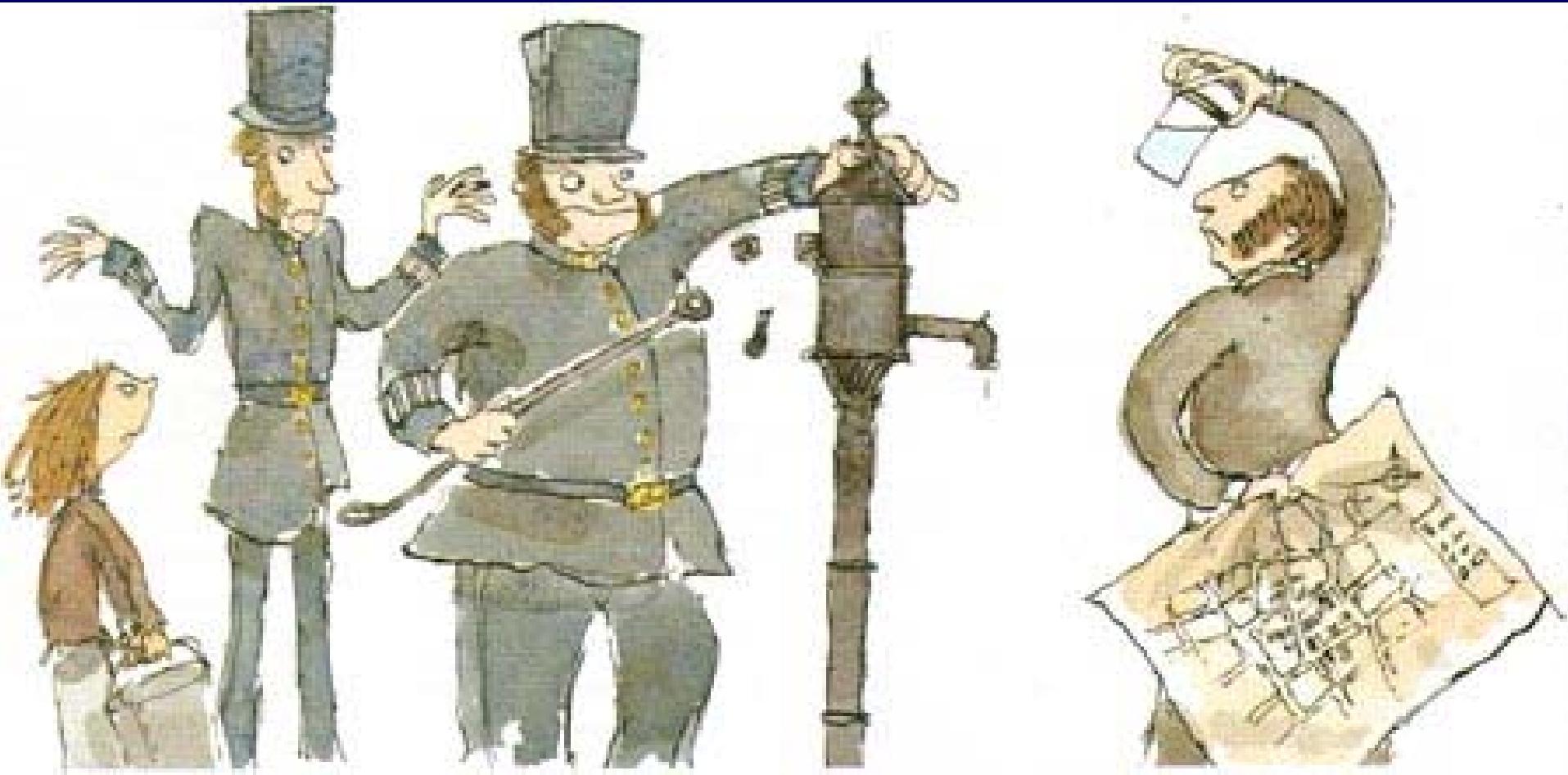
?



Possible cracks
and crevices

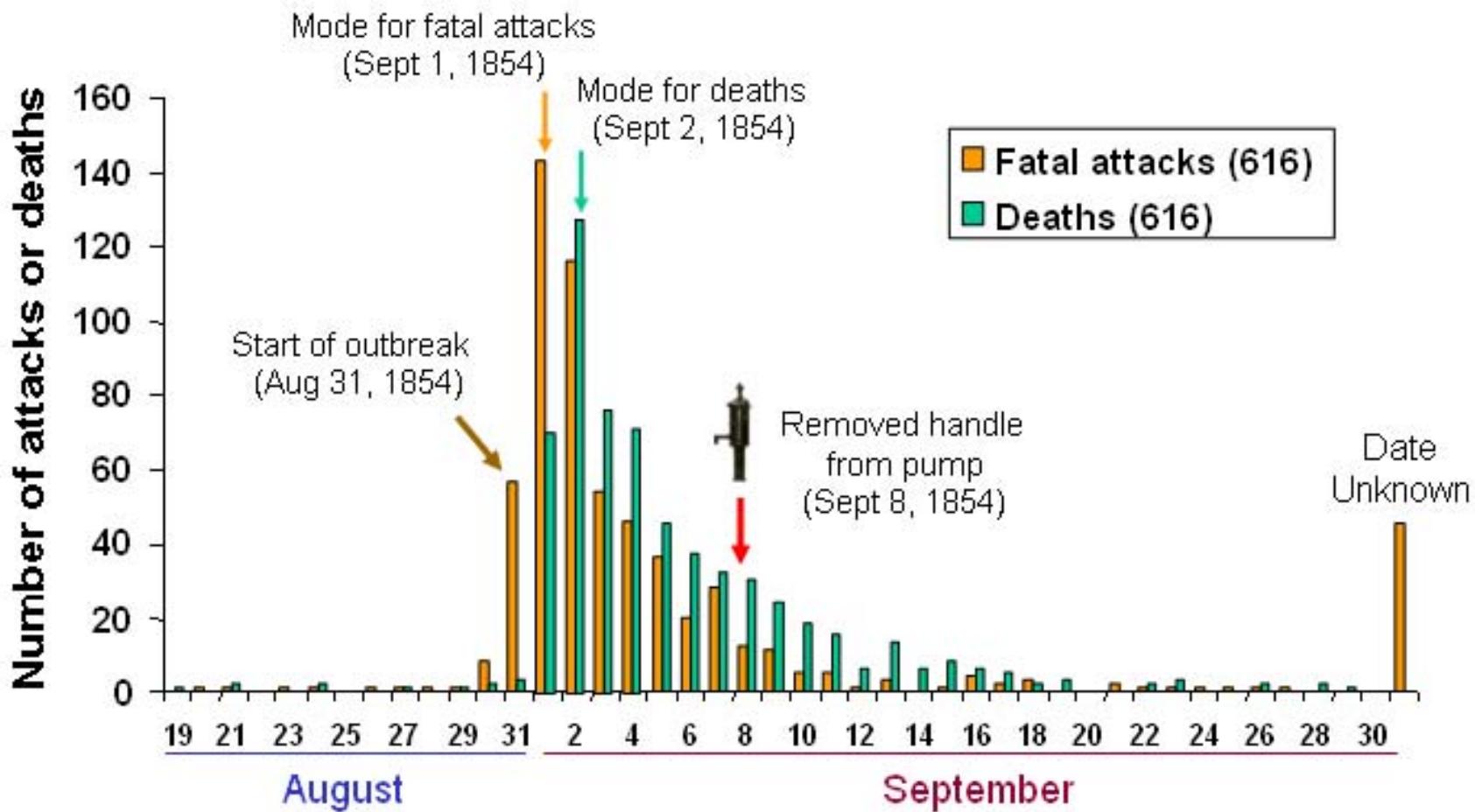


- Snow also investigated groups of **people who did not get cholera** and tracked down whether they drank pump water.
- That information was important because it helped Snow **rule out** other possible sources of the epidemic besides pump water.



On 7 September 1854, Snow took his research to the town officials and convinced them to take the handle off the pump, making it impossible to draw water. The officials were reluctant to believe him, but took the handle off as a trial only to find the outbreak of cholera almost immediately trickled to a stop. Little by little, people who had left their homes and businesses in the Broad Street area out of fear of getting cholera began to return. 84

The Complete Outbreak



John Snow and cholera in London

In 1883 a German physician, Robert Koch, took the search for the cause of cholera a step further when he isolated the bacterium *Vibrio cholerae*, the “poison” Snow contended caused cholera.

Dr. Koch determined that cholera is not contagious from person to person, but is spread only through unsanitary water or food supply sources, a major victory for Snow’s theory.

The cholera epidemics in Europe and the United States in the 19th century ended after cities finally improved water supply sanitation.

John Snow and cholera in London

Remember that in Snow's day the enterotoxic *Vibrio cholerae* was unknown .

Snow's conclusion that contaminated water was associated with cholera was entirely on observational data.

The point is that although it is extremely important for us to maximize our knowledge of the biology and pathogenesis of disease, it is not always necessary to know every detail of the pathogenic mechanism to be able to prevent a disease.

Today, scientists consider, Dr John Snow (1813-1858) , a surgeon [actually an anesthesiologist] to be the pioneer of public health research in a field known as epidemiology.



Broad Street
pump



Search PubMed

for |

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LinkOut

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Resources

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NLM Gateway

TOONET

□ 1: Bull Environ Contam Toxicol. 1995 Mar;54(3):337-41.

Related Articles, Links

Endemic fluorosis in China from ingestion of food immersed in hot spring water.**Xu RH, Yuan HH, Fan A.**

Department of Environmental Health, Health and Epidemic Prevention Station of Guangdong Province, Guangzhou, P. R. China.

PMID: 7749263 [PubMed]

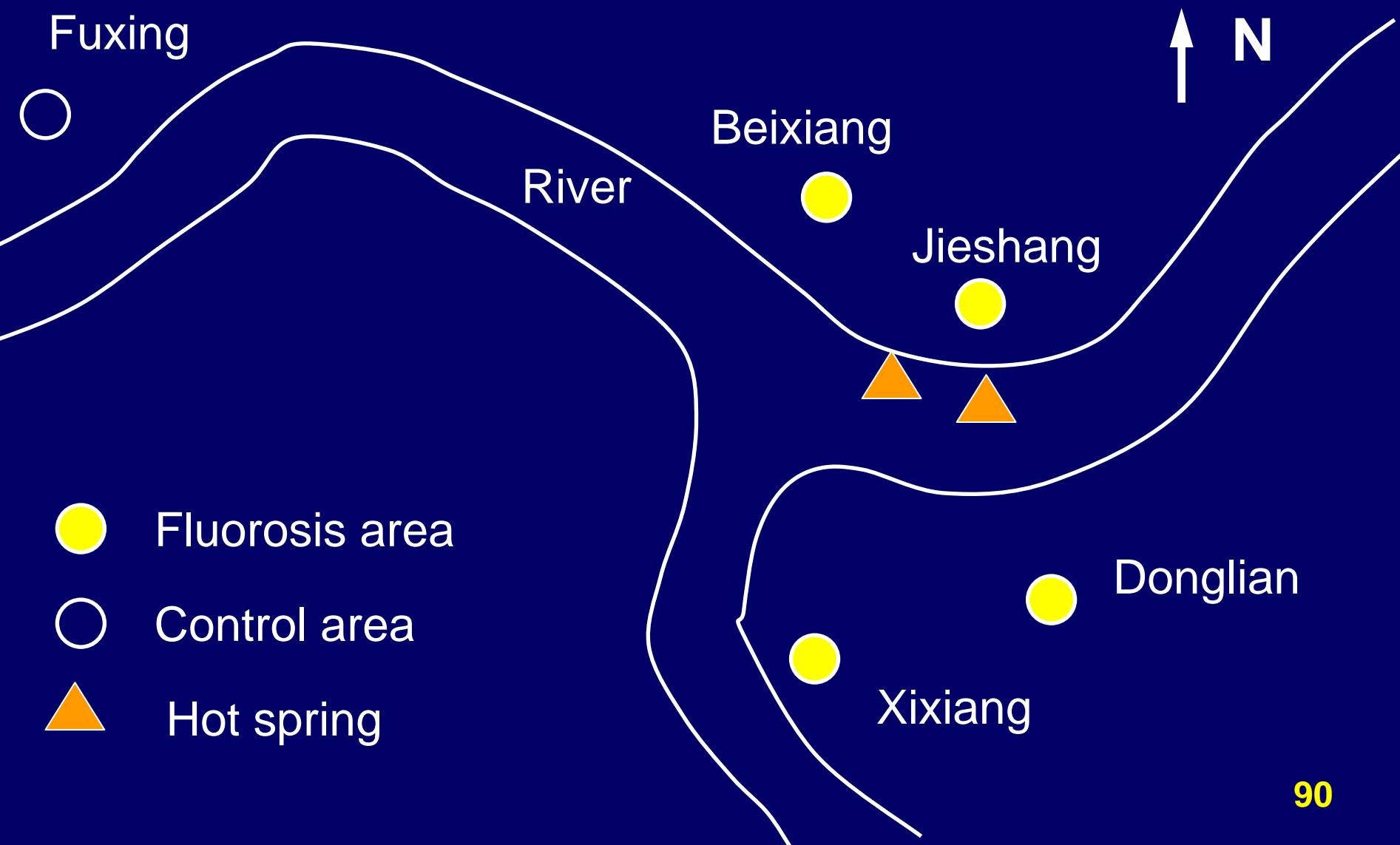
Display Abstract

Show: 20

Sort

Send to Text

Map showing the geographical location of fluorosis area, control area and two hot springs





Residents in the fluorosis villages habitually immerse vegetables in hot springs water ($>95^{\circ}\text{C}$)

Children dental fluorosis prevalence and urine fluoride content in five sites and distance between sites and hot spring

Residential Sites	Distance between Site and Hot Spring (M)	Dental Fluorosis			Urine	
		No. of Children	Positive	%	No. of Samples	Mean (F ⁻ , ppm)
Fluorosis Area						
JS	50	499	270	54.11	32	2.98
BX	500	67	33	49.25	35	2.17
DL	600	198	90	45.45	30	2.03
XX	800	73	30	41.10	32	1.31
Control						
FX	3000	283	3	0.01	58	0.67

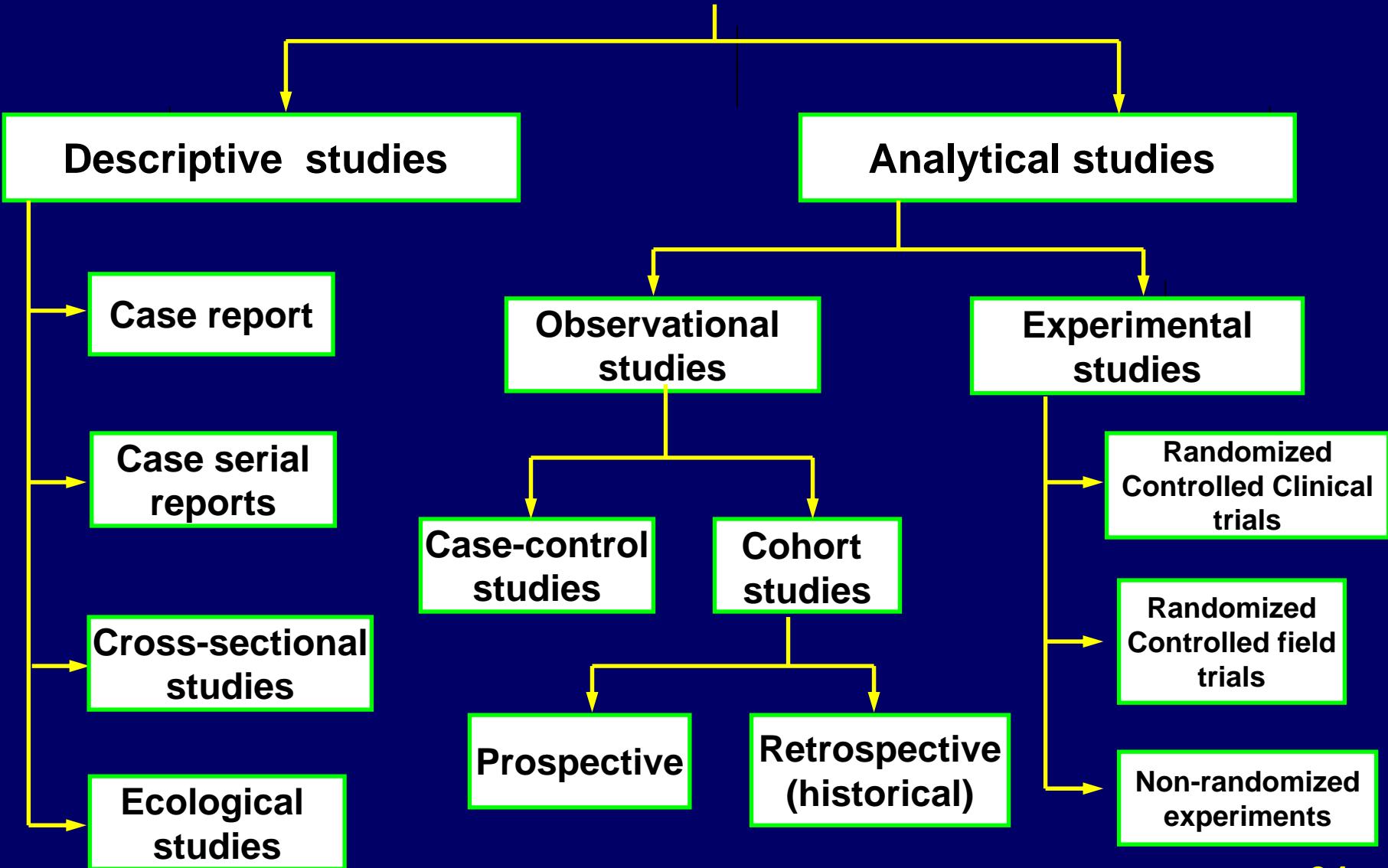
Endemic fluorosis in China from ingestion of food immersed in hot spring water
 Bull. Environ. Contam. Toxicol. (1995) 54:337-341

Fluoride content (ppm) in vegetables immersed in hot spring water and well water

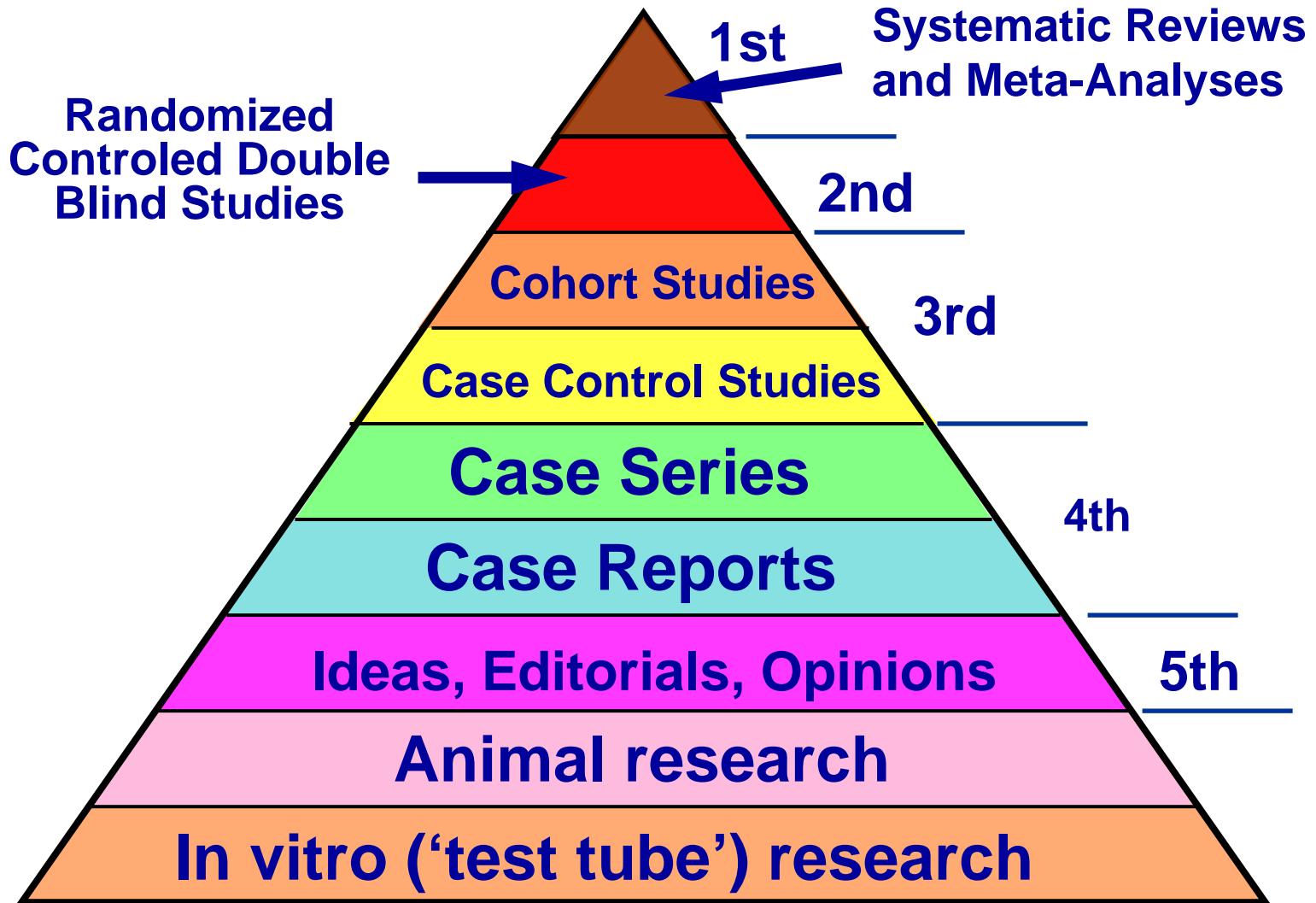
Vegetable	Immersion		
	Hot spring Water (F ⁻ , 20.33 ppm)	Well water (F ⁻ , 0.12 ppm)	H / W
I	147	2.53	58.1
II	151	9.53	15.8
III	115	8.17	14.1

Endemic fluorosis in China from ingestion of food immersed in hot spring water
Bull. Environ. Contam. Toxicol. (1995) 54:337-341

Study Design



The Evidence Pyramid



Clinical observations



Available data

Ecological or Cross-Sectional Studies



Case - control studies



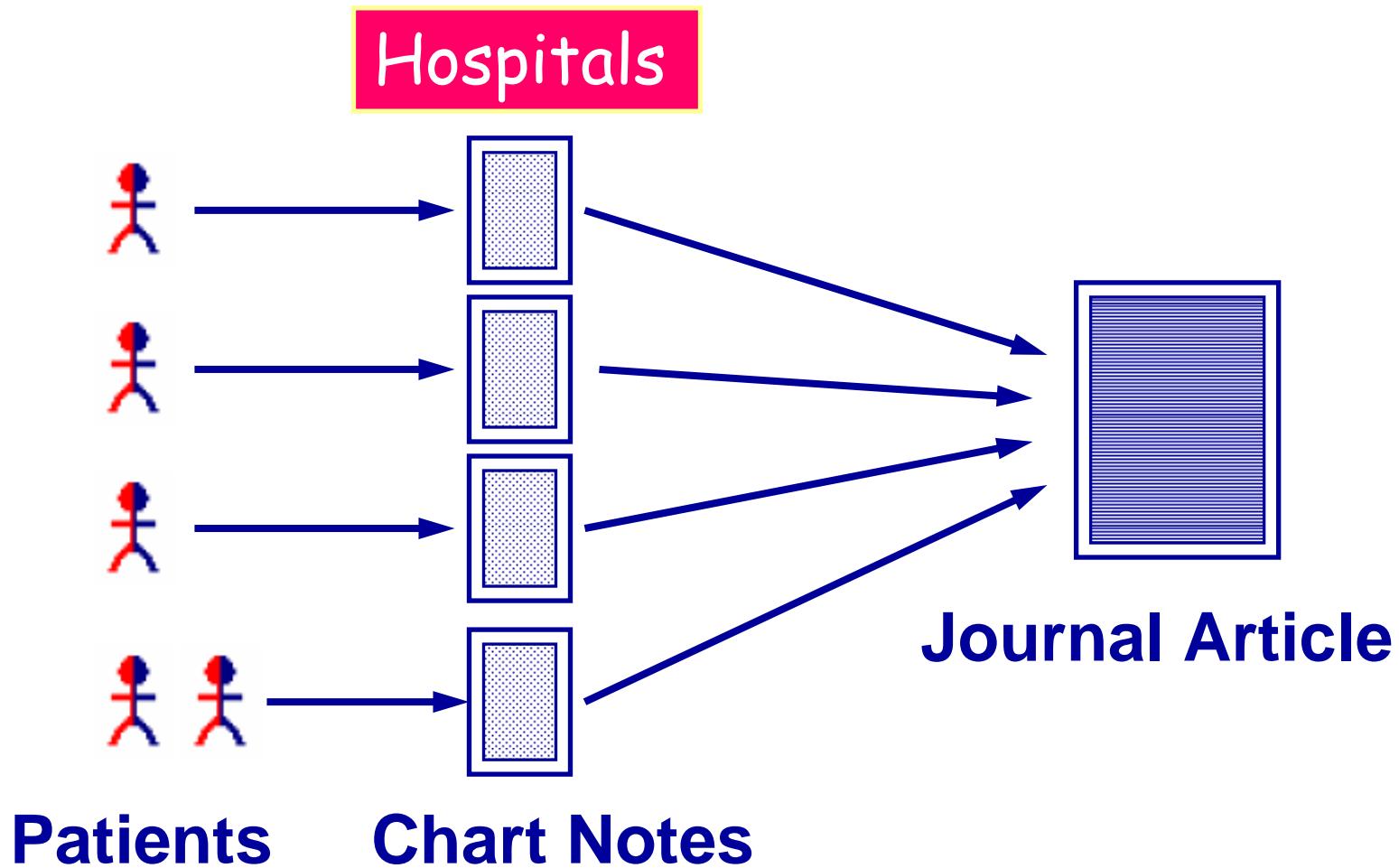
Cohort studies



Randomized trials

(only used for potentially beneficial treatments)

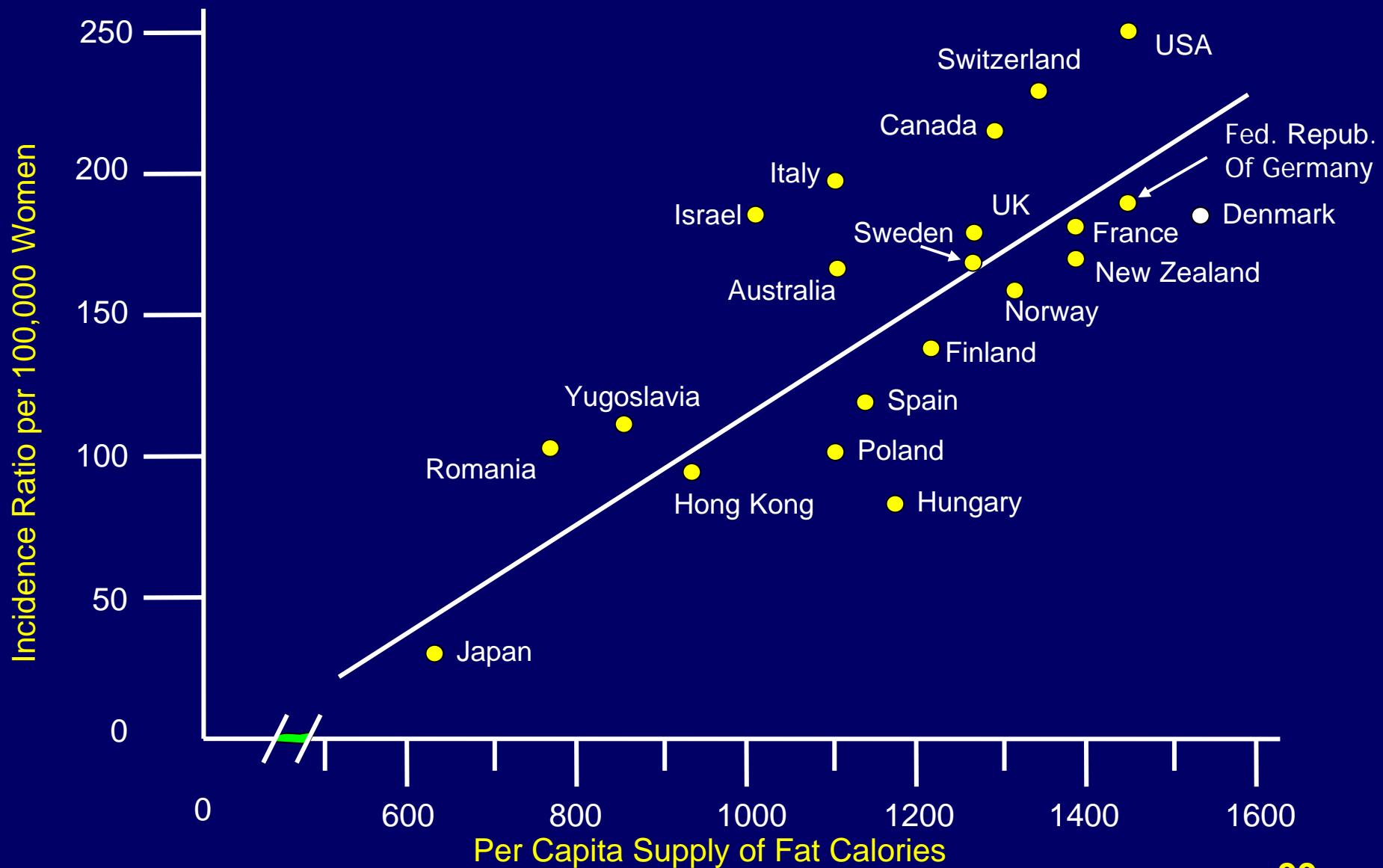
Case Series and Case Reports



Ecologic studies

- A study in which the units of analysis are populations or groups of people, rather than individuals.
- Usually takes advantage of pre-existing data collected for other purposes- an efficient and economical study design
- No time element- a “snapshot” of populations- think cross-sectional studies of populations, not individual

Correlation between dietary fat intake and breast cancer by country



Study Without Comparison

A very important Boston surgeon visited the school and delivered a great treatise on a large number of patients who had undergone successful operation for vascular reconstruction.

At the end of the lecture

Student : Do you have any controls ?

Surgeon : Do you mean did I not operate on half of the patients ?

Student : Yes, that's what I had in mind.

Surgeon : Of course not. That would have doomed half of them to their death.

Student : Which half ?

Simultaneous Nonrandomized Control

- A sea captain was given samples of anti-nausea pills to test during a voyage.
- The need for controls was carefully explained to him.

Upon return to the ship, the captain reported the results enthusiastically.

“Practically every one of the controls was ill, and not one of the subjects had any trouble. Really wonderful.”

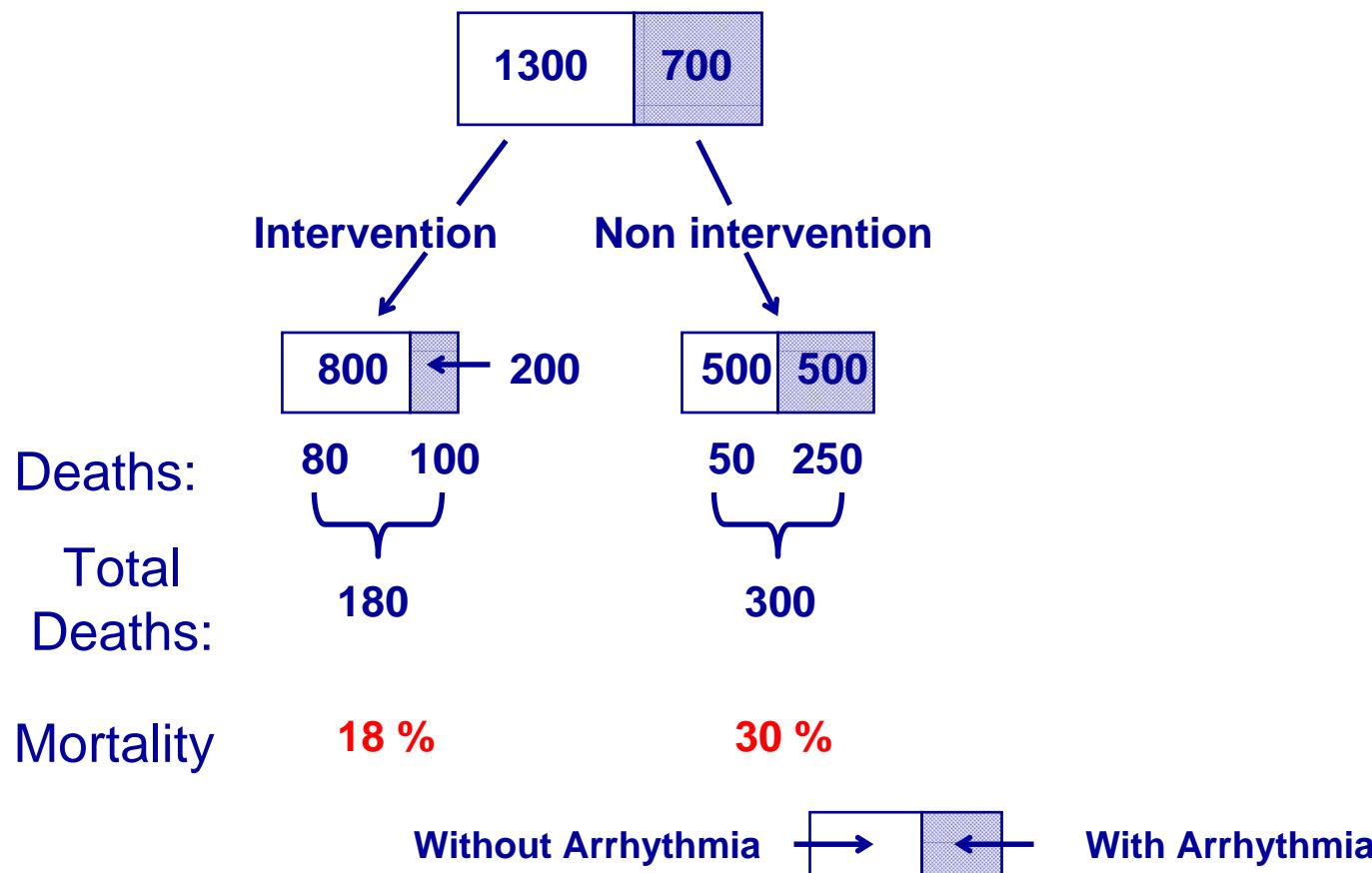
A skeptic asked how he had chosen the controls and the subjects.

“Oh, I gave the stuff to my seamen and used the passengers as controls”

Randomzation

1. Observational Study

n=2,000 Myocardial infarction

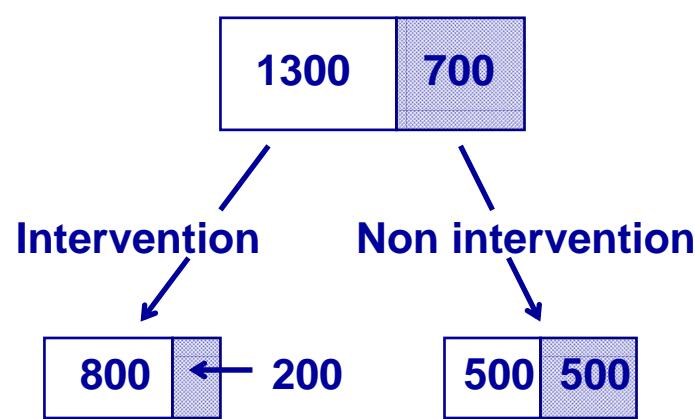


Randomization

1. Observational Study

n=2,000

Myocardial infarction



Deaths:

80 100

50 250

80
100
180

50
250
300

Total Deaths:

Mortality

18 %

30 %

24 %

24 %

Randomization

- Randomization increases the likelihood that the groups will be comparable
- not only in terms of variables that we recognize and can measure
- but also in terms of variables that we may not recognize and may not be able to measure but nevertheless may affect prognosis.

Analytic Studies

- Case control studies
- Cohort studies
 - Prospective cohort study
 - Concurrent cohort study
 - Historical cohort study
 - Retrospective cohort study
 - Ambispective cohort study
- Intervention studies
- Clinical trials

Case control studies

- Evaluation of risk factors
- Case control studies compare a group of people with a disease or condition to another group of people without it.

The Doll and Hill (1950) study of cigarette smoking and cancer in Britain is a classic example, And is credited with starting our current series of efforts to control tobacco use.

Case control studies

- Persons with a specified condition (the **cases**) and persons without the condition (the **controls**) are selected for study.
- The proportion of cases and controls with certain characteristics or **exposure** is then **measured** and compared.
- **Comparison** is an **essential component** of epidemiologic investigation and is well exemplified by the case-control study design.

For example, knowing that there are **10 school children with purple spots** in grade 3, a set of other third grade children from the same school but **without purple spots** would be identified **as controls**, and **analysis** done to see **what different exposures** the purple-spotted children had than the non-spotted.

Case control studies

At the beginning of the case control study

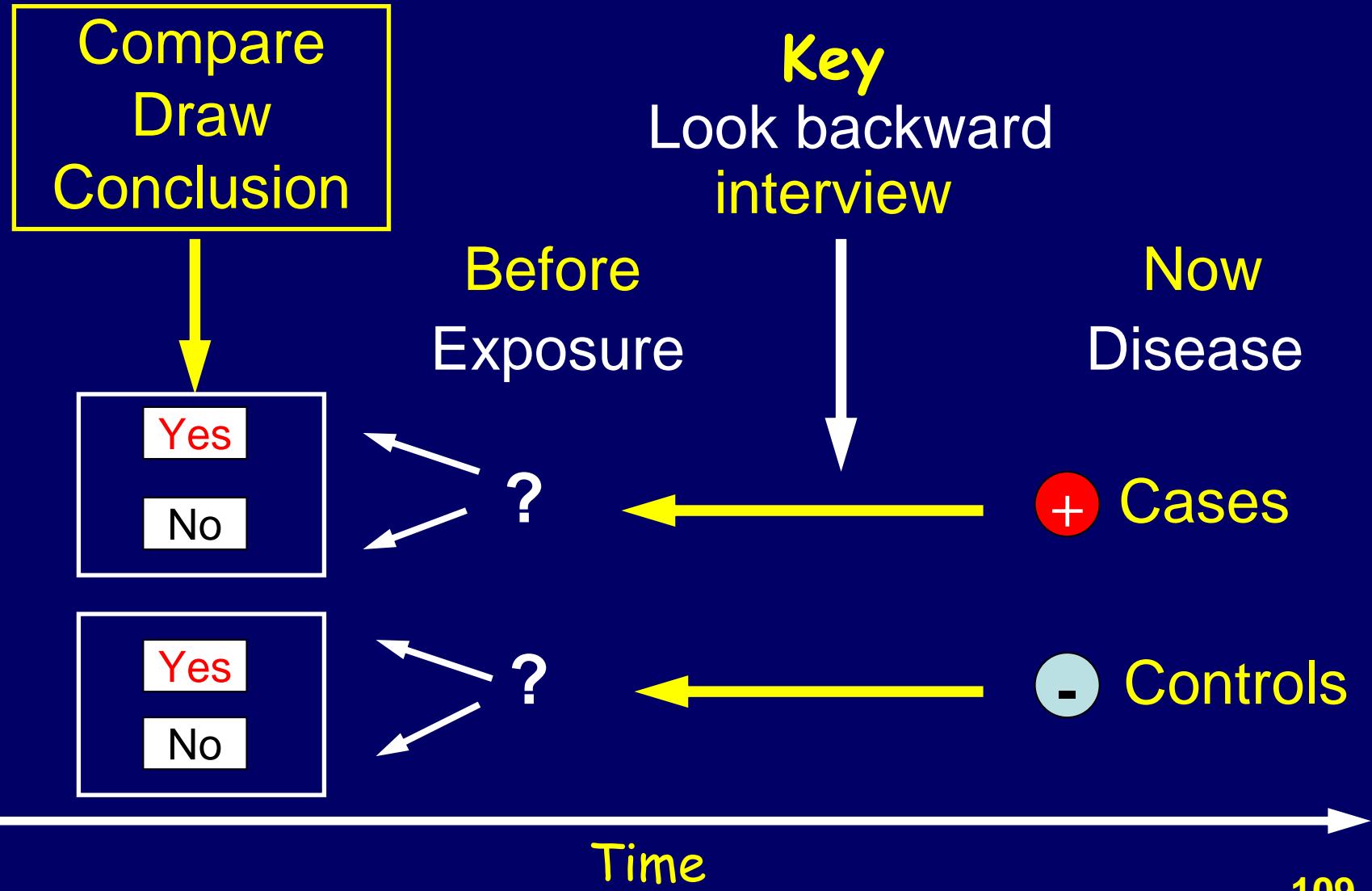
The investigator knows that there are some people with a disease(**cases**);

they are matched with similar individuals (**controls**) who do not have the disease.

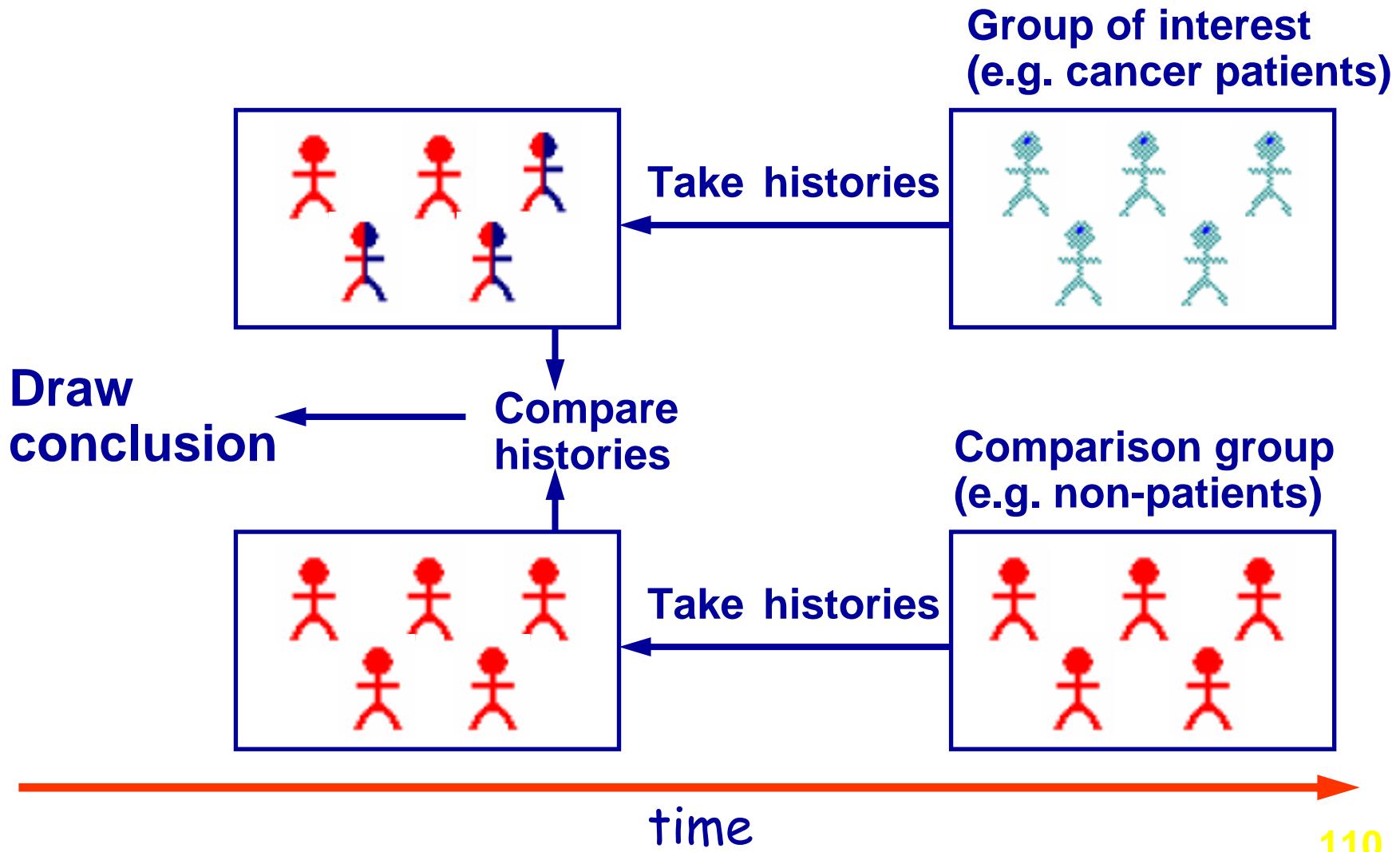
The investigator **looks backward** to identify what different exposures the two groups might have had.

For example, when some individuals attending a picnic become ill, they could be matched with controls who also attended the picnic but did not become ill, and all interviewed about what was eaten, to identify a possible source of food-borne illness.

Case control studies



Case Control Studies



Cohort studies

Long term population studies

In cohort studies, subjects are categorized on a predetermined basis and followed over time for the development of health conditions.

One well-known example is the Framingham Heart Study in which 5200 residents were followed over 35 years. Findings of this study have been used to develop improved cardiovascular disease prevention methods.

Cohort studies

- Groups of individuals with some common feature (age and geography, for example) are identified for study over time to learn about differing health and illness experiences.
- Comparison of outcome(s) in an exposed group and a non-exposed group (or with / without a certain characteristic) is the hallmark of the cohort design

For example, one might enroll in a study all third graders in a school and follow them until graduation, attempting to identify the differences in experiences of those who maintained a body weight close to recommended and those who did not.

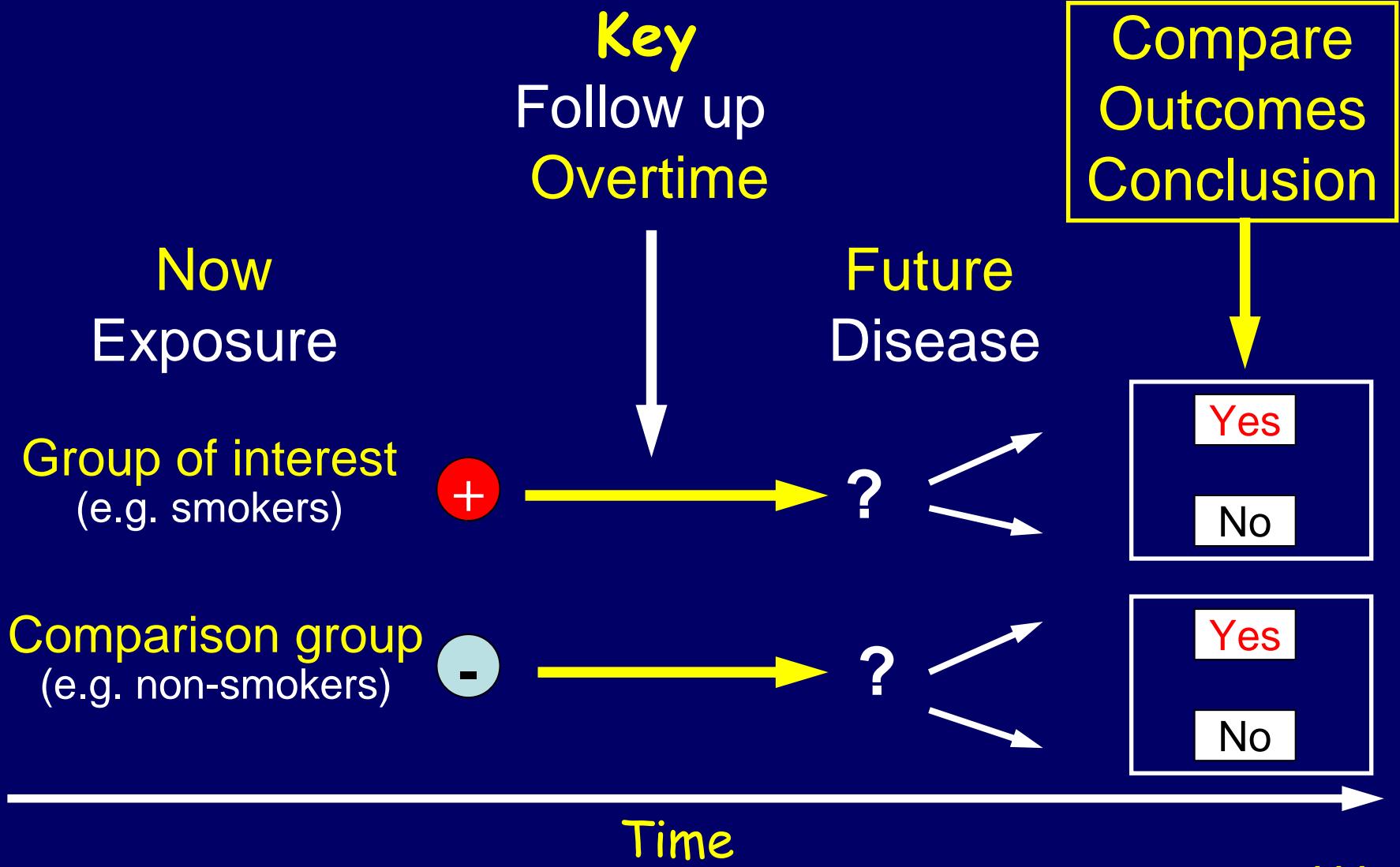
Cohort studies

- At the beginning of a prospective cohort study the investigator is aware of a group of individuals, some of whom have been exposed to a hazard.
- All members of the cohort will be followed over time to see if those exposed and those unexposed have different disease experiences.

For example, a public health department may be informed of the exposure of a portion of a school class to an individual with an active case of a communicable disease in the course of a field trip.

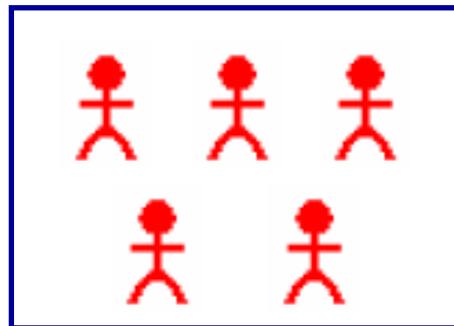
The entire class (the cohort) would be observed over time to identify any cases of disease that arise, and any difference in disease rate between the two groups

Cohort studies

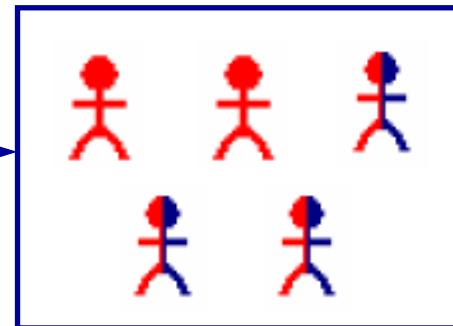


Prospective Cohort Studies

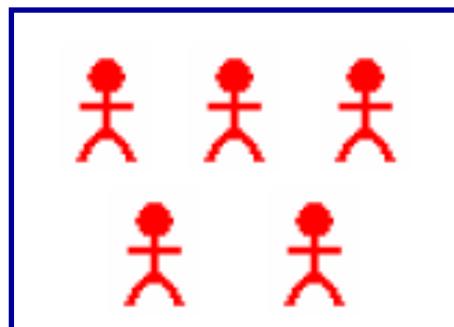
Group of interest
(e.g. smokers)



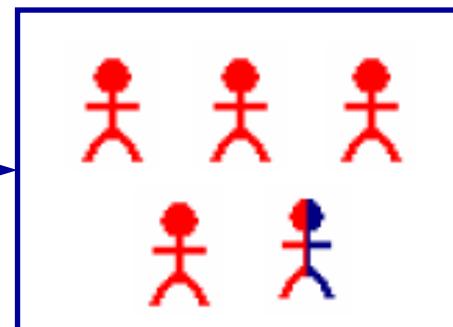
Follow
over time



Comparison group
(e.g. non-smokers)



Follow
over time



Compare
outcomes

time

Retrospective cohort study

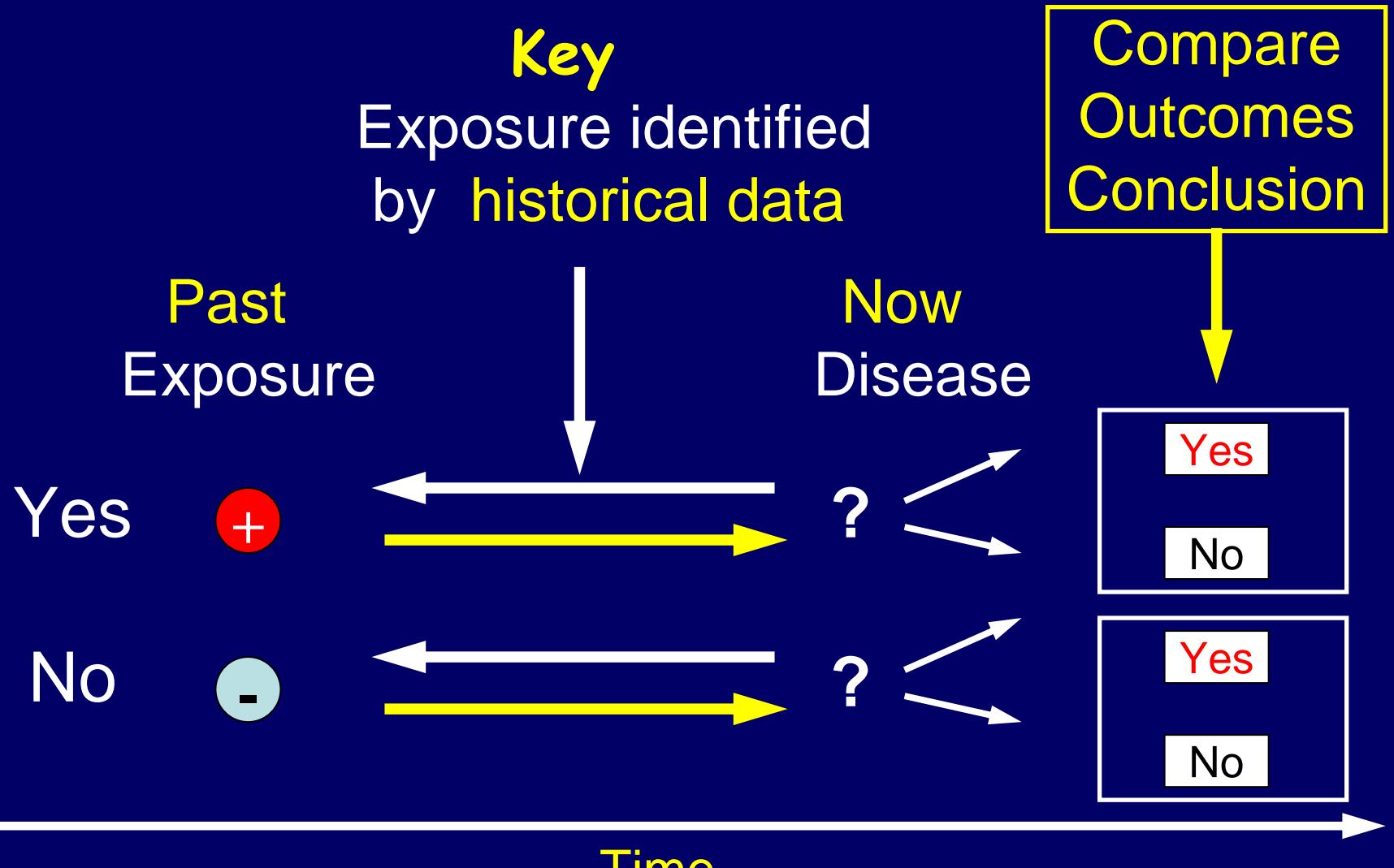
At the beginning of a retrospective cohort study

the investigator is aware of an **exposure** to a hazard that occurred at some time in the past, sufficiently long ago that if **disease** were to have occurred, it should by now be evident.

A cohort that includes the **exposed individuals** is identified, and the health histories of all members explored to **identify** the presence or absence of disease in all individuals, and the **difference in rate** between exposed and non-exposed.

Many of the studies of association between **environmental exposures and disease** have been of this type. A cohort of individuals who lived or worked in an area but had **different experiences of exposure/non-exposure** to a chemical will be identified. Their **health histories** in the intervening years will be **examined to identify differences**, if any, in their rates of disease.

Retrospective cohort study

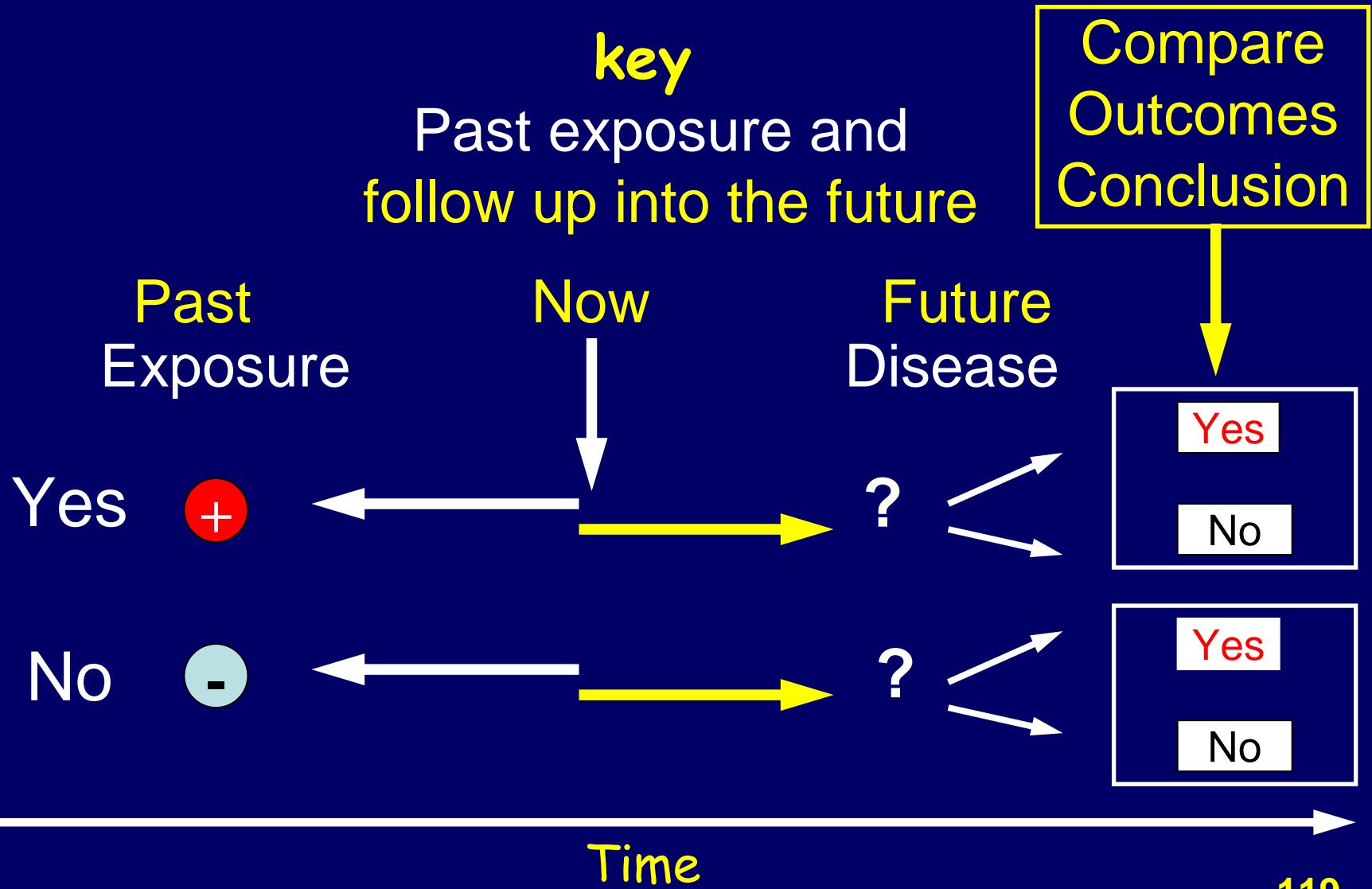


Ambispective cohort study

Combination of concurrent cohort and retrospective cohort designs

Exposure is ascertained from objective records **in the past** (as in a historical cohort study), and follow-up and measurement of outcome continue **into the future**

Ambispective cohort study



Past

Now

Future

Case Control Studies



Prospective cohort study



Retrospective cohort study



Ambispective cohort study



Time

Clinical trials

To evaluate interventions

Clinical trials in humans are conducted to determine whether methods found effective in laboratory conditions can be safely applied to a large population under normal conditions to demonstrate its application to the control of disease.

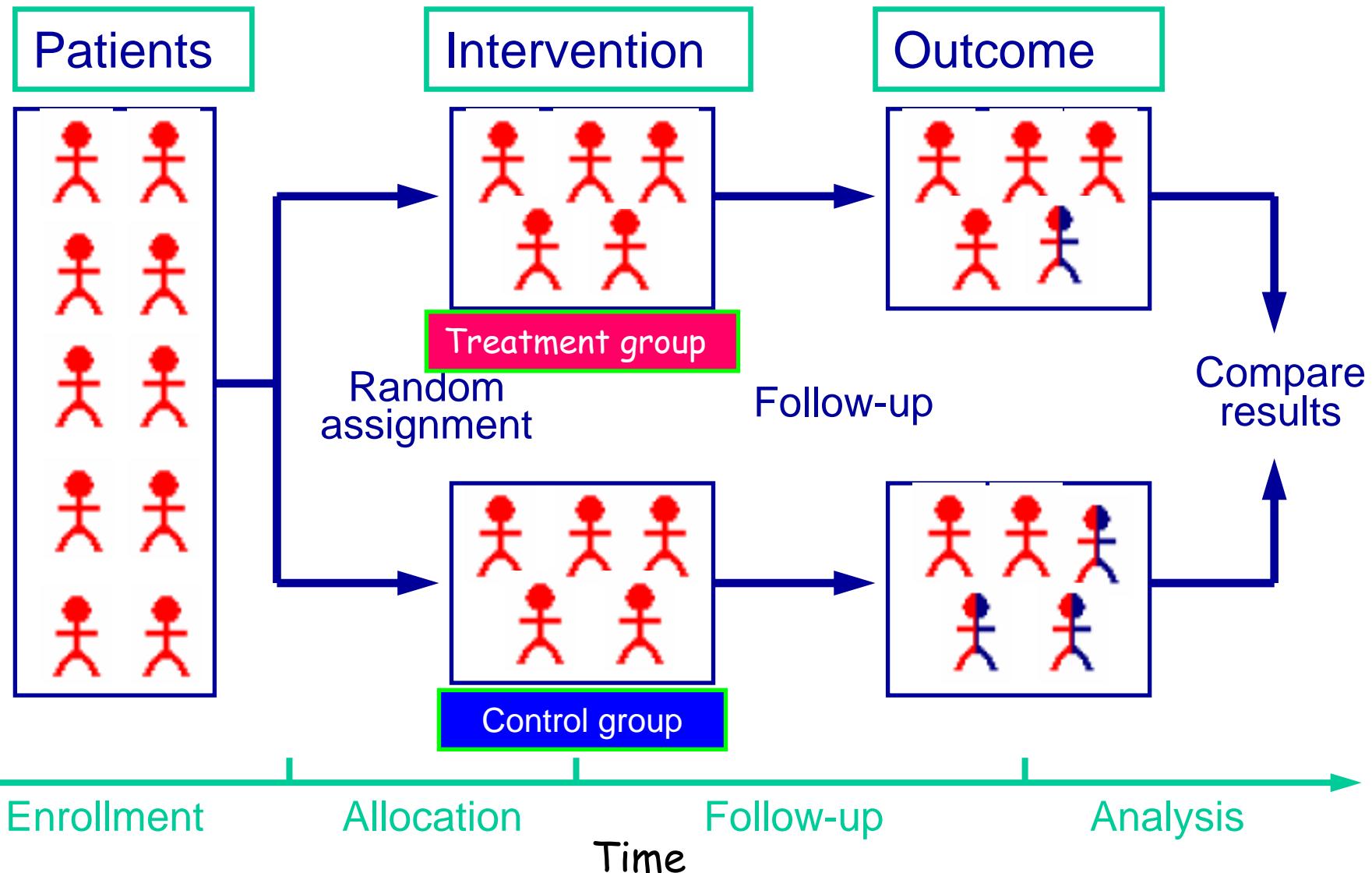
Randomized control blind trial

RCT Randomized control trial
Randomized clinic trial

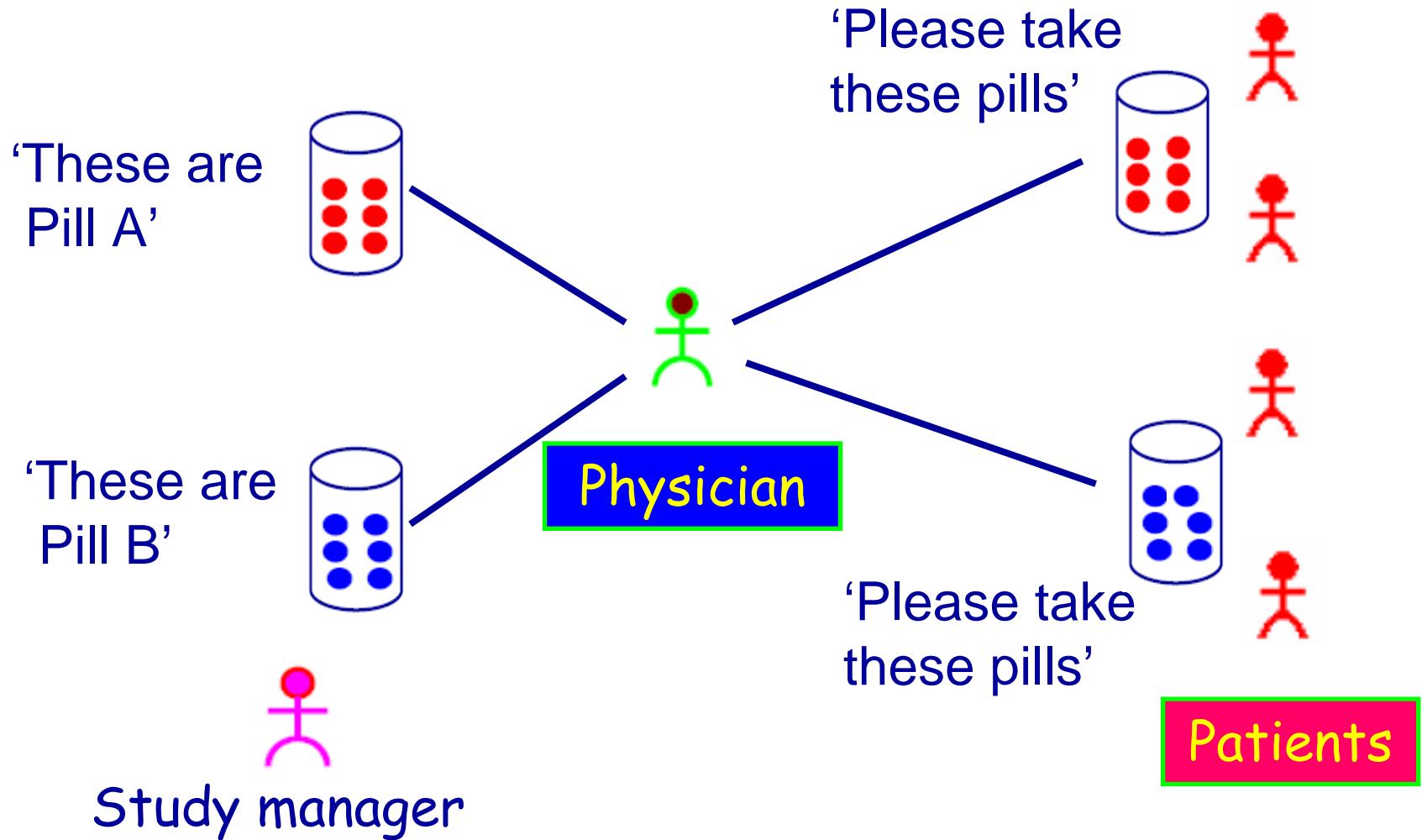
RCT is the **gold standard** for evaluating efficacy of therapeutic, preventive, and other **measures**, both in **clinical medicine** and public health.

the **most ideal design** for evaluating efficacy and side effect of new intervention measure

Randomized Controlled Studies



The Double Blind Method



Interpreting Results

Measurement Errors

- Bias
 - information
 - selection
- Confounding
 - extraneous factors
- Effect modification
 - statistical interaction

Paper/Article Format

Title

Authors Contributors Institute / agency

Abstract / Summary

Key words

I M R A D

Introduction

Material and Methods

Results and

Discussion

Acknowledgments

References

4. Disease / Public health surveillance

Influenza surveillance

Definition of Surveillance

- The **ongoing systematic** collection, collation, analysis and interpretation of data and
- The **dissemination** of information to those who need to know in order that **action** may be taken.

Disease / Public health surveillance

Public health surveillance
is the ongoing,
systematic collection,
analysis, interpretation,
and dissemination of data
about a health-related event
for use in public health action to reduce
morbidity and mortality and to improve health

MMWR 2004;53:RR-5

Surveillance serves at least eight public health functions

1. Supporting case detection and public health interventions,
2. Estimating the impact of a disease or injury,
3. Portraying the natural history of a health condition,
4. Determining the distribution and spread of illness,
5. Generating hypotheses and stimulating research,
6. Evaluating prevention and control measures,
7. Facilitating planning,
8. Outbreak detection , (i.e., identifying an increase in frequency of disease above the background occurrence of the disease).

Purposes of Public Health Surveillance

1. Assess public health status
2. Define public health priorities
3. Evaluate programs
4. Stimulate research

Uses of Public Health Surveillance

1. Detect epidemics / define a problem
2. Determine geographic distribution of illness
3. Portray the natural history of a disease
4. Estimate magnitude of the problem
5. Generate hypotheses, stimulate research
6. Monitor changes in infectious agents
7. Detect changes in health practices
8. Facilitate planning
10. Evaluate control measures

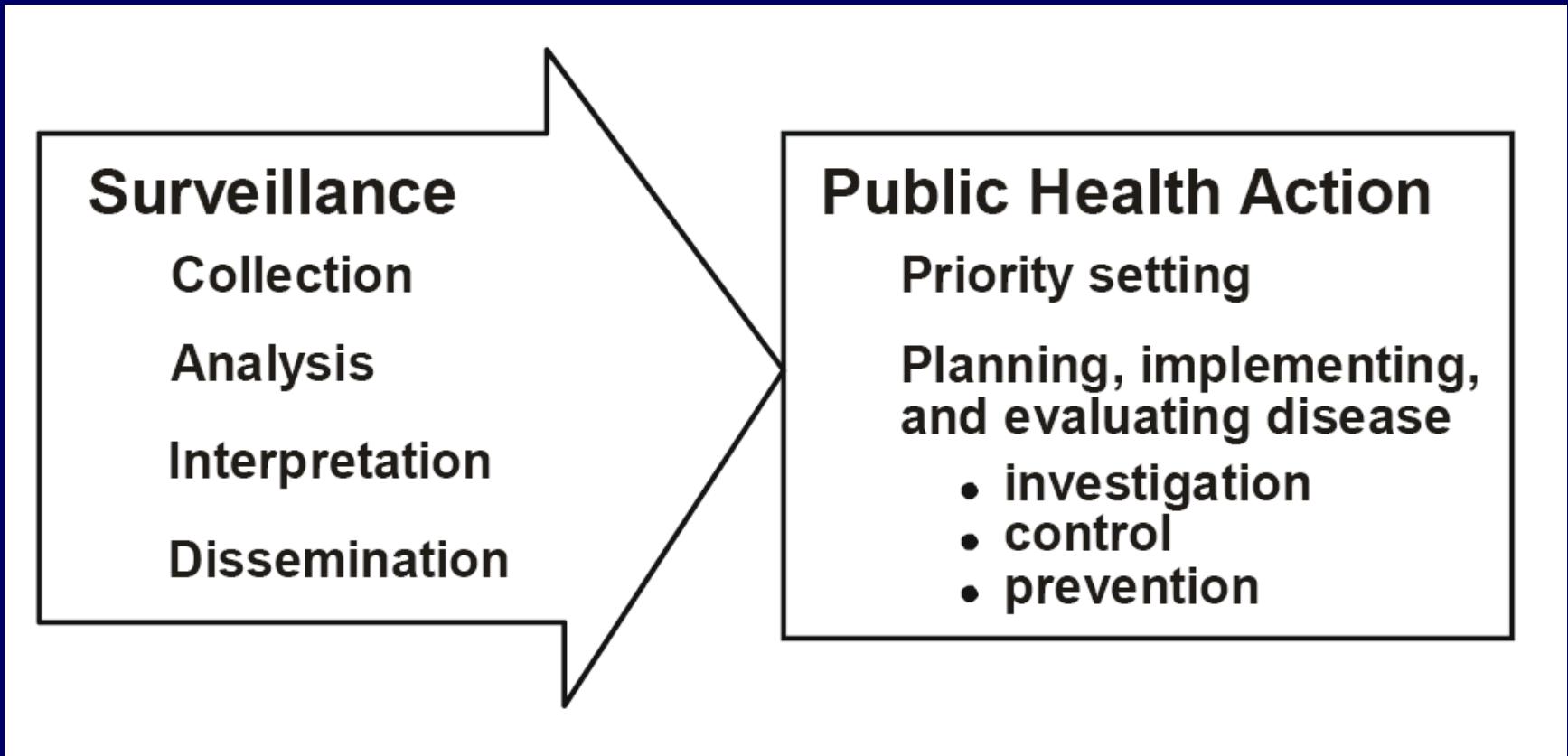
Objectives of surveillance

1. Monitoring **trends** and estimate **magnitude** of health problem
2. Epidemic (outbreak) **detection** and **prediction**
3. Monitor **progress** towards a control objective
4. Monitor programme **performance**
5. **Evaluating** an intervention
6. Forecast **future** disease **impact**
7. **Understand** characteristics of health events
 - Distribution and spread
 - Natural history
8. Facilitate **planning**

Components of an effective surveillance system

1. Clear objectives
2. Well-defined health event(s)
with clear widely-known case definitions
3. Data sources
4. Laboratory support
5. Established data collection and reporting mechanism
6. Regular data analysis and interpretation
7. Rapid response mechanism
8. Feedback and dissemination of information
9. Monitoring and Evaluation

The components of surveillance and resulting public health action



The goal of surveillance is not merely to collect data for analysis, but to guide public health policy and action.

Sources of Surveillance Data

1. Reports of health events affecting individuals
2. Vital statistics on the entire population
3. Reporting from laboratories
4. Registries
5. Vital statistics
6. Information on the health status, risk behaviors, and experiences of populations
7. Information on potential exposure to environmental agents
8. Information on existing public health programs
9. Information on the health care system
10. Information from other organizations

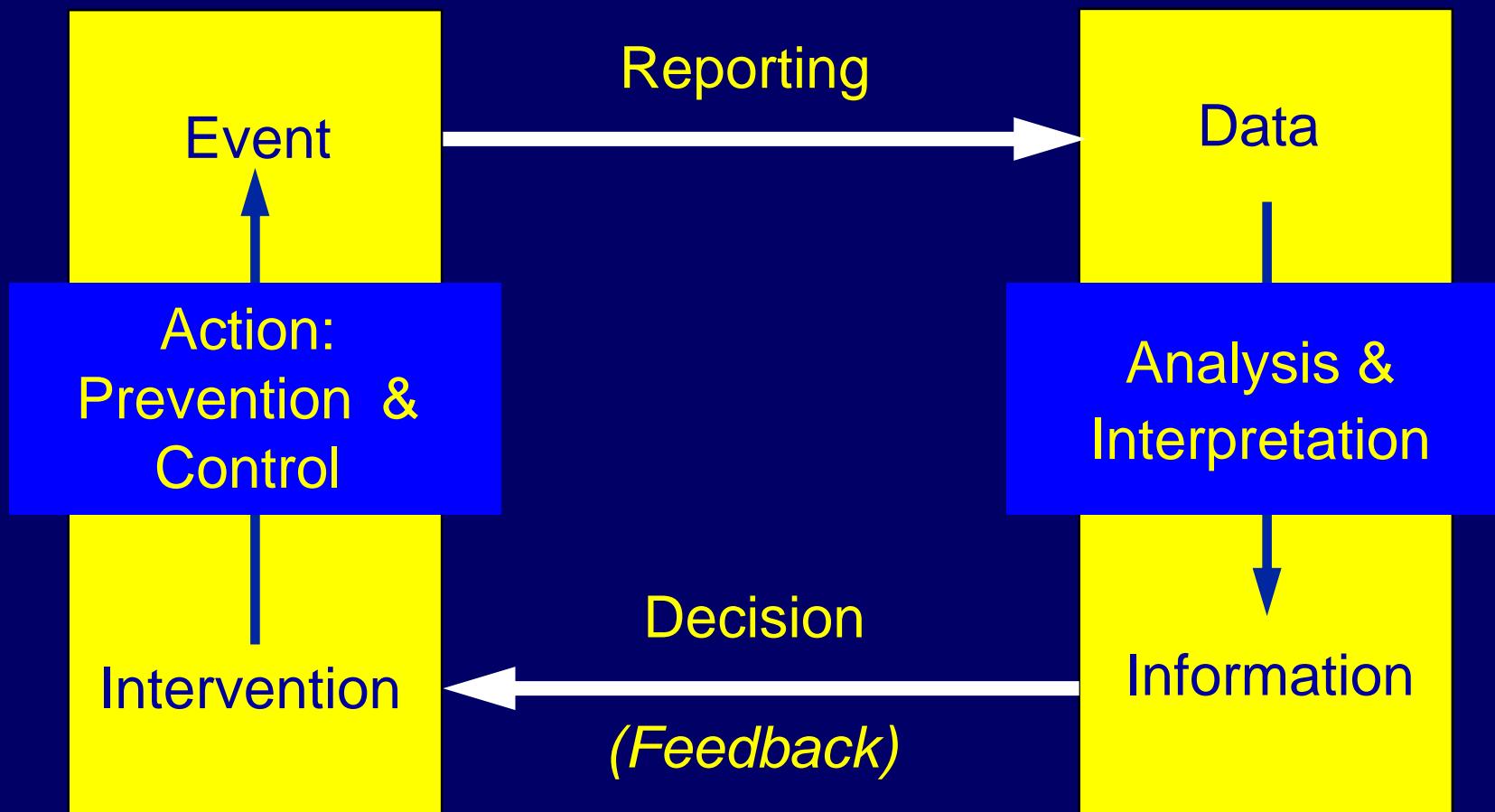
Community Screening Programs

1. Defining the target population
2. Setting priorities among diseases and conditions
3. Choosing effective screening tests
4. Assessing the effectiveness of screening programs

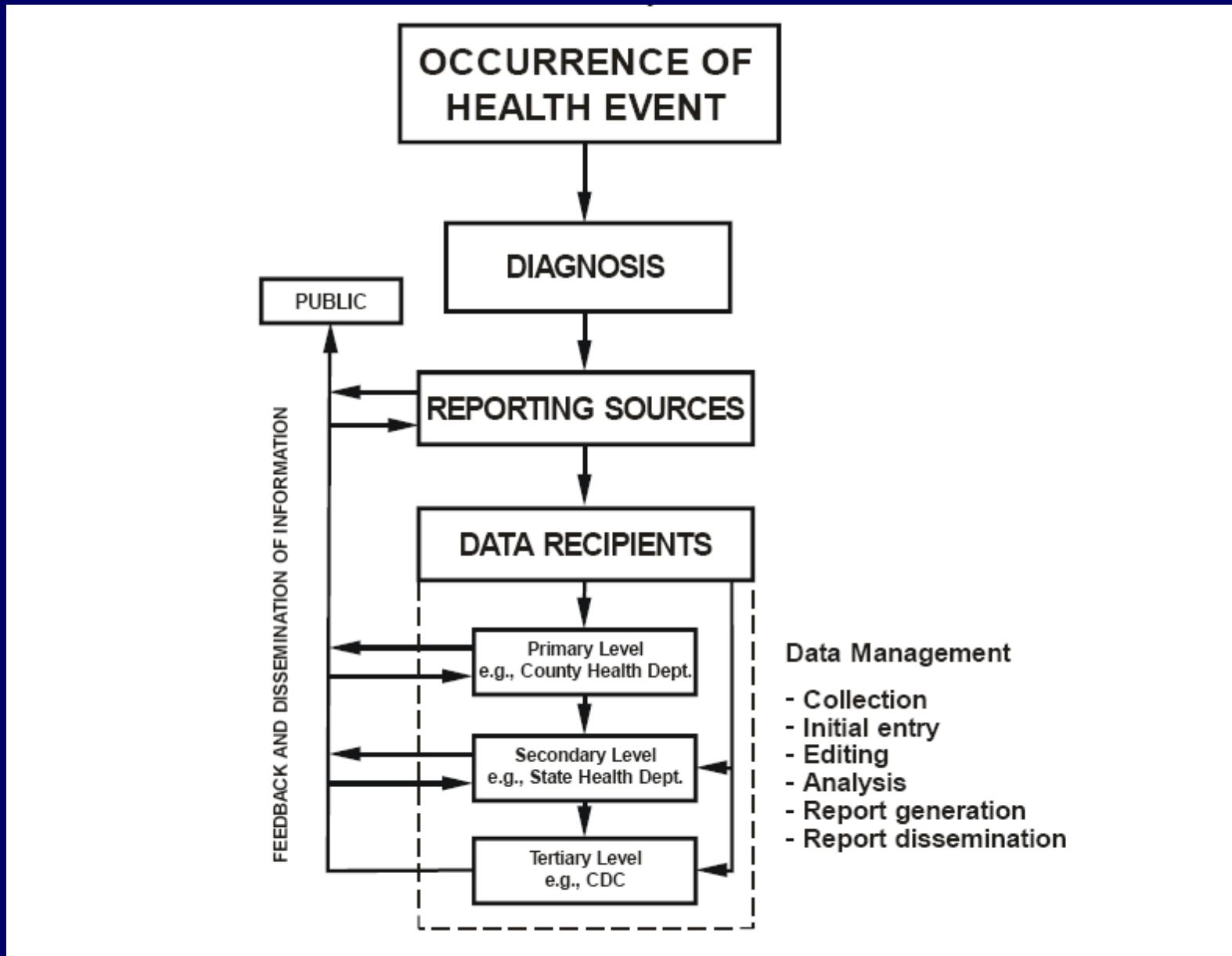
Surveillance Cycle

Health Care System

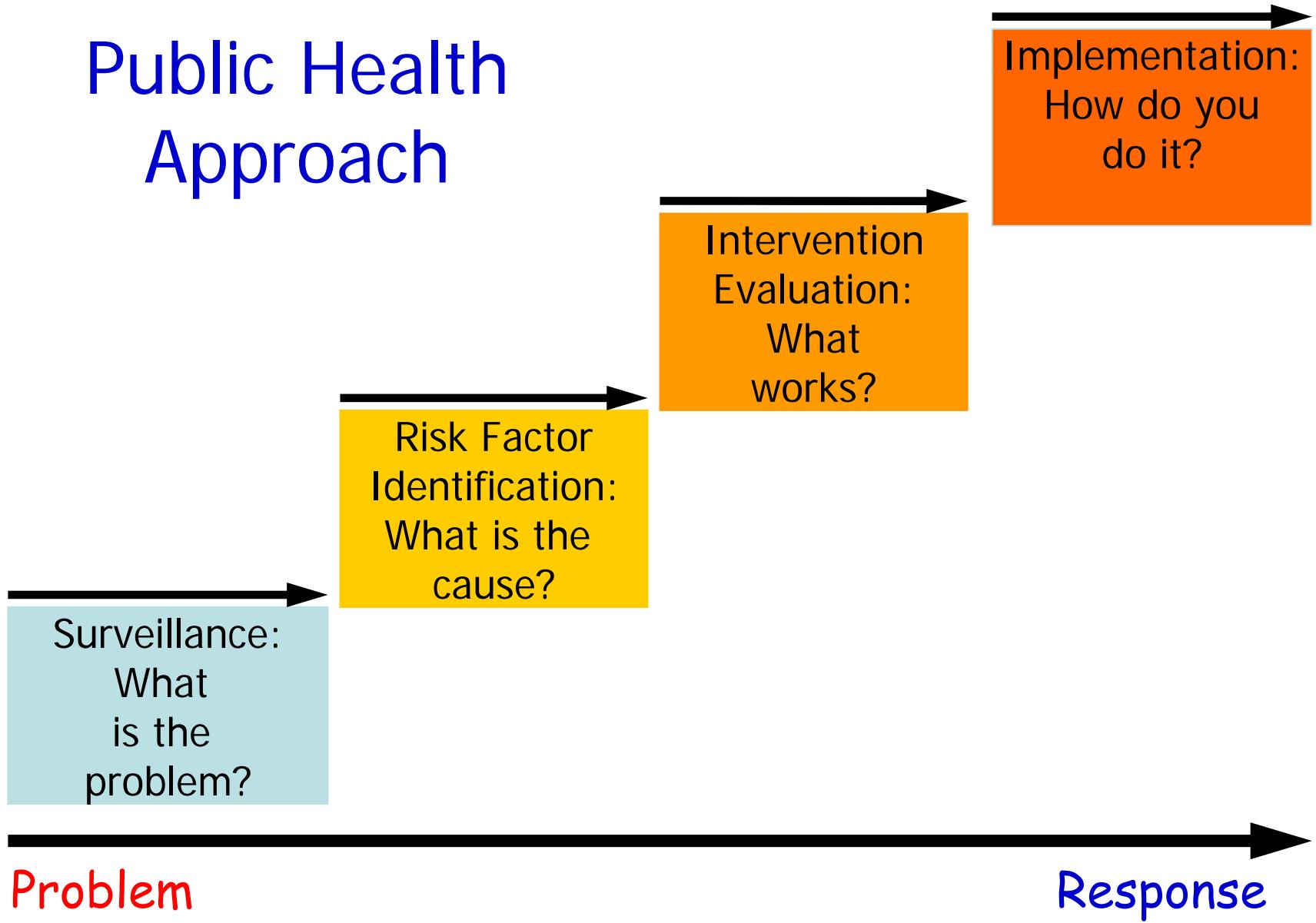
Public Health Authority



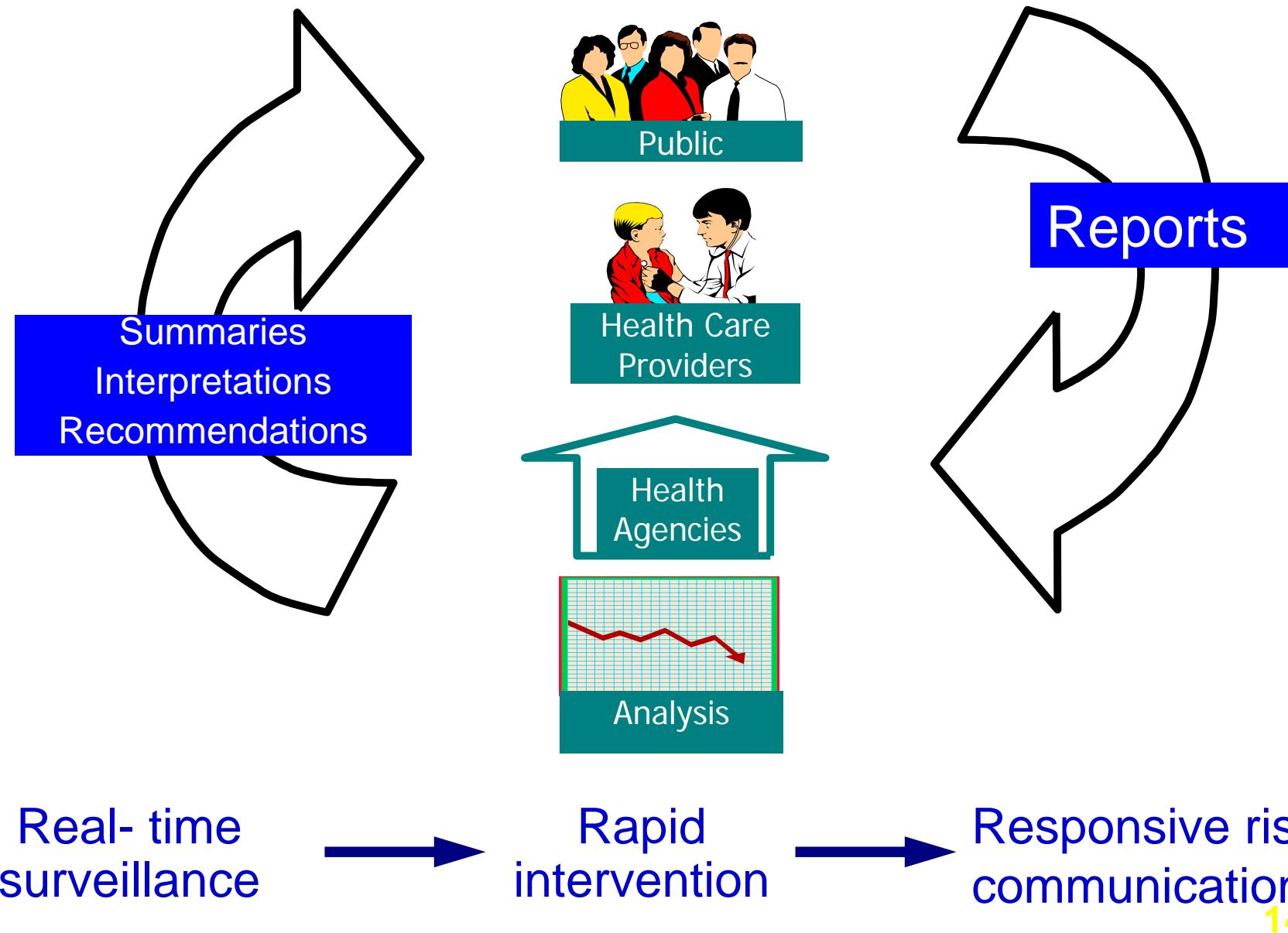
Surveillance system flow chart



Public Health Approach



Information Loop of Public Health Surveillance



WHO Western Pacific Regional Office Conceptualized a Framework for Action

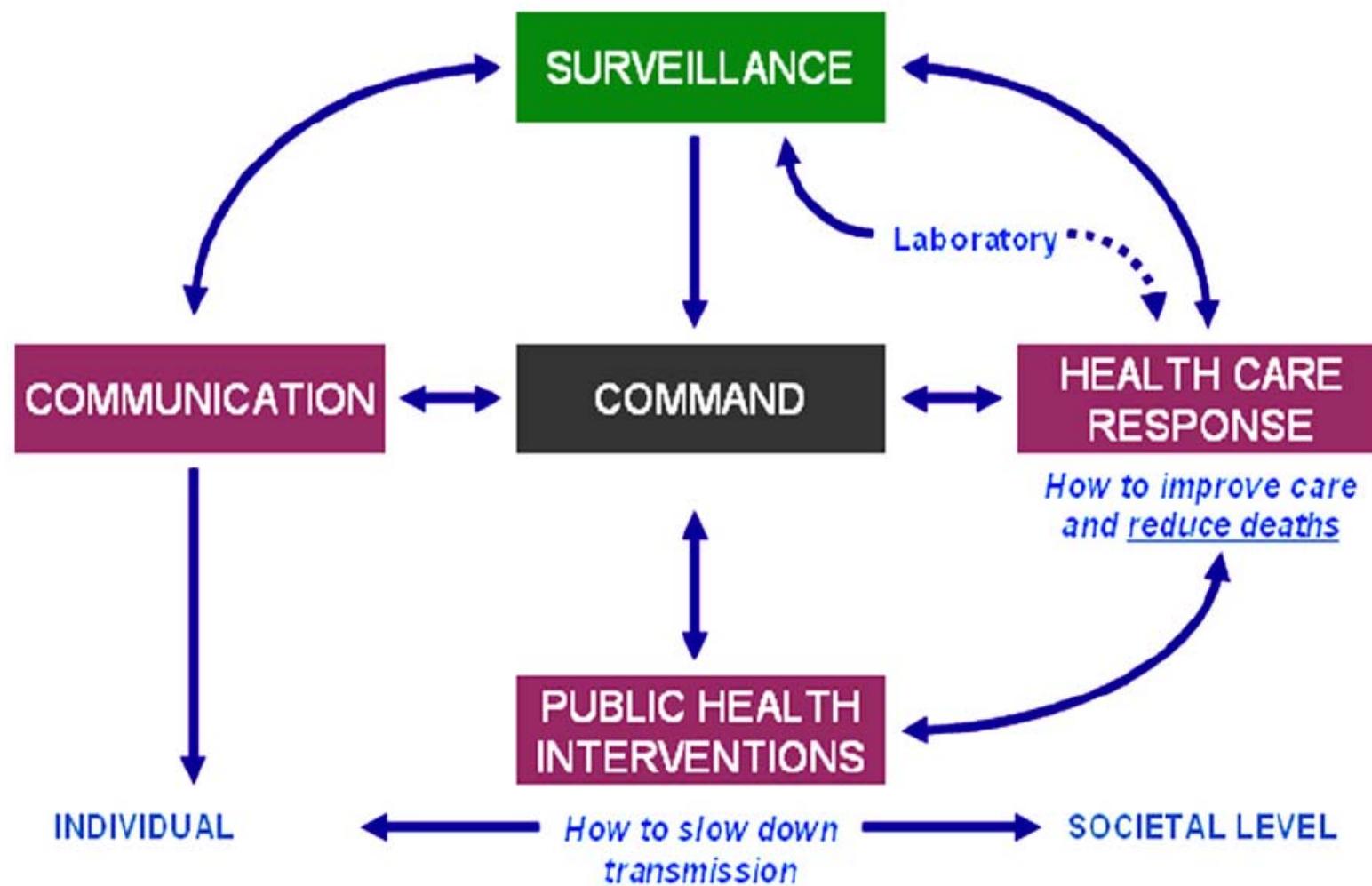
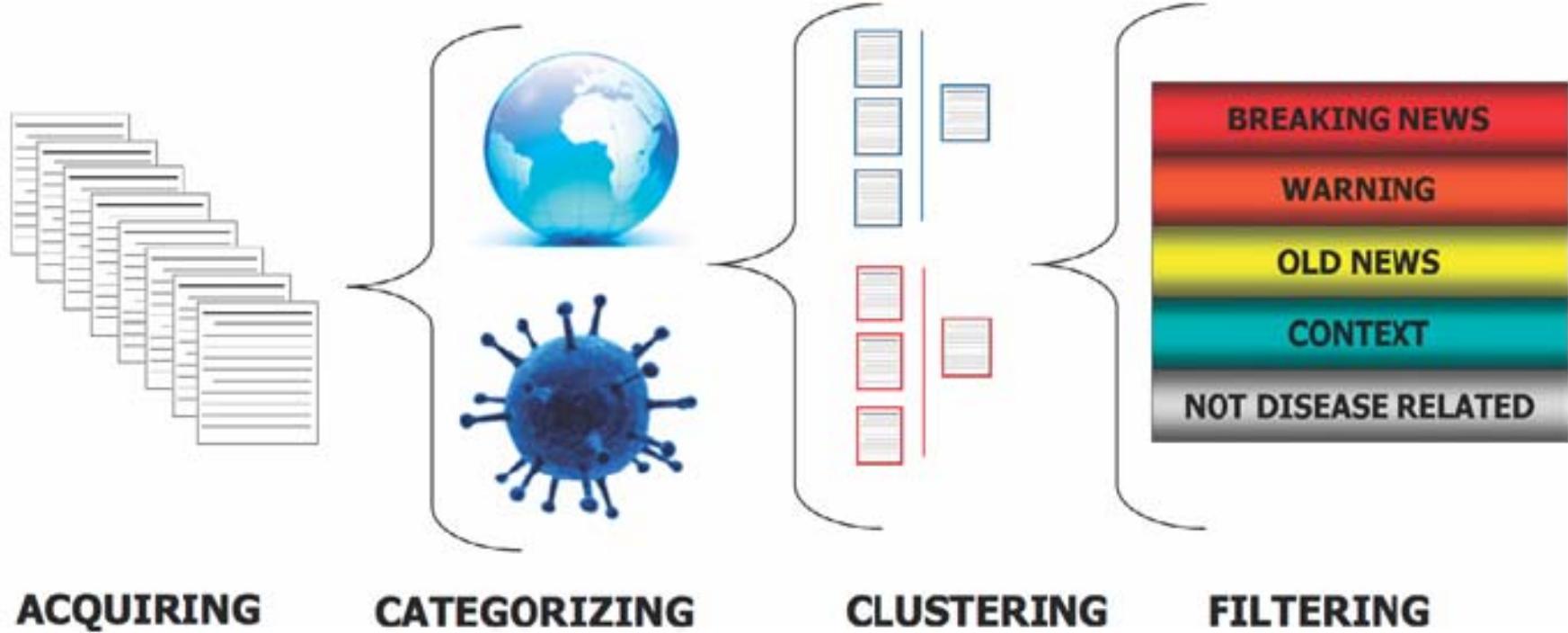


Figure 1 – Framework for Action.

Stages of HealthMap Surveillance



ACQUIRING

doi:10.1371/journal.pmed.0050151.g002

CATEGORIZING

CLUSTERING

FILTERING

Global Influenza Surveillance and Response System (GISRS)

- Established in 1952,
- the network currently comprises
 - 6 WHO Collaborating Centres,
- 4 WHO Essential Regulatory Laboratories and
- 139 institutions in 109 WHO Member States, which are recognized by WHO as National Influenza Centres, in addition to ad hoc groups established to address specific emerging issues.

Global Influenza Surveillance and Response System (GISRS)

- Global influenza virological surveillance has been conducted through WHO's Global Influenza Surveillance and Response System (GISRS) for over half a century.
- Formerly known as the Global Influenza Surveillance Network (GISN), the new name came into effect following the adoption of the Pandemic Influenza Preparedness (PIP) Framework in May 2011.
- WHO GISRS monitors the **evolution of influenza viruses** and provides recommendations in areas including **laboratory diagnostics**, **vaccines**, **antiviral susceptibility** and **risk assessment**.
- WHO GISRS also serves as a global alert mechanism for the **emergence of influenza viruses with pandemic potential**.

WHO Global Influenza Surveillance and Response System

31 August 2012



- ▲ National Influenza Centre
- WHO Collaborating Centre for Reference and Research on Influenza
- WHO Collaborating Centre for the Surveillance, Epidemiology and Control of Influenza
- WHO Collaborating Centre for Studies on the Ecology of Influenza in Animals
- * WHO Essential Regulatory Laboratory
- ◆ WHO H5 Reference Laboratory

- [Light gray square] Data not available
- [Dark gray square] Not applicable

0 900 1,800 3,600 Kilometers

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: Global Influenza Surveillance and Response System (GISRS), WHO
Map Production: WHO GISRS Team
World Health Organization



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China , the first country in the developing world
to host a WHO Collaborating Center
for Reference and Research on Influenza

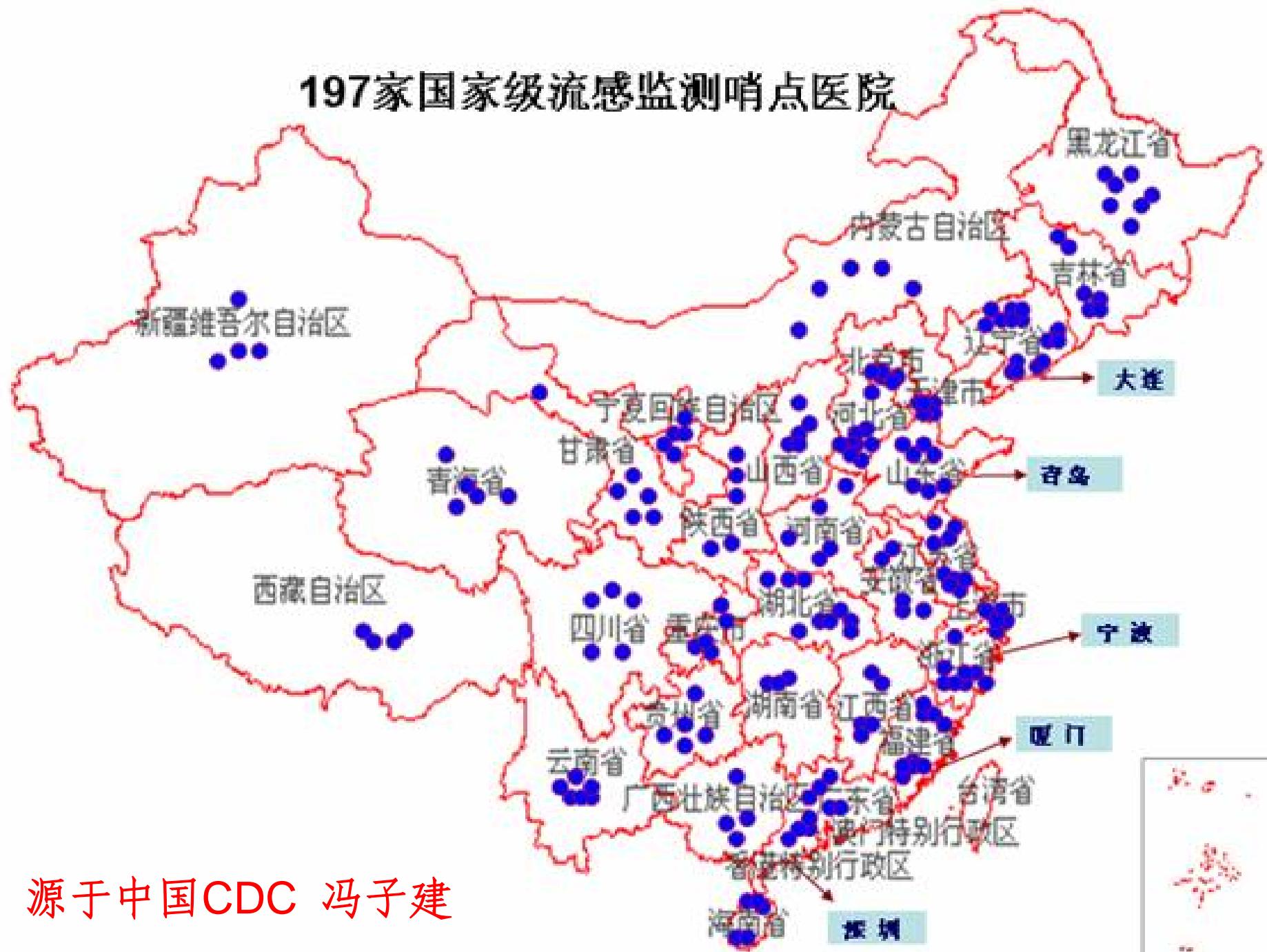


Flu-ent Chinese: The National Influenza Center.

147

China's new WHO flu monitoring center seeks to reverse criticism, nature medicine vol 17, 5 ,2011

197家国家级流感监测哨点医院



源于中国CDC 冯子建

我国流感监测网络实验室（63个）



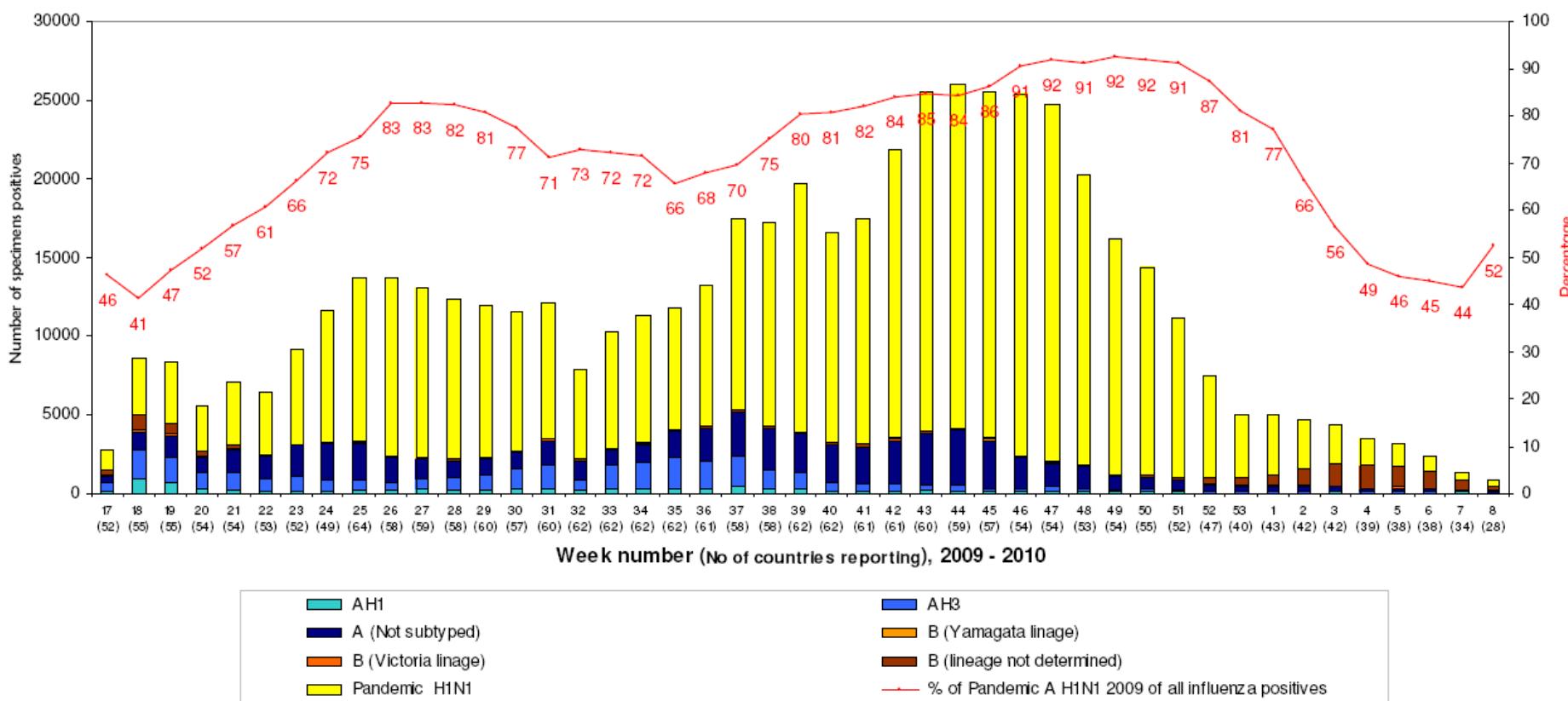
源于中国CDC 冯子建

Global circulation of influenza viruses

Number of specimens positives for influenza by subtypes

week 17 (2009) - 8 (2010) from 19 April 2009 to 27 February 2010

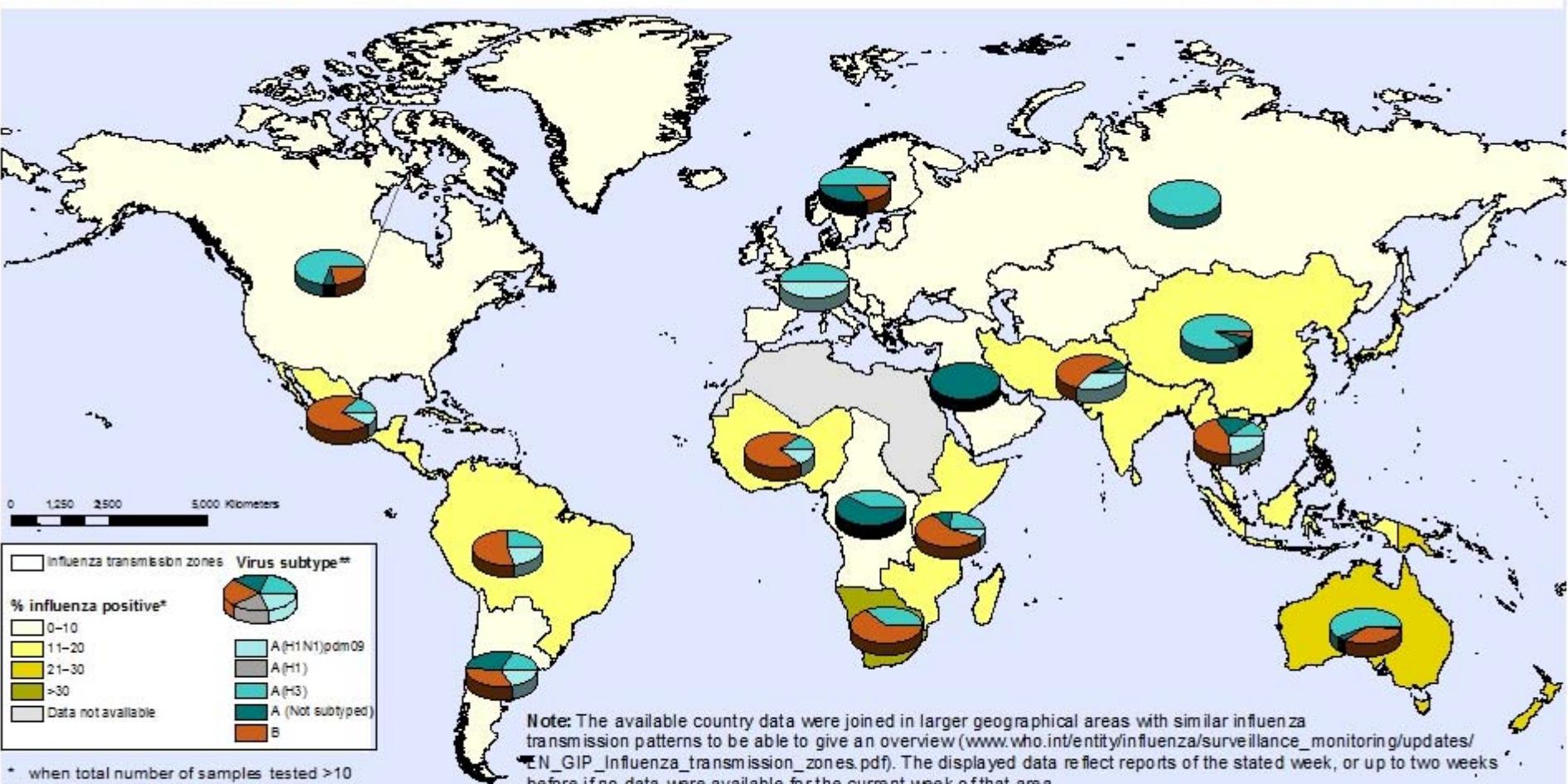
2009.04.19 ~ 2010.02.27



Percentage of respiratory specimens that tested positive for influenza By influenza transmission zone

Status as of week 35

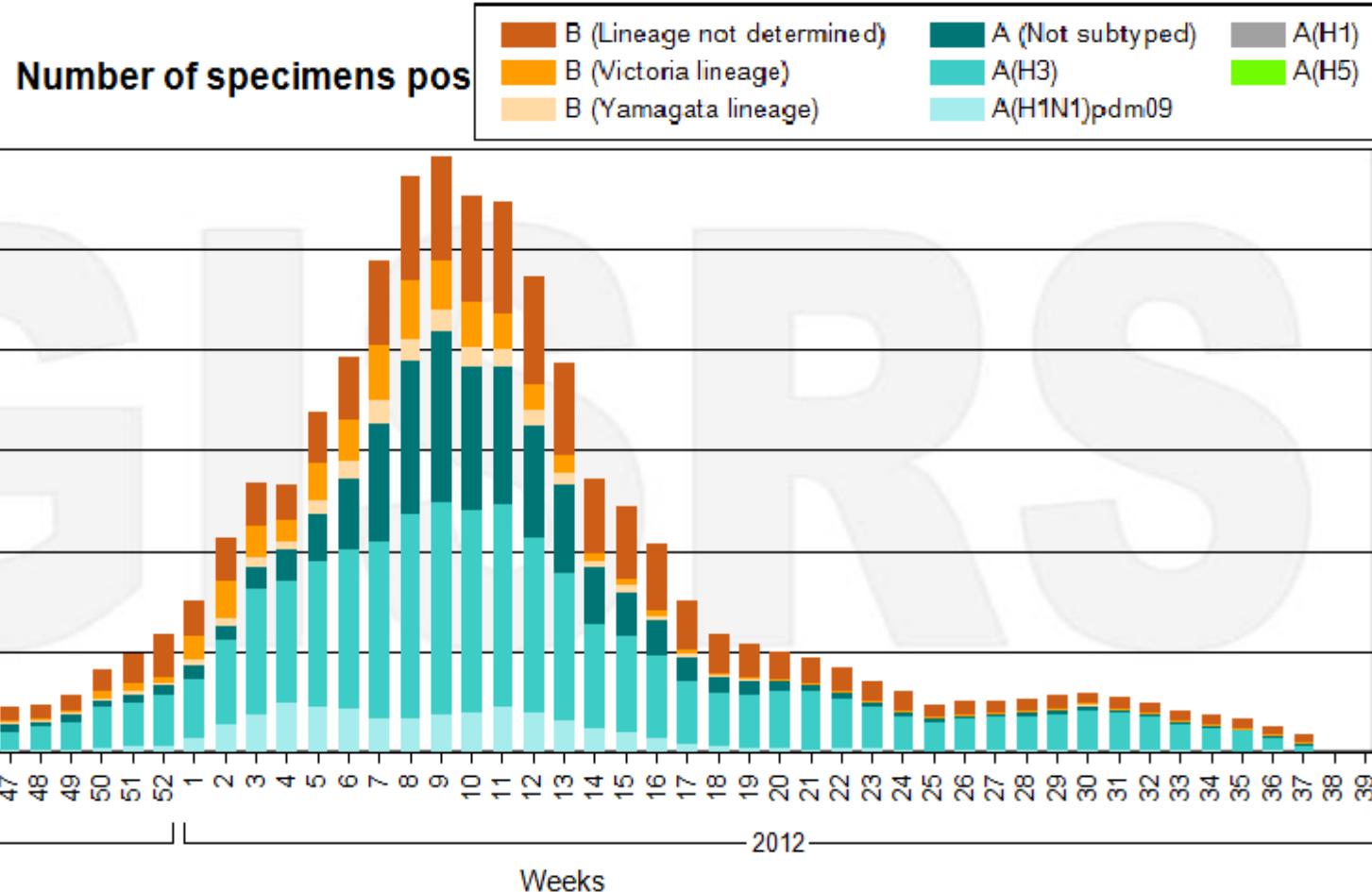
26 August – 01 September 2012



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: WHO/HIP, data in HQ as of 11 September 2012.
Data used are from FluNet (www.who.int/fluNet), 16:04 UTC snapshot, from WHO regional offices and/or ministry of health websites.

Northern hemisphere



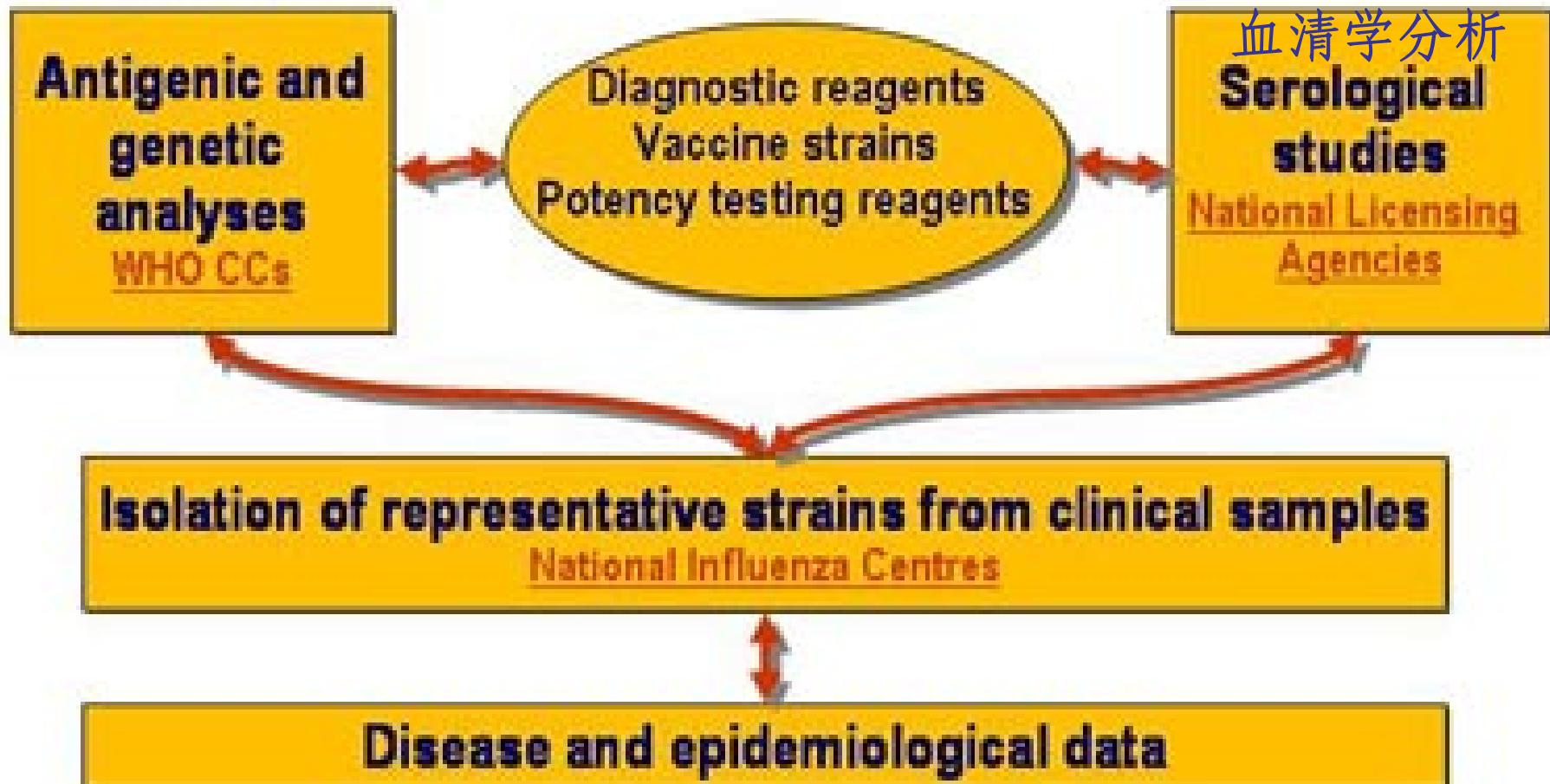
<http://gamapserver.who.int/gareports/Default.aspx?ReportNo=5&Hemisphere=Northern>

WHO recommended that the Northern Hemisphere's 2012-2013 seasonal influenza vaccine be made from the following three vaccine viruses:

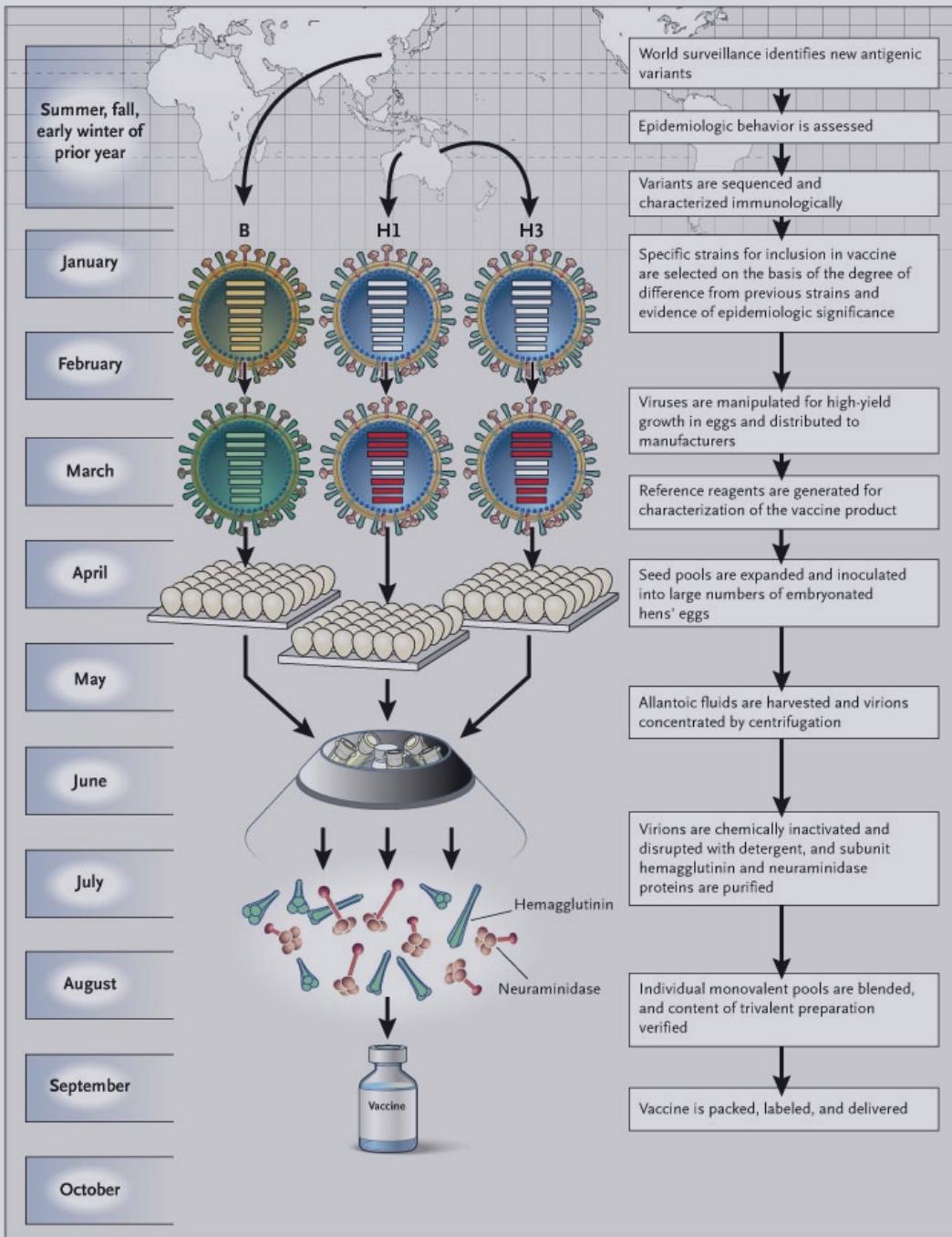
- an A/California/7/2009 (H1N1)pdm09-like virus;
- an A/Victoria/361/2011 (H3N2)-like virus;
- a B/Wisconsin/1/2010-like virus
(from the B/Yamagata lineage of viruses).

WHO Global Influenza Surveillance Network

Make recommendations on the influenza vaccine formulation



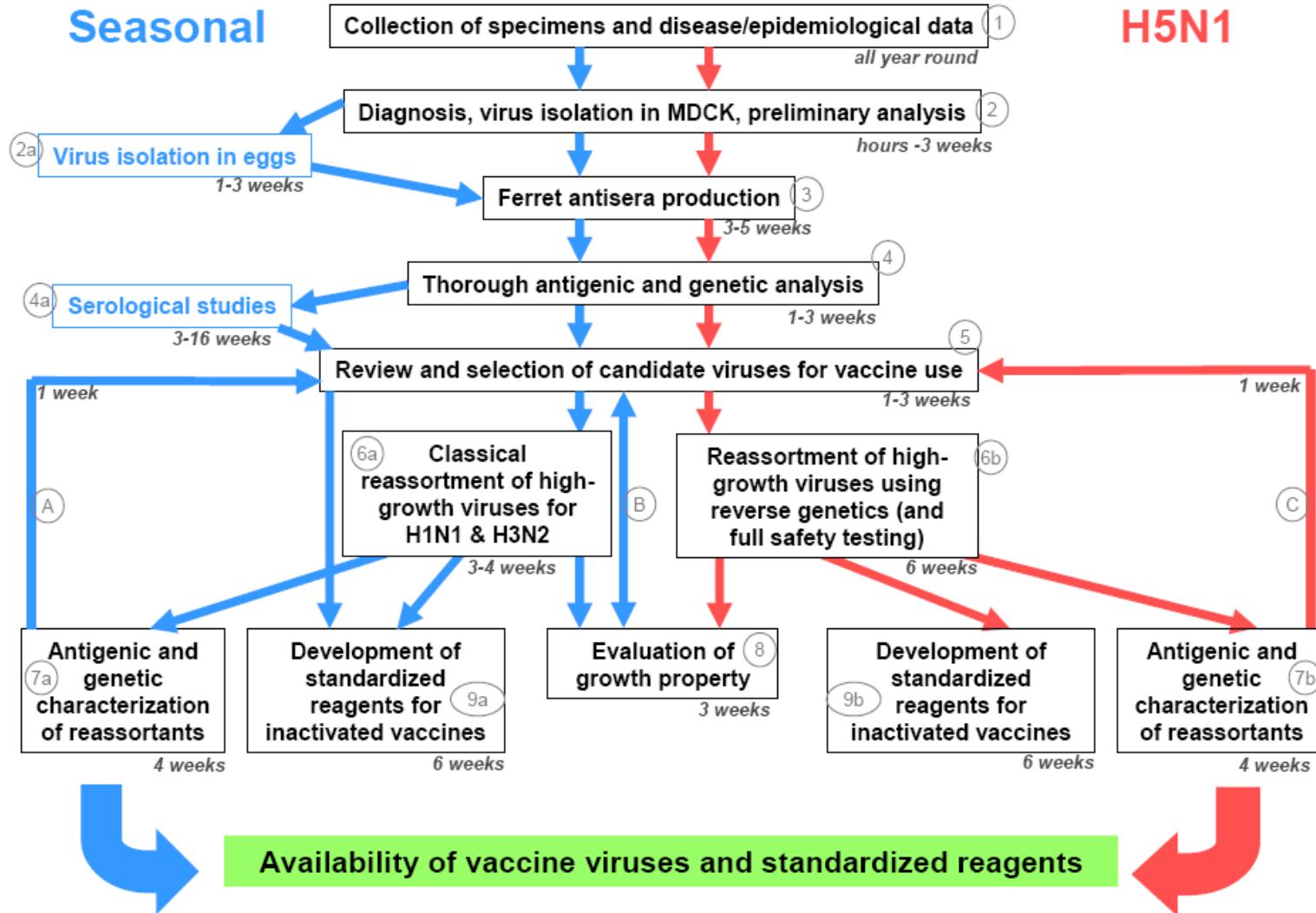
Influenza Vaccine Manufacturing Process



RTI International is a trade name
of Research Triangle Institute.

A description of the process of seasonal and H5N1 influenza vaccine virus selection and development

Process of influenza vaccine virus selection and development

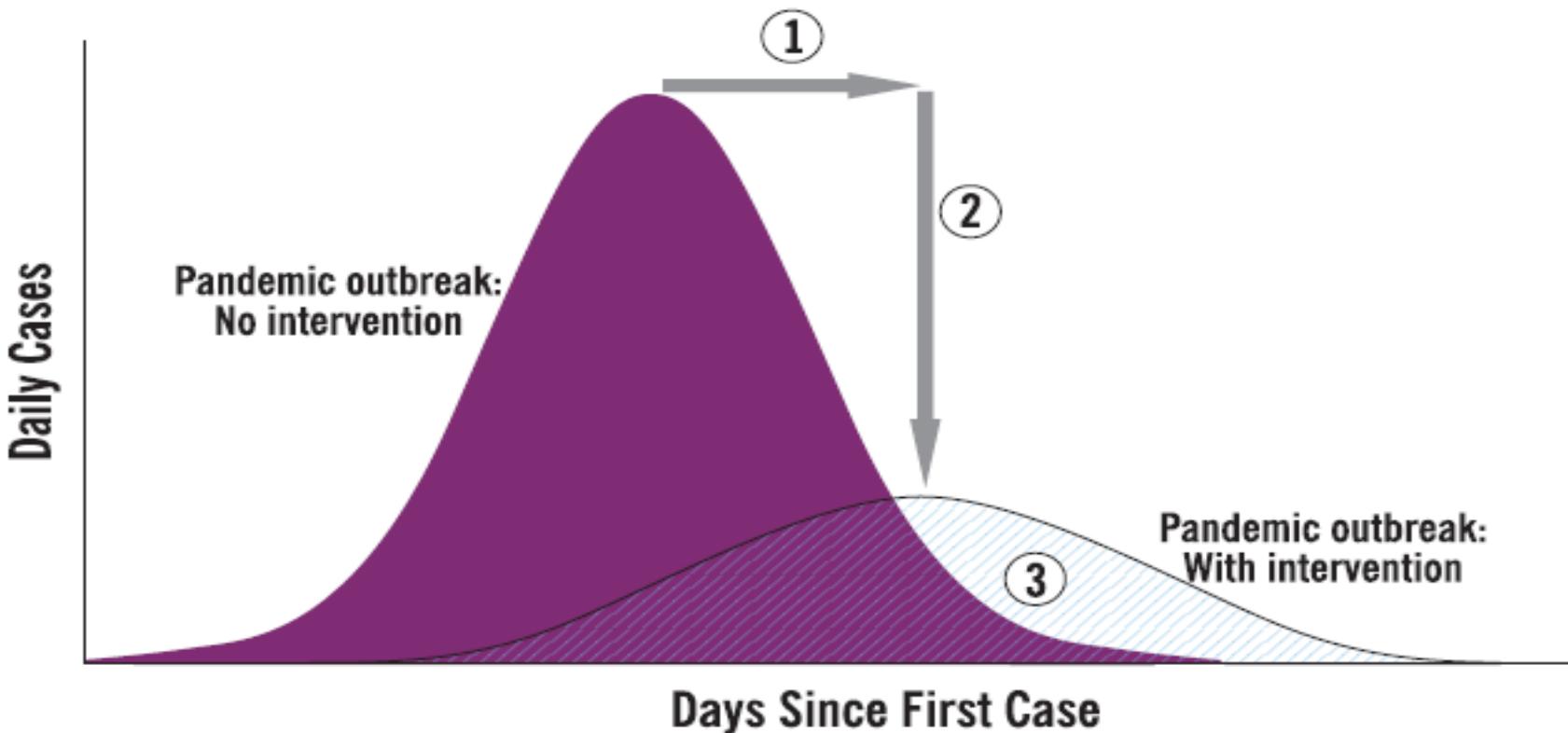


Goals of Community Mitigation

Figure 1.

Goals of Community Mitigation

- ① Delay outbreak peak
- ② Decompress peak burden on hospitals / infrastructure
- ③ Diminish overall cases and health impacts



HIV/AIDS Surveillance

- Invest in second-generation monitoring systems to better identify the drivers of the epidemic.
- Study the behavioural patterns of specific at risk groups, and adjust prevention and care policies based on knowledge generated by these studies.

4 key high risk groups:

- Injecting drug users
- Men who have sex with men
- Sex workers
- Prisoner

One in five Americans currently living with HIV doesn't know it.
If our President and First Lady can get tested -- you can too.

The image is a promotional graphic for National HIV Testing Day. It features a large American flag in the background. In the upper right corner, there is a portrait of President Barack Obama. Overlaid on the image is the text "Take the Test. Take Control." in large, bold, white letters. Below this, in a smaller white box, is the text "President Obama Takes an HIV Test." To the right of this box is a large, bold "GO»" button. At the bottom of the image, there are three tabs with gold borders: "HIV Funding", "Prevention Efforts", and "HIV Testing".

Take the Test. Take Control.

President Obama Takes an HIV Test.

GO»

HIV Funding Prevention Efforts HIV Testing »

The 14th commemoration of National HIV Testing Day, 2009.06.27 ,
President Obama release a special video

*Get test it! You can take control not only your health
but the health of those around you!*
<http://www.whitehouse.gov/blog/GetTested/>

Objectives of Epidemic Preparedness and Response

1. Anticipation/prediction

so that epidemics be prevented
e.g. meningitis, measles

2. Early detection

to know when there is a problem
e.g. EWARS (Early Warning and Reporting System)

3. Rapid Response

Guidelines / trained staff / supplies
in place before epidemic

4. Effective Response

appropriate control methods
adequate resources and logistics

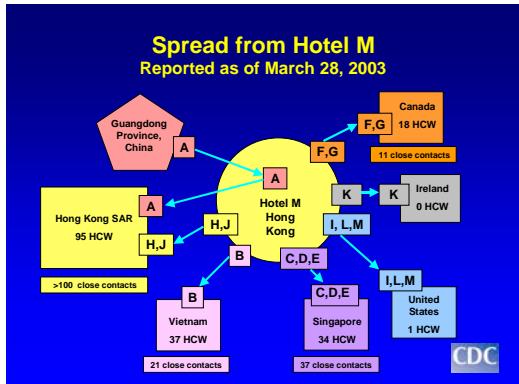
5. Outbreak Investigations

Emerging Infectious Diseases

SARS

Health Communication

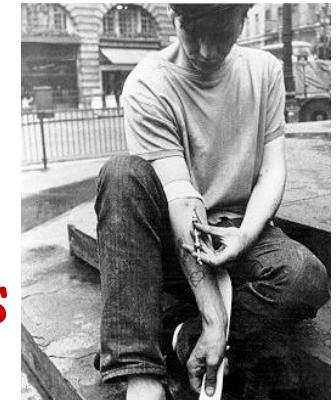
GUANGDONG



ANCIENT



MODERN MENACE



Youngster gives himself fix of heroin
Courtesy of The World Health Organization

CHOLERA
CLONORCHIASIS
SARS

PREVENTION



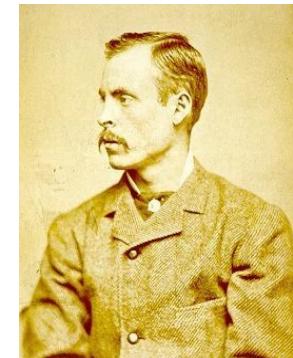
& CONTROL

Ancient Disaster
Modern Threat

FIGHT



Patient before treatment.



Patient after treatment.

BACK

Examples of modern and historically important emerging infectious diseases



- (A) Caused by war and famine. Plague in an Ancient City, 430 ~ 426BC
- (B) Associated with intent to harm. Black Death (bubonic/pneumonic plague) associated with a bioterrorist attack, Europe, 14th century
- (C) Due to travel and trade. Cholera epidemic, spread from Asia to Europe, Paris, 1832
- (D) Associated with microbial adaptation and change. Influenza pandemic. 1918~1919

Emerging infectious diseases

An emerging disease is one that has appeared in a population for the first time,

or that may have existed previously but is rapidly increasing in incidence or geographic range.



Emerging and re-emerging diseases

- Emerging infectious diseases
newly identified or
previously unknown infections
- Re-emerging infectious diseases
re-appearance of, or
increase in number of,
infections from a disease previously known

What are emerging infectious diseases?

According to the National Institute of Allergy and Infectious Diseases, emerging infectious diseases are commonly defined as:

- Diseases that have newly appeared in a population.

AIDS	Lyme disease
Escherichia coli O157:H7 (E. coli)	
Hantavirus	SARS and others
- Diseases that have existed in the past, but are rapidly increasing in incidence or geographic range.
- Re-emergence may also occur because of breakdowns in public health measures for previously controlled infections.

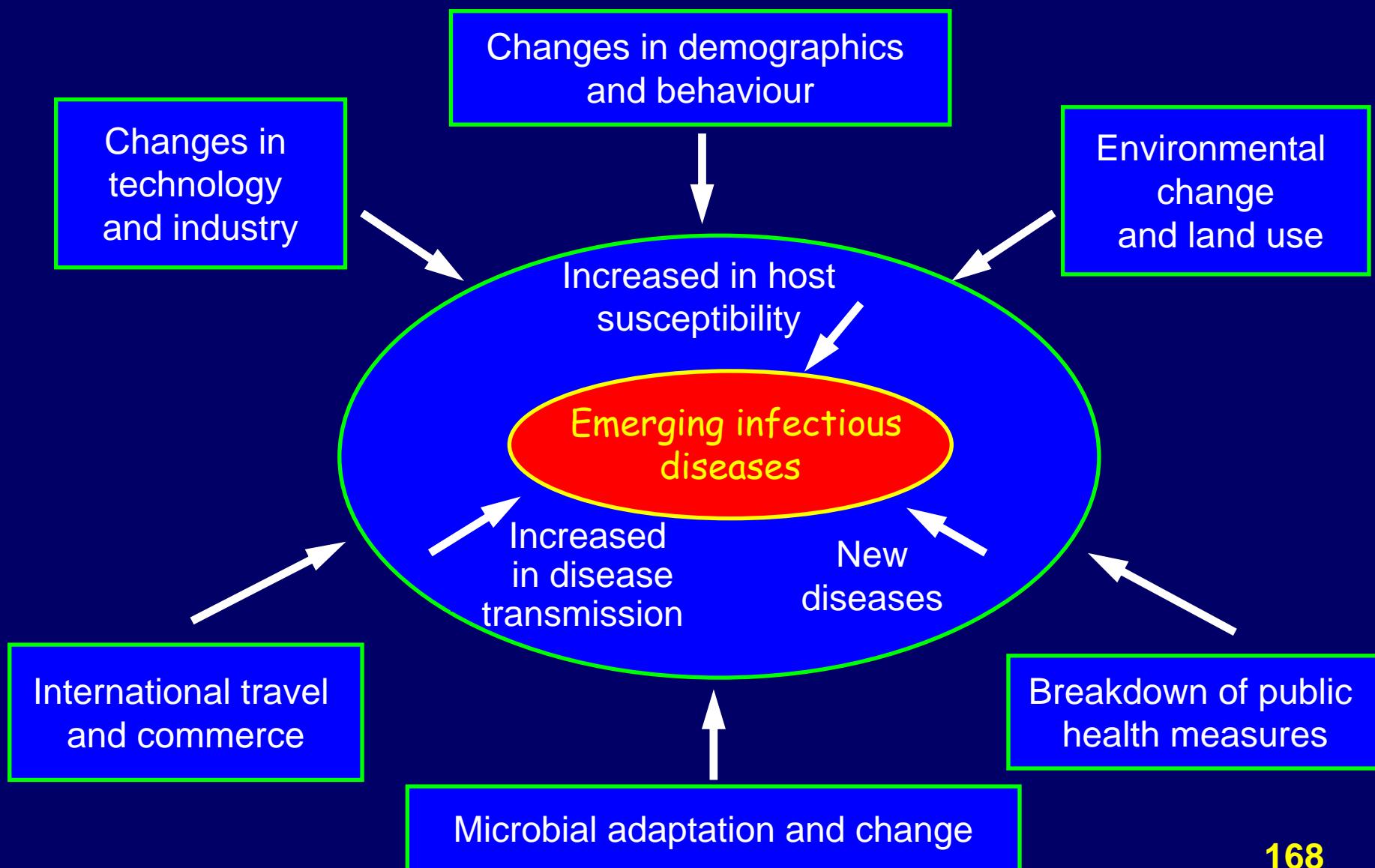
Schistosomiasis	Tuberculosis	Malaria
Cholera	Plague	Influenza
Pneumococcal disease	gonorrhea	and others

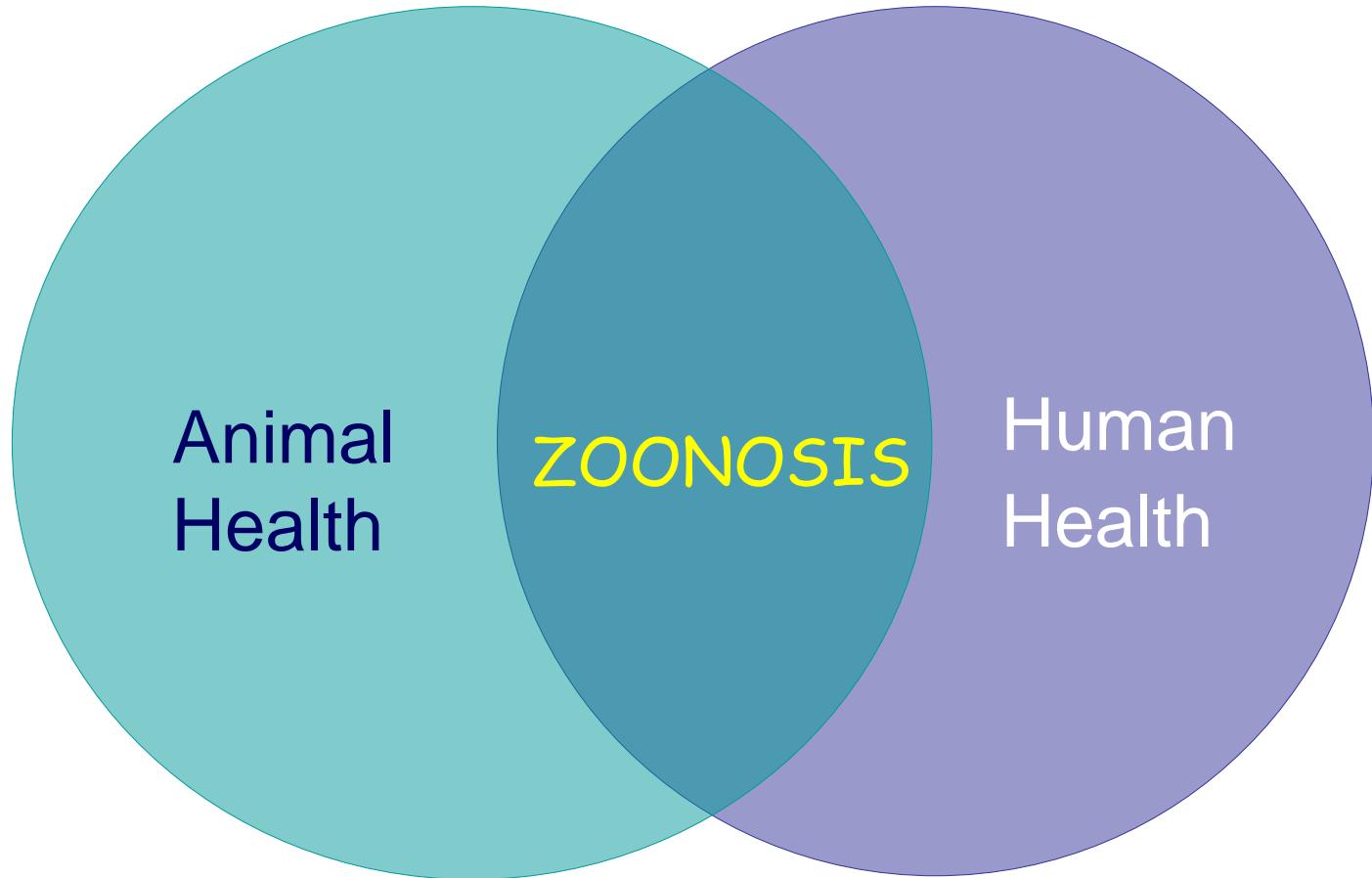
Preventing Emerging Infectious Diseases

“As we face the new millennium,
we must **renew our commitment** to the
prevention and control of infectious diseases,
recognizing that the competition
between humans and microbes
will continue long past
our lifetimes and those of our children.”

Jeffrey P. Koplan, Director, US CDC

Factors leading to the emergence of infectious diseases



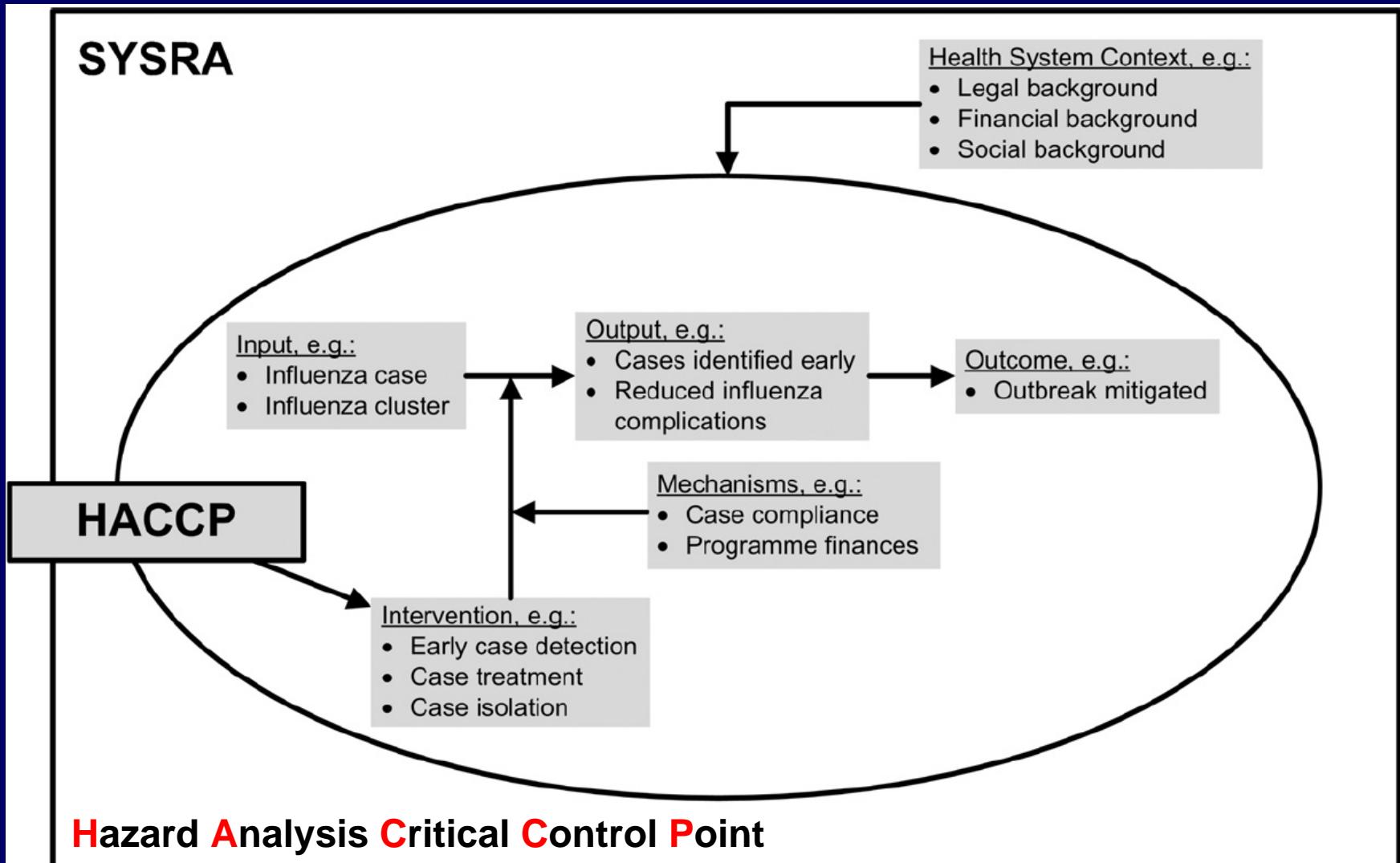


Zoonosis (Zoonotic Diseases) - all diseases naturally transmissible from animals to man

Factors that affect the emergence of disease

1. Human behavior and demographics
2. Microbial adaptation and change
3. International travel and commerce
4. Human susceptibility to infection
5. Technology and industry
6. Changing ecosystems
7. Climate and weather
8. Breakdown of public health measures
9. Poverty and social inequality
10. Economic development and land use
11. War and famine
12. Lack of political will
13. Intent to harm

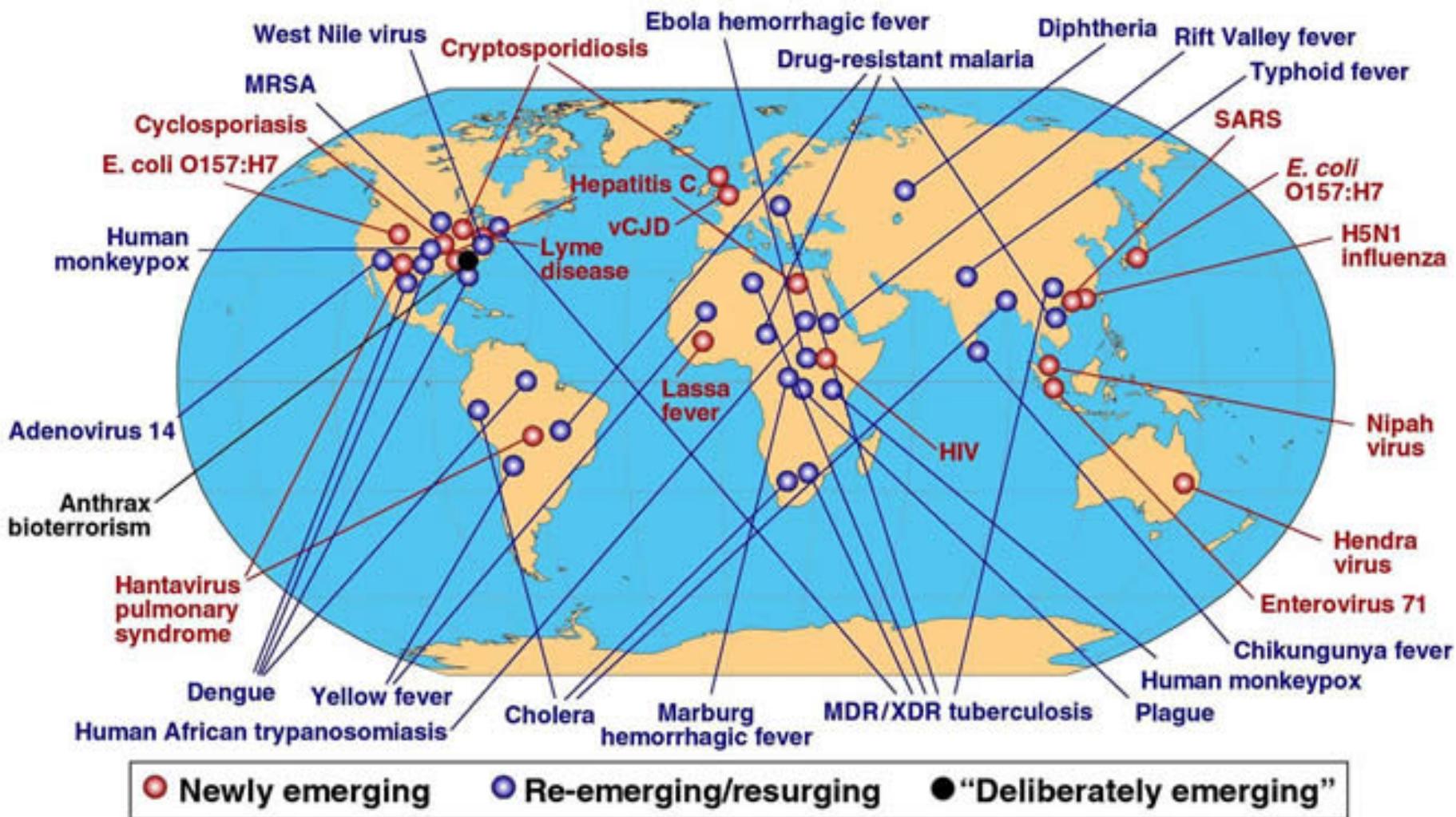
Systemic Rapid Assessment Toolkit (SYSRA)



EMERGING AND RE-EMERGING INFECTIOUS DISEASES, 1996–2001



Newly emerging, re-emerging/resurging, and deliberately emerging diseases , 1977~2007



Emerging infectious diseases

Conclusion

- Emerging and re-emerging diseases are not new
- Their control does **not require new approaches** but determination and vigilance at all levels
- Key to success
 - Sound public health **practices**
 - Awareness and commitment of **decision makers**
 - **Synergy**

Outbreak investigations

- Usually retrospective, often relying upon recall of affected persons to identify causal linkages.
- Because they begin without clear hypotheses, outbreak investigations require descriptive studies to generate hypotheses before analytic studies can be conducted.
- Since outbreak investigations are driven by an immediate health concern in the community, the need for responsiveness to community needs and effective risk communication is heightened.
- Require public health officials to weigh the evidence, often in the absence of a clear etiologic connection, and determine when the data are sufficient to take controversial and sometimes unwelcome actions.
- Outbreak investigations often attain national or international prominence (eg, toxic shock syndrome, Escherichia coli or O157:H7(E. coli), food contamination, SARS and Avian flu)
- Generally involve infectious disease and laboratory confirmation

Cluster investigators

Clustering of disease is **intriguing** and some cluster investigations have led to **important scientific discoveries**.

For example,

Investigation of the spatial clustering of **enamel discoloration** led to the discovery of the relation between **fluoride levels in drinking water and dental caries**.

Most cluster investigations focus on **cancer**.

Many **carcinogens** have been discovered through occupational or medical cluster investigations.

Cluster investigators

Studies of disease clusters often are **challenging** because of the **constraints** of information available to investigators. Some of the **biggest issues** include:

- Rare health events
- Vague definition and/or heterogeneity of cases
- Lack of a population base for rate calculation
- Weak association and multiple risk factors
- Long induction periods
- Multiple comparisons
- Low-level, long-term, heterogeneous exposures
- Intense publicity
- Resource intensiveness of full investigations

Global Outbreak Alert & Response Network

Guiding Principles for International Outbreak Alert and Response

عربی | 中文 | English | Français | Русский | Español

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Global Alert and Response (GAR)

[GAR Home](#)[Alert & Response Operations](#)[Diseases](#)[Global Outbreak Alert & Response Network](#)[Biorisk Reduction](#)

Global Outbreak Alert & Response Network

The Global Outbreak Alert and Response Network (GOARN) is a technical collaboration of existing institutions and networks who pool human and technical resources for the rapid identification, confirmation and response to outbreaks of international importance. The Network provides an operational framework to link this expertise and skill to keep the international community constantly alert to the threat of outbreaks and ready to respond.

[Video](#)

Highlights

[Avian influenza](#)[Latest information](#)

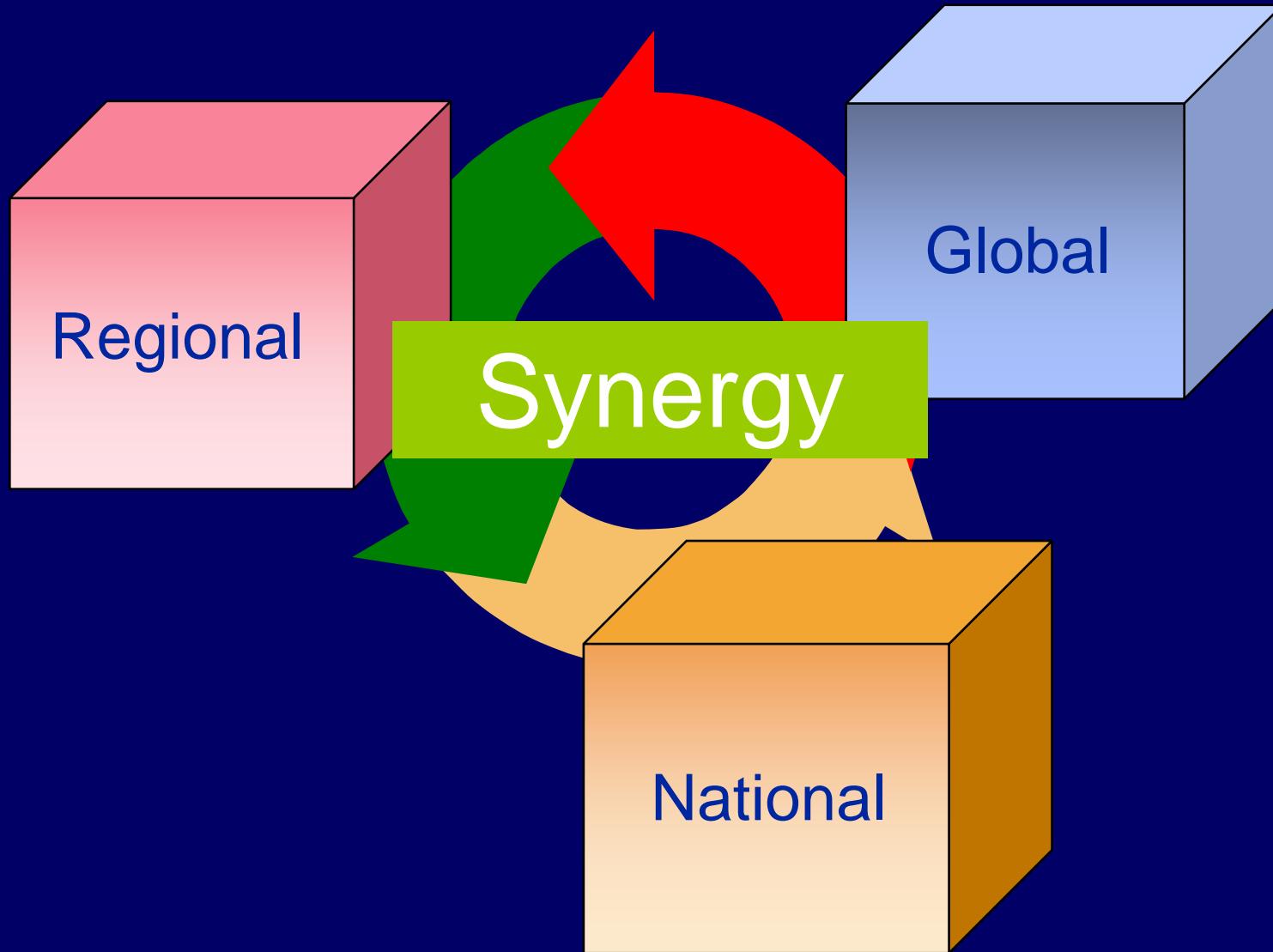
Disease outbreaks

[17 October 2012](#)[Dengue Fever in Madeira, Portugal](#)[10 October 2012](#)[Novel coronavirus infection - update](#)[8 October 2012](#)

Planning for a Contingency Health Emergency



Key tasks - carried out by whom?

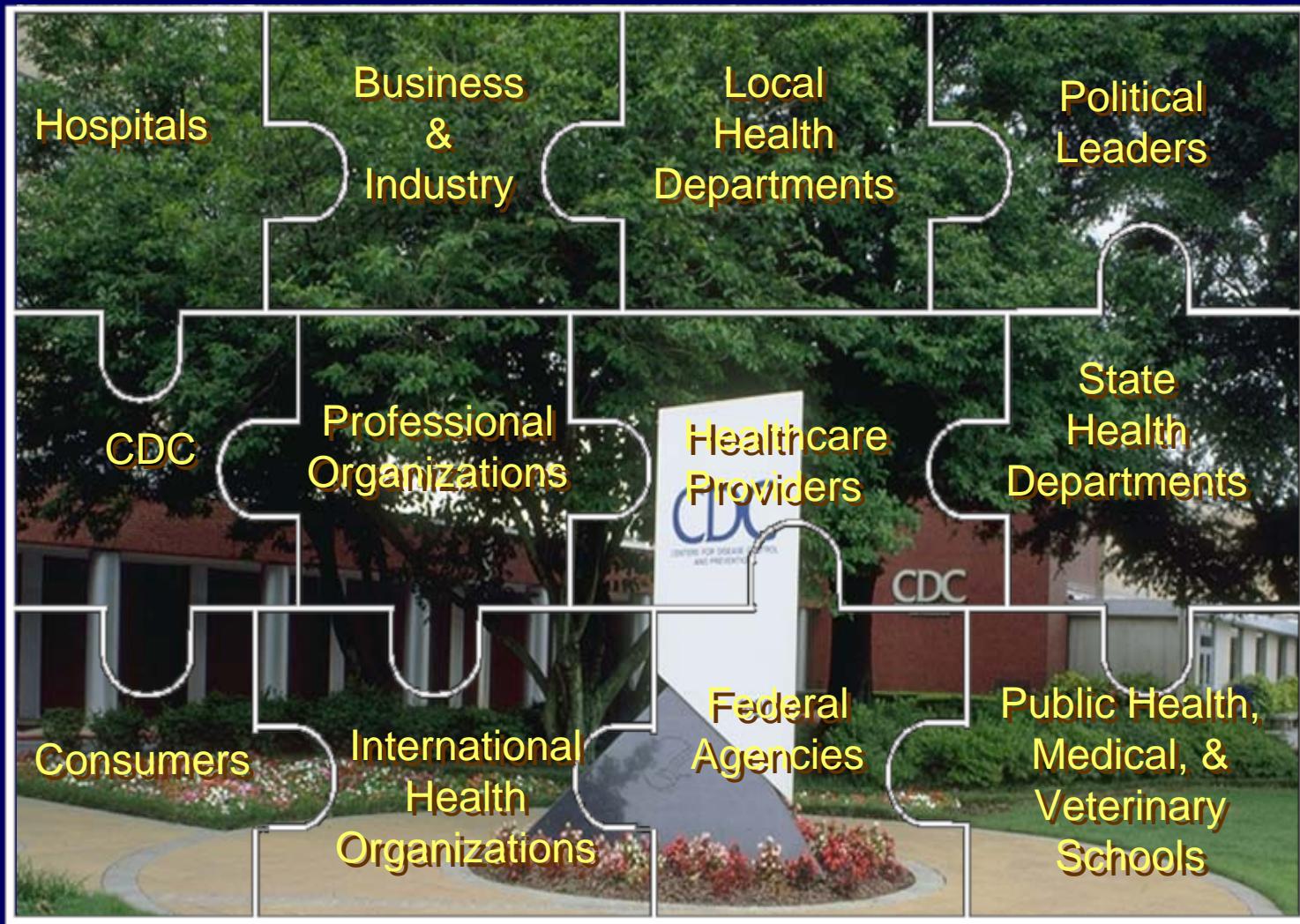


What skills are needed?

- Infectious diseases
- Clinical
- medicine
- Epidemiology
- Laboratory
- Public Health
- International field experience
- Telecom. & Informatics
- Information management
- Ecology
- Anthropology
- Logistics
-

Multiple expertise needed !

Prevention Partners



Prevention of Emerging Infectious Diseases Will Require Action in Each of These Areas

1. Surveillance and Response
2. Applied Research
3. Infrastructure and Training
4. Prevention and Control

Preventing Emerging Infectious Diseases

1. Surveillance and Response

- Detect, investigate, and monitor emerging pathogens, the diseases they cause, and
- the factors influencing their emergence, and
- respond to problems as they are identified.

Preventing Emerging Infectious Diseases

2. Applied Research

Integrate laboratory science and epidemiology to increase the effectiveness of public health practice.

Preventing Emerging Infectious Diseases

3. Infrastructure and Training

- Strengthen public health **infrastructures** to support surveillance, response, and research and to implement prevention and control programs.
- Provide the public health work force with the **knowledge and tools** it needs.

Preventing Emerging Infectious Diseases

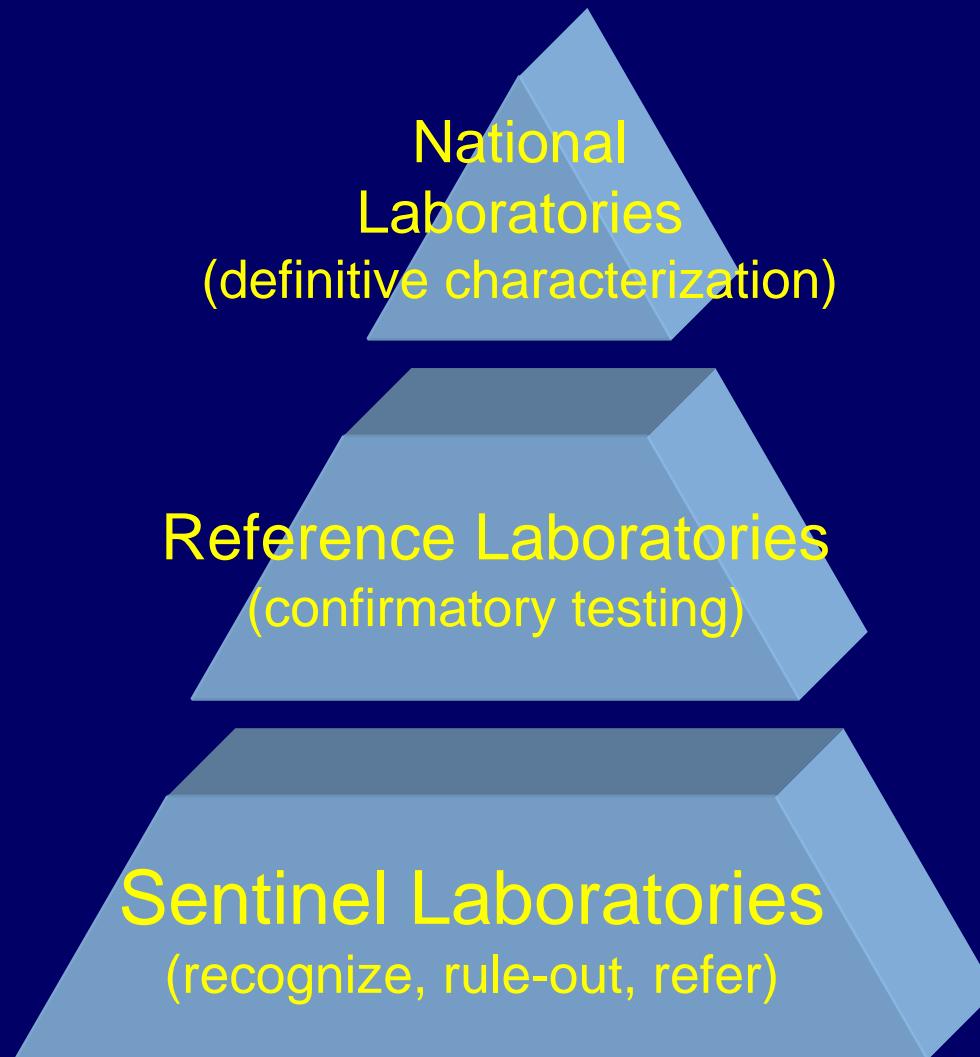
4. Prevention and Control

- Ensure prompt implementation of prevention strategies and
- Enhance communication of public health information about emerging diseases.

Key tasks in dealing with emerging diseases

- Surveillance at national, regional, global level
 - Epidemiological
 - Laboratory
 - Clinical
 - Ecological
 - Anthropological (e.g., behaviours)
- Investigation and early control measures
- Implement prevention measures
 - behavioural, political, environmental
- Monitoring & Evaluation

Laboratory Response Network (LRN)



Early detection of outbreaks can be achieved in three ways

1. by timely and complete receipt, review, and investigation of disease case reports.

Electronic reporting system will improve the timeliness and completeness of reporting notifiable conditions

2. by improving the ability to recognize patterns indicative of a possible outbreak early in its course.

- Statistical / analytic tools for pattern recognition and aberration detection can be applied to screen data for patterns warranting further public health investigation and to enhance recognition of subtle or obscure outbreak patterns .
- Automated analysis and visualization tools can lessen the need for frequent and intensive manual analysis of surveillance data

Early detection of outbreaks can be achieved in three ways

3. through receipt of new types of data that can signify an outbreak earlier in its course.

- These new types of data might include health-care product purchases, absences from work or school, presenting symptoms to a health-care provider, or laboratory test orders .
- Many new surveillance systems, loosely termed *syndromic surveillance systems*, use data that are not diagnostic of a disease but that might indicate the early stages of an outbreak

AFP (Acute flaccid paralysis)	→	Polio
ILI (Influenza - like illness)	→	Influenza
?	→	SARS

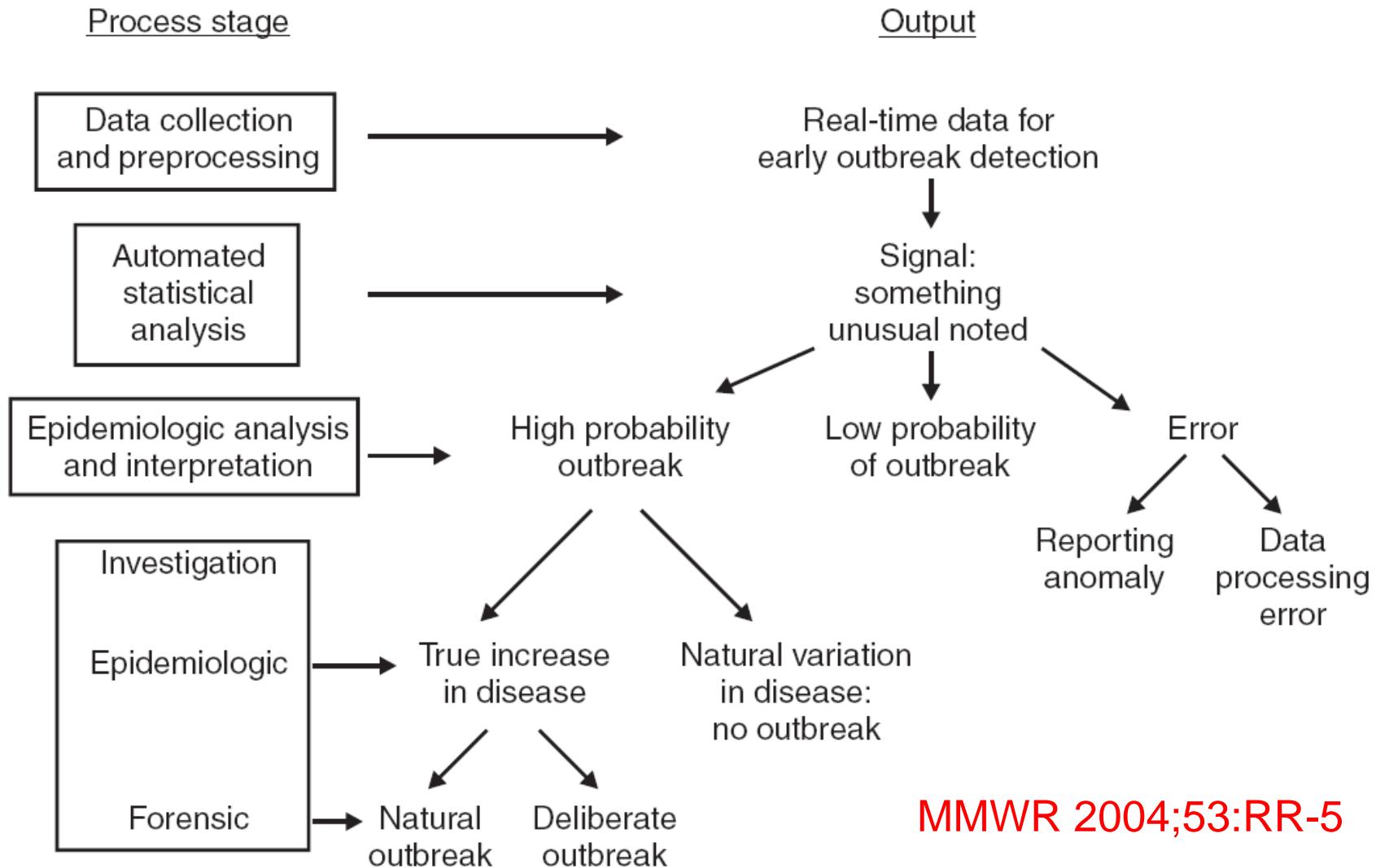
Global Disease Detection (GDD) Operations Center

The GDD Operations Center
is an innovative epidemic
intelligence and response
operations unit
located at CDC headquarters.



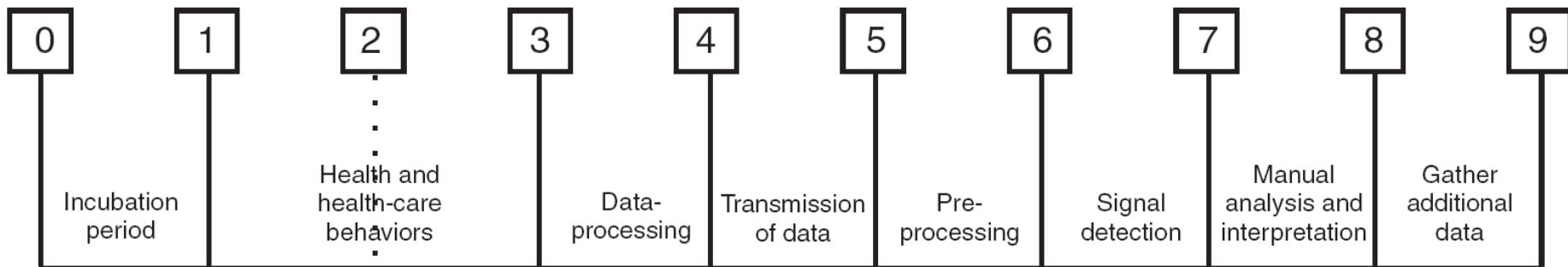
It uses non-traditional surveillance methods to provide early warning about international disease threats so that CDC can rapidly respond to protect public health in the United States and the global community.

Process model for early outbreak detection



MMWR 2004;53:RR-5

Timeline milestones for early outbreak detection



0. Onset of exposure
1. Onset of symptoms
2. Onset of behavior
3. Capture of data
4. Completion of data processing
5. Capture of data in surveillance system
6. Application of pattern recognition tools/algorithms
7. Generation of automated alert
8. Initiation of public health investigation
9. Initiation of public health intervention

MMWR 2004;53:RR-5

Communicable Disease Outbreak Investigation

Outbreak

A localised epidemic of two or more cases of disease related in time and or place in excess of normal expectancy.

Objectives

1. Identify source and mode of spread
2. Interrupt further transmission
3. Prevent secondary spread
4. Educate
5. Introduce future preventative measures
6. (prosecute)

Steps of an Outbreak Investigation

1. Prepare for field work
2. Establish the existence of an outbreak
3. Verify the diagnosis
4. Define and identify cases
5. Describe and orient the data in terms of
 person place time
6. Develop hypotheses
7. Evaluate hypotheses
8. Refine hypotheses and
 carry out additional studies
9. Implement control and prevention measures
10. Communicate findings

Speed !
Right Answer !
Effective !

Steps of an Outbreak Investigation

- The steps are presented here in conceptual order
- In practice, however, several may be done at the same time, or
 - The sequence is not important !**
 - they may be done in a different order.**
- For example, control measures should be implemented as soon as the source and mode of transmission are known, which may be early or late in any particular outbreak investigation.

Steps in Outbreak Investigation

The sequence is not important !

Descriptive steps

1. Determine existence of an outbreak
2. Confirm the diagnosis:
Which diseases are we talking about?
3. Define a case; find and count cases
4. Orient data as to:
 - Person Who?
 - Place Where?
 - Time When?

Steps in Outbreak Investigation

The sequence is not important !

- Analyse
 - 5. Generate hypotheses
 - 6. Test the hypotheses
 - 7. Compare each hypothesis with facts
 - 8. Plan a more systematic study
- Synthesis and action
 - 9. Write a report, communicate findings
 - 10. Control measure and prevention

Steps of outbreak investigation

1. Prepare for field work
2. Establish the existence of an outbreak
3. Verify the diagnosis
 - a. clinical features: is the disease known ?
 - b. what are its serologic or cultural aspects ?
4. Define and identify cases
 - a. establish a case definition
 - b. identify and count cases and calculate the attack rates

**Do not wait for laboratory results
to start treatment and control activities!**
5. Perform descriptive epidemiology
 - a. time and place distributions of cases
 - b. look for time – place interactions
 - c. timely collect samples related to the pathogens
6. Look for combinations (interactions) of relevant variables

Steps of outbreak investigation

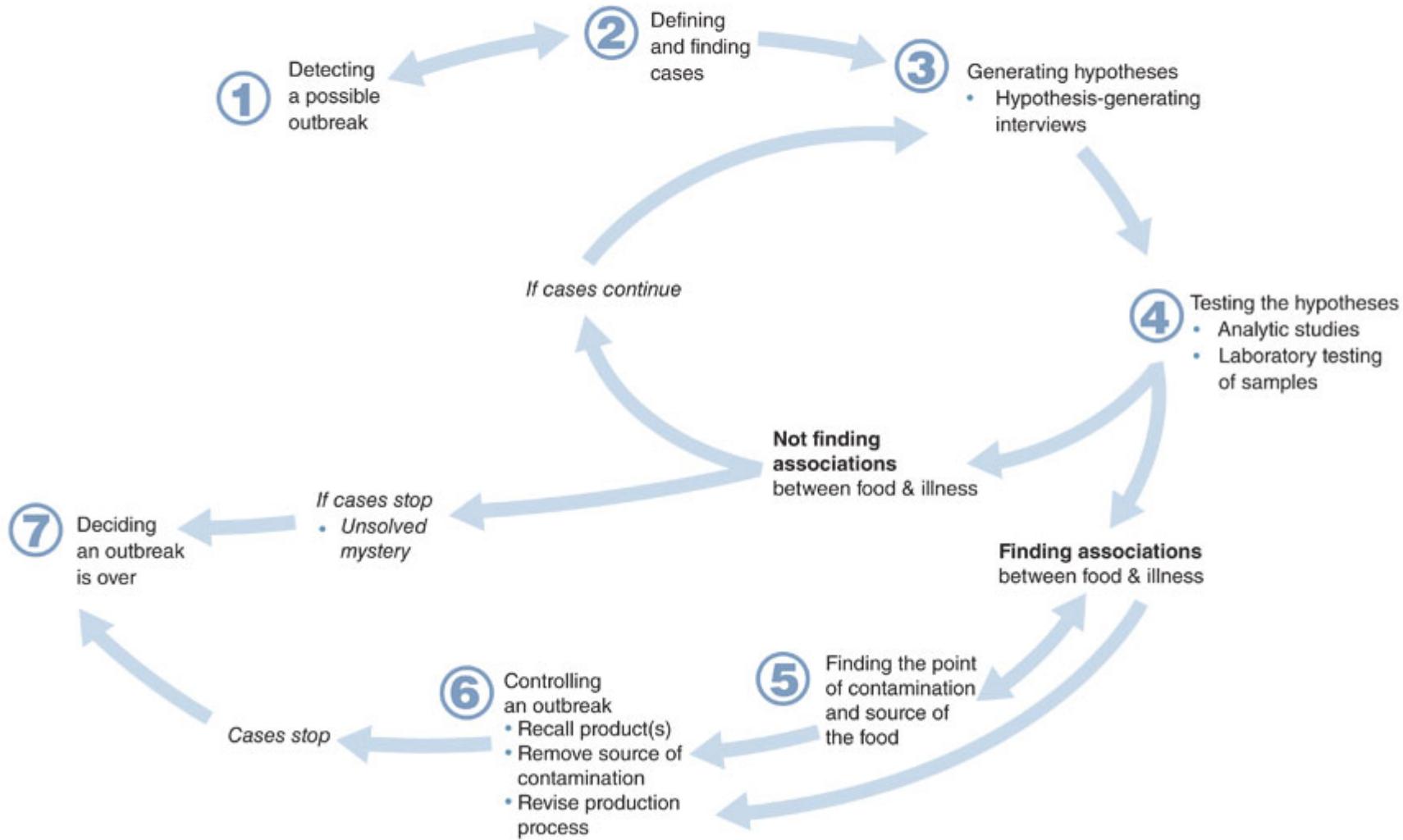
7. Develop hypotheses based on the following
 - a. existing knowledge (if any) of the disease
 - b. analogy to diseases of known etiology
(food-, water-, air-, and vector-borne)
8. Test hypotheses
 - a. further analyze existing data
(case – control studies)
 - b. collect additional data
 - c. as necessary, reconsider / refine hypotheses and execute additional studies
(epidemiologic, laboratory, environmental)
9. Recommend control and prevention measures
 - a. control of present outbreak
 - b. prevention of future similar outbreaks
10. Communicate findings
 - a. share information with public officials
 - b. interactions with the Public and Press

Steps of an outbreak investigation

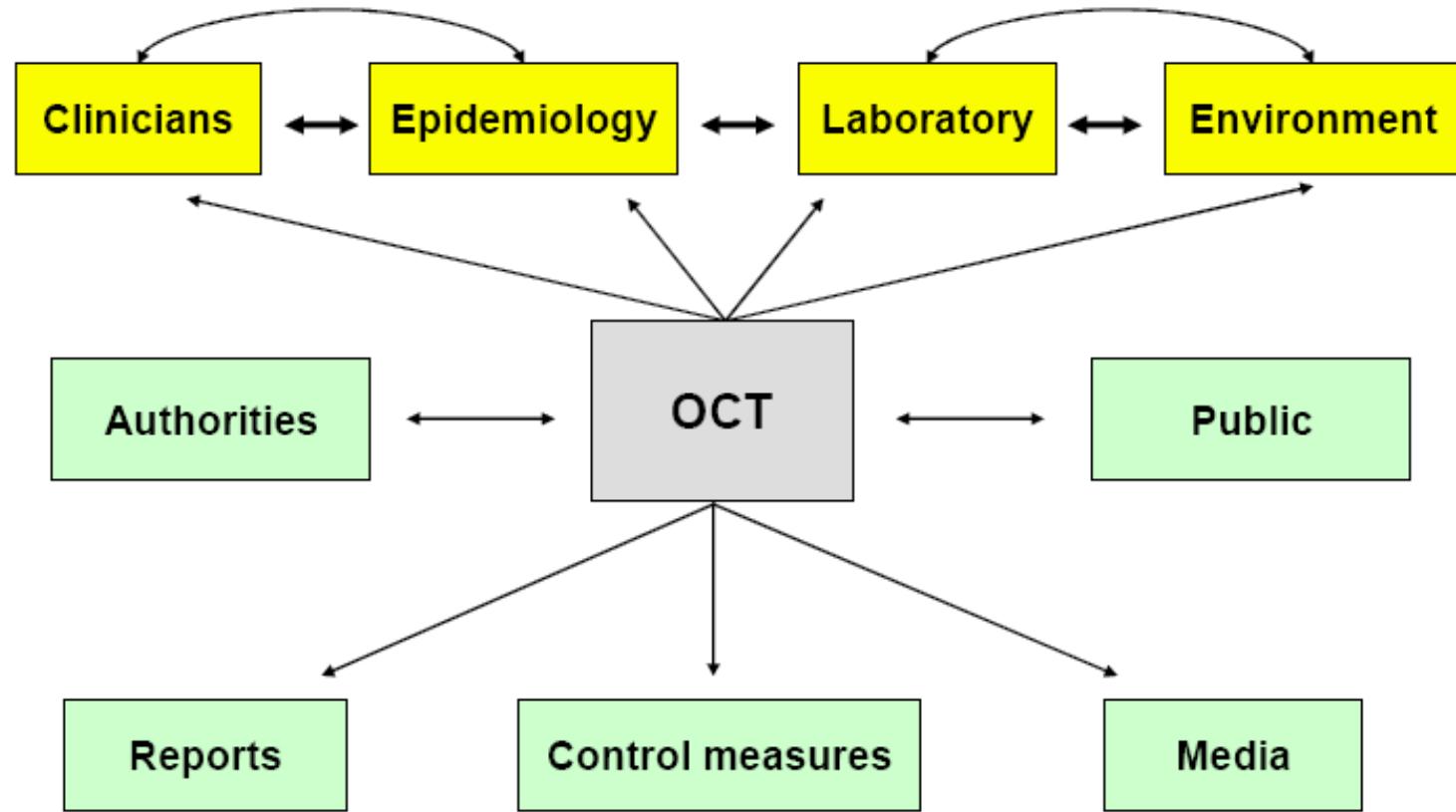
1. Confirm outbreak and diagnosis
2. Define case
3. Identify cases and obtain information
4. Descriptive data collection and analysis
5. Develop hypothesis
6. Analytical studies to test hypotheses
7. Special studies
8. Communicate, including outbreak report
9. Evaluate

Implement control measures

Steps in a Foodborne Outbreak Investigation



Coordinating role of the outbreak control team (OCT) in an outbreak investigation



Preparedness

Committee
Priorities
Plan
Co-ordination
Responsibilities
Resources
Supplies
Training
Surveillance
Rapid Response

Outbreak control

Detect & Confirm

Investigate

Analyse

Predict & Prevent

Evaluate

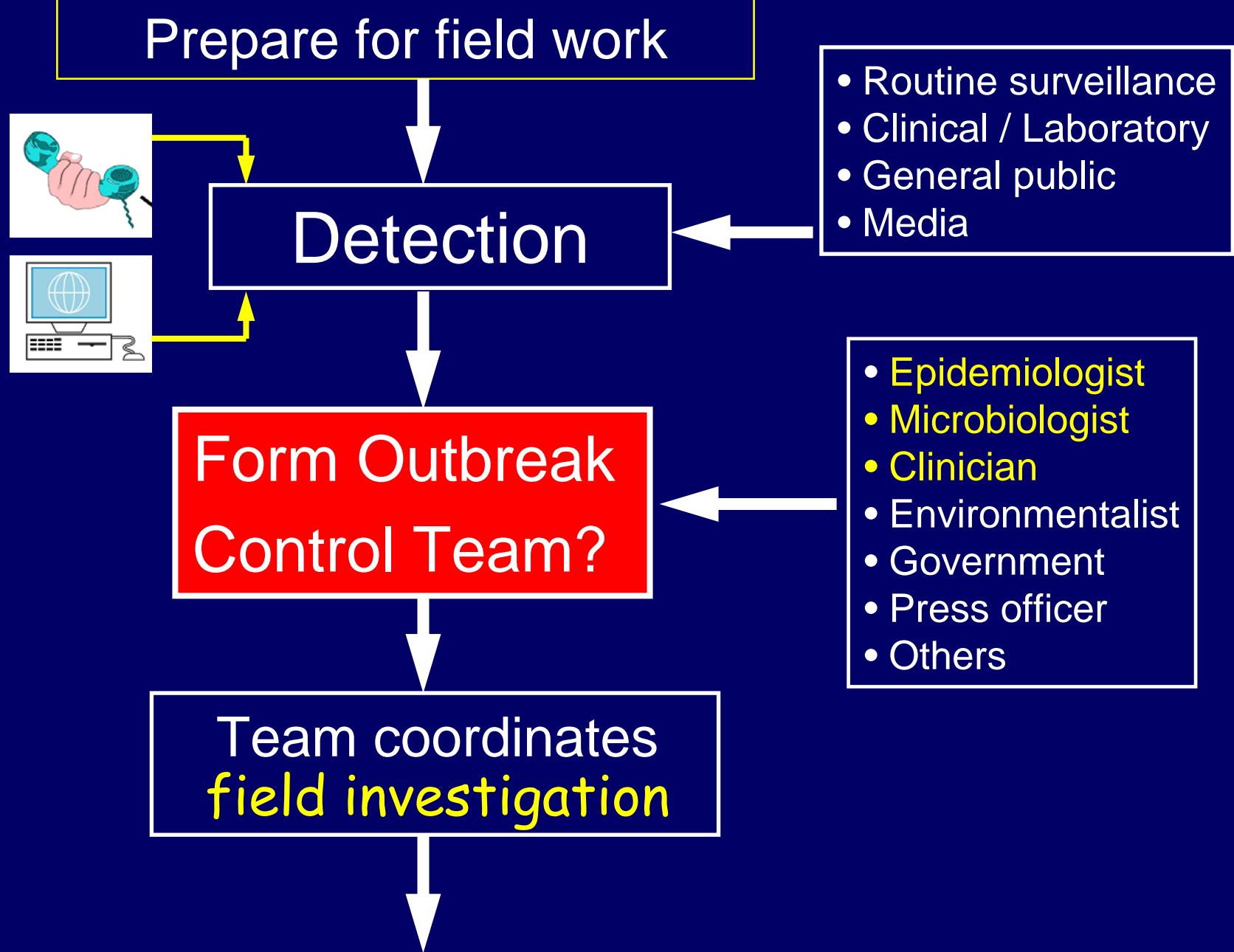
Respond
Treat
Control

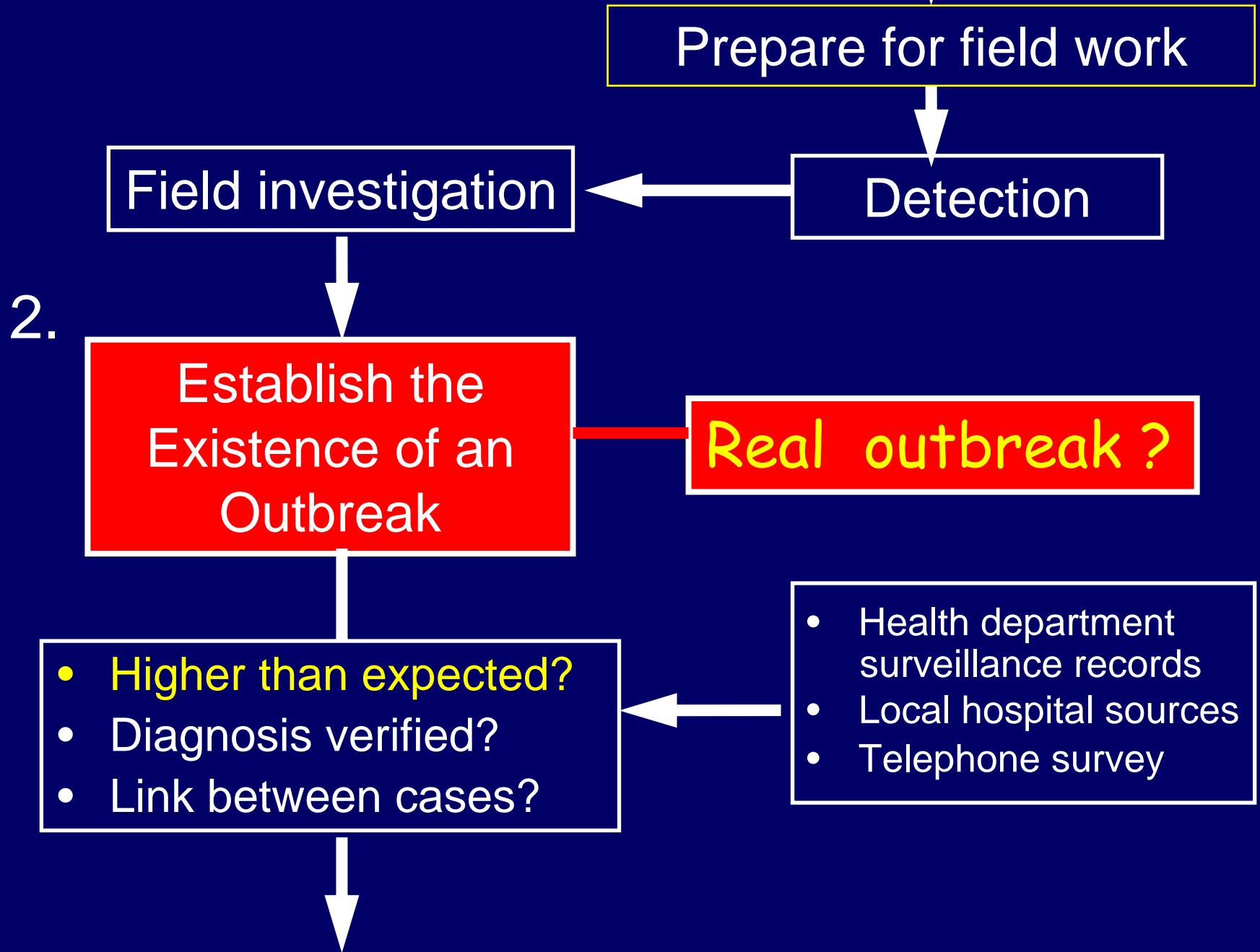
1.

Prepare for field work

- Literature and Technique
- Training
- Coordination
- Investigation group
 - What should be done ?
- Responsibility
 - Who should do it ?
- Resources / Supplies / Equipment
- Administrative and personal arrangements
- Local contacts

1.





2.

Real Outbreak Confirmed



Immediate control
measures?

Further
investigation?



- Prophylaxis
- Exclusion / Isolation
- Public warning
- Hygienic measures
- Others

- Unknown aetiology
- Cases serious
- Cases still occurring
- Public pressure
- Training opportunity
- Scientific interest

Real Outbreak Confirmed

3.

- Clinical findings
- Laboratory results
- Appropriate specimens
- Talk to some of patients
- Questionnaire

Verify the
diagnosis

Verify the diagnosis

Case definition

- Confirmed
Laboratory verification
- Probable
Typical clinical features of the disease without laboratory confirmation
- Possible
Usually has fewer of the typical clinical features

"Get it while you can."

- Identifying information
- Demographic information
- Clinical information
- Risk factor information

Define and Identify Cases

4.

5.

Define and Identify Cases

Describe and Orient the Data

Descriptive epidemiology

Person - Who are the cases?

Place - Where do they live?

Time - When did they become ill ?

Define and Identify Cases

Describe and Orient the Data
Summarize what you know

Explain why and how

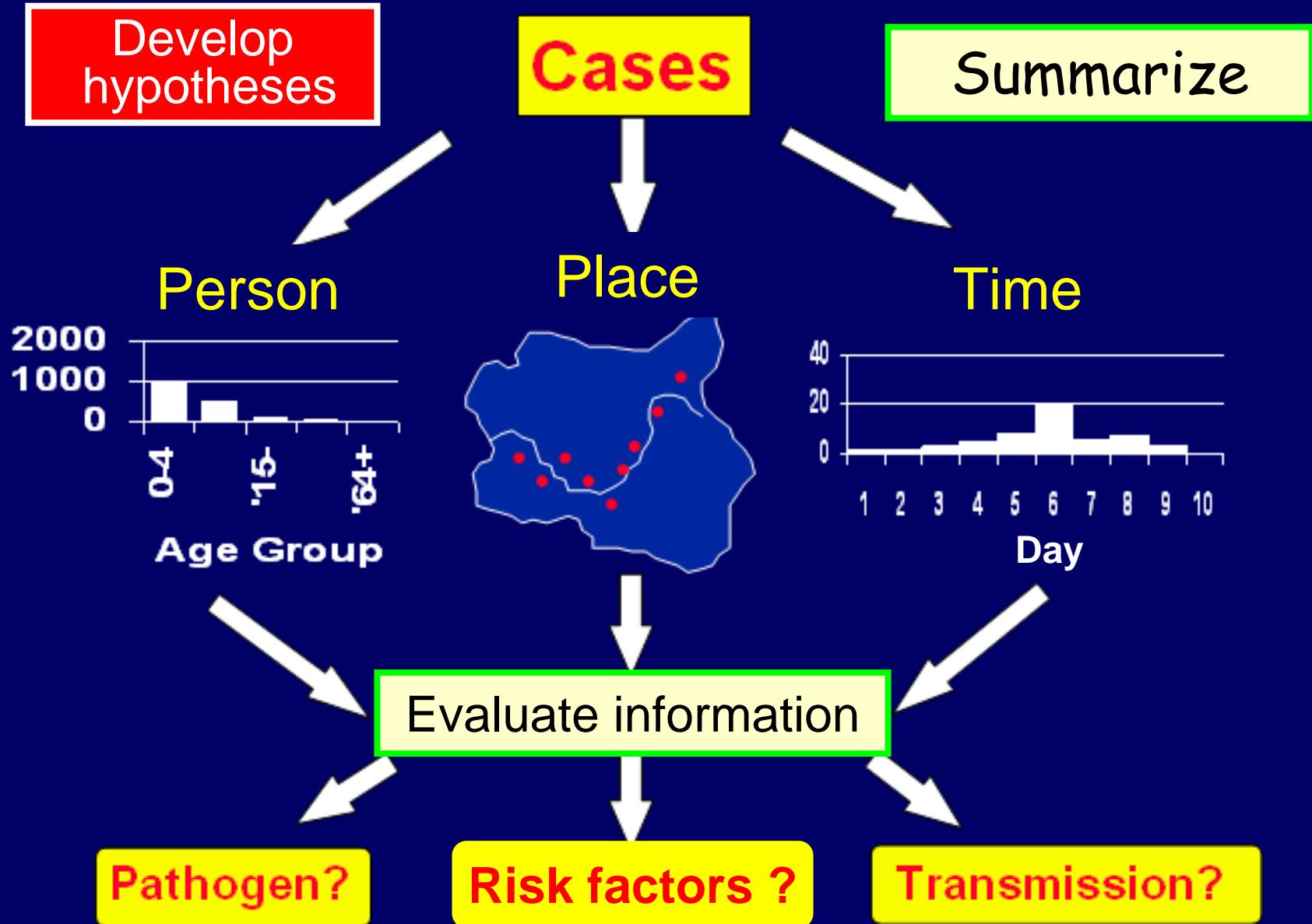
- The outbreak occurred
- Source of the agent
- Mode of transmission
- Exposures caused the disease

Visit the homes of people who became ill
Questionnaire

6.

Develop hypotheses

6.



Develop hypotheses

7.

Evaluate Hypotheses

Comparison hypotheses
with facts

- test hypotheses
 - cohort studies
 - case-control studies
- Statistical test

Analytic epidemiology

Food – specific Attack Rate for Items Consumed

Item Consumed	Ate				Did Not Eat			
	Sick	Total	Sick %	(Attack Rate)	Sick	Total	Sick %	(Attack Rate)
Beverage	179	264	67.8		22	50	44.0	
Egg salad	176	226	77.9		27	73	37.0	

- For both beverage and egg salad, attack rates are clearly higher among those who ate (or drink) than among those who did not
- This table dose not permit us to determine whether the beverage or the egg salad accounted for the outbreak

Gordis L: Epidemiology, ed 2. Philadelphia, W.B. Saunders Company, 2000

Cross - Table Analysis for Egg Salad and Beverage Consumed

		Ate Egg Salad			Did Not Ate Egg Salad			
Drank Beverage	Sick	Well	Total	Sick %	Sick	Well	Total	Sick %
				(Attack Rate)				(Attack Rate)
Yes	152	49	201	75.6	19	53	72	26.4
No	12	3	15	80.0	7	21	28	25.0

- In order to answer this question, we use the technique of **cross-tabulation**
- Looking at the data **by columns**, drinking the beverage did not increase the incidence of streptococcal illness (75.6% vs. 80% and 26.4% vs. 25%)
- By **horizontal**, eating egg salad significantly increased the attack rate of the illness (75.6% vs. 26.4% and 80% vs. 25%).

Thus, the egg salad is clearly implicated.

Gordis L: Epidemiology, ed 2. Philadelphia, W.B. Saunders Company, 2000

Evaluate Hypotheses

- When analytic epidemiological studies do not confirm initial hypotheses
- **Reconsider the hypotheses**

- Additional epidemiological studies
- Laboratory and environmental studies

8.

Refine Hypotheses and Carry Out Additional Studies

Refine Hypotheses and Carry Out Additional Studies

- Control the source of pathogen
- Risk factors
- Interrupt transmission
- Immunization
- Chemoprophylaxis

9.

Implementing Control and Prevention Measures

Should do at any time during the outbreak !!

Implementing Control and Prevention Measures



Right channel
Right audience
Right message
Right time

10.

Communicate Findings

Steps of Communicable Disease outbreak investigation

1. Preliminary assessment

- Is it an outbreak?
- Confirm numbers
- Is further investigation needed?
- Literature review
- Form Outbreak control team (OCT)
- Initiate immediate control measures

2. Case definition and case findings

Person	Place	Time
Clinical symptoms	Laboratory results	

3. Descriptive study

data collection and analysis

Epidemic curve

Generation of hypothesis

- Count Cases
- Control outbreak
- Diagnosis verify
- Communicate result
- Surveillance continues to evaluate control
- Hypothesis formulation
- Additional studies Micro / Env
- Test hypothesis Analytic study
- Epidemic Conform exists
- Identify cases Create case definition
- Tabulate and orientate data Person / Place / Time
- Describe epidemic

Steps of Communicable Disease outbreak investigation

4. Analytical study

cohort or case control
to test hypothesis

5. Verify hypothesis

microbiological or environmental tests

6. Initiate control measures

- Remove source Isolate / Treat case
- Destroy food Close shop
- Protect those at risk Hygiene Hand washing
- Water boiling Prophylaxis e.g. hepatitis B injections
- Prevent recurrence
- Recommendations Guidelines

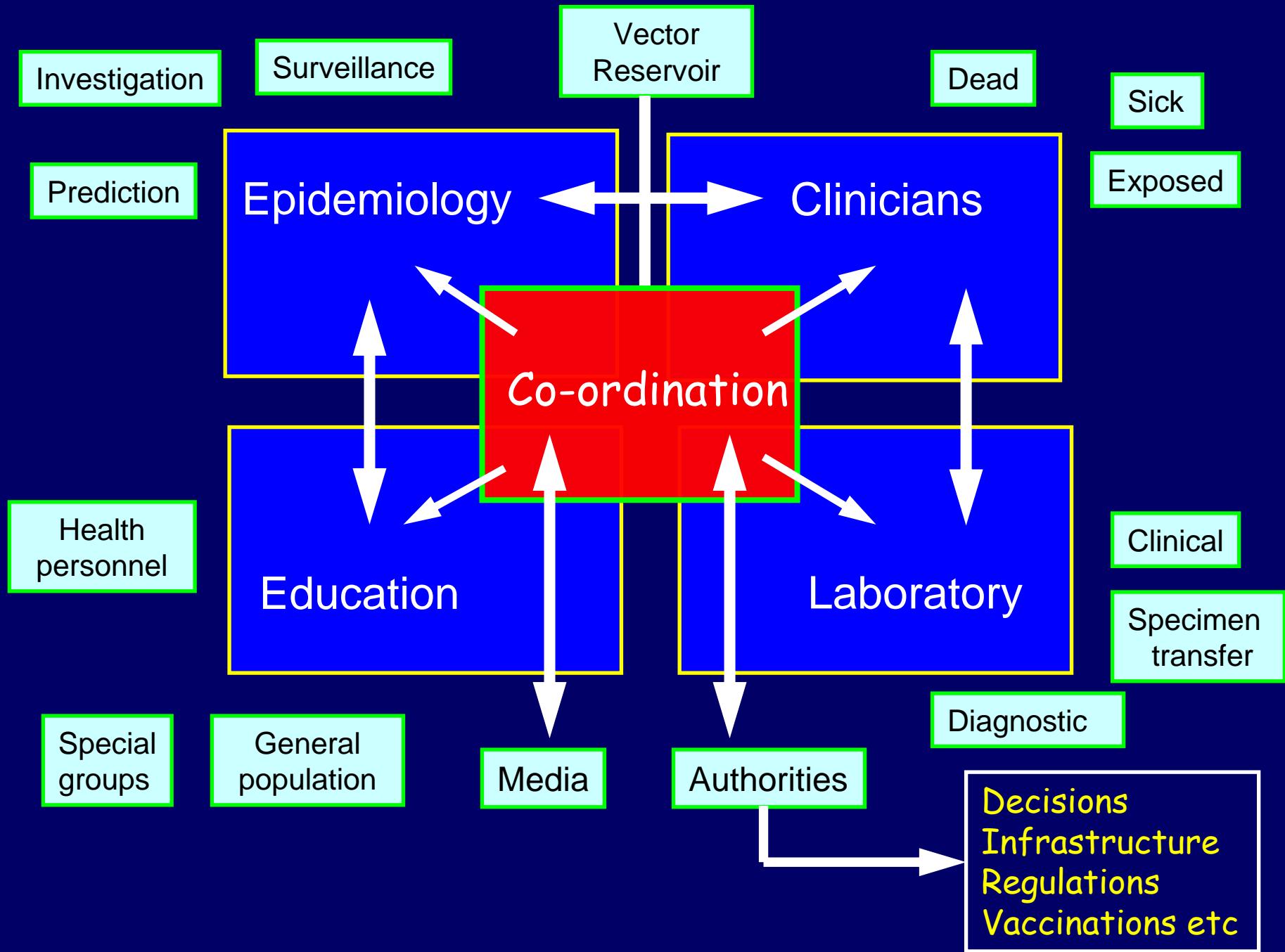
7. Communication

Media Reports Guidelines

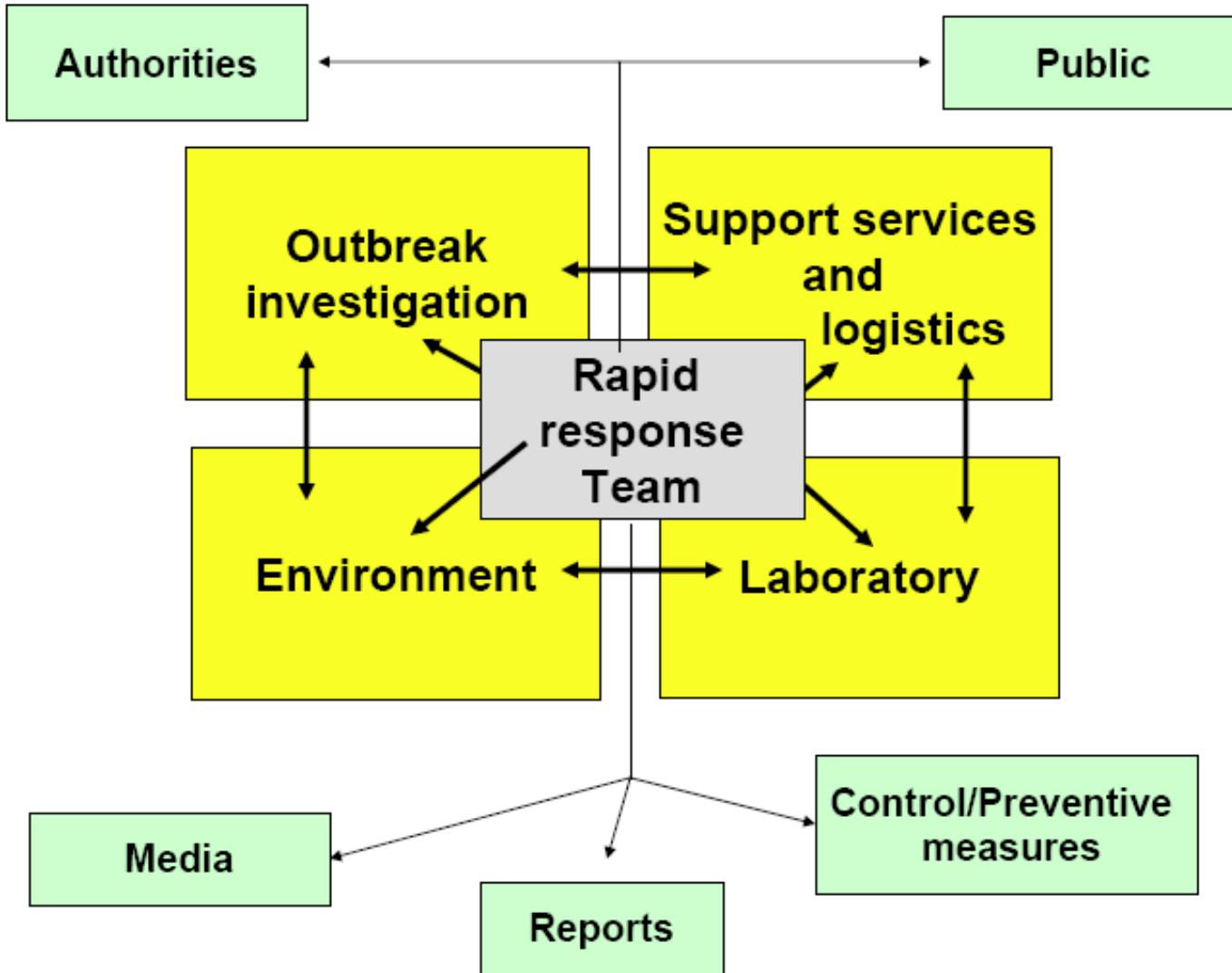
Better information leads to better results

- A good **description** of
 - Person
 - Place
 - Time
- Good **data collection and preservation of samples**
- A well coordinated multidisciplinary team

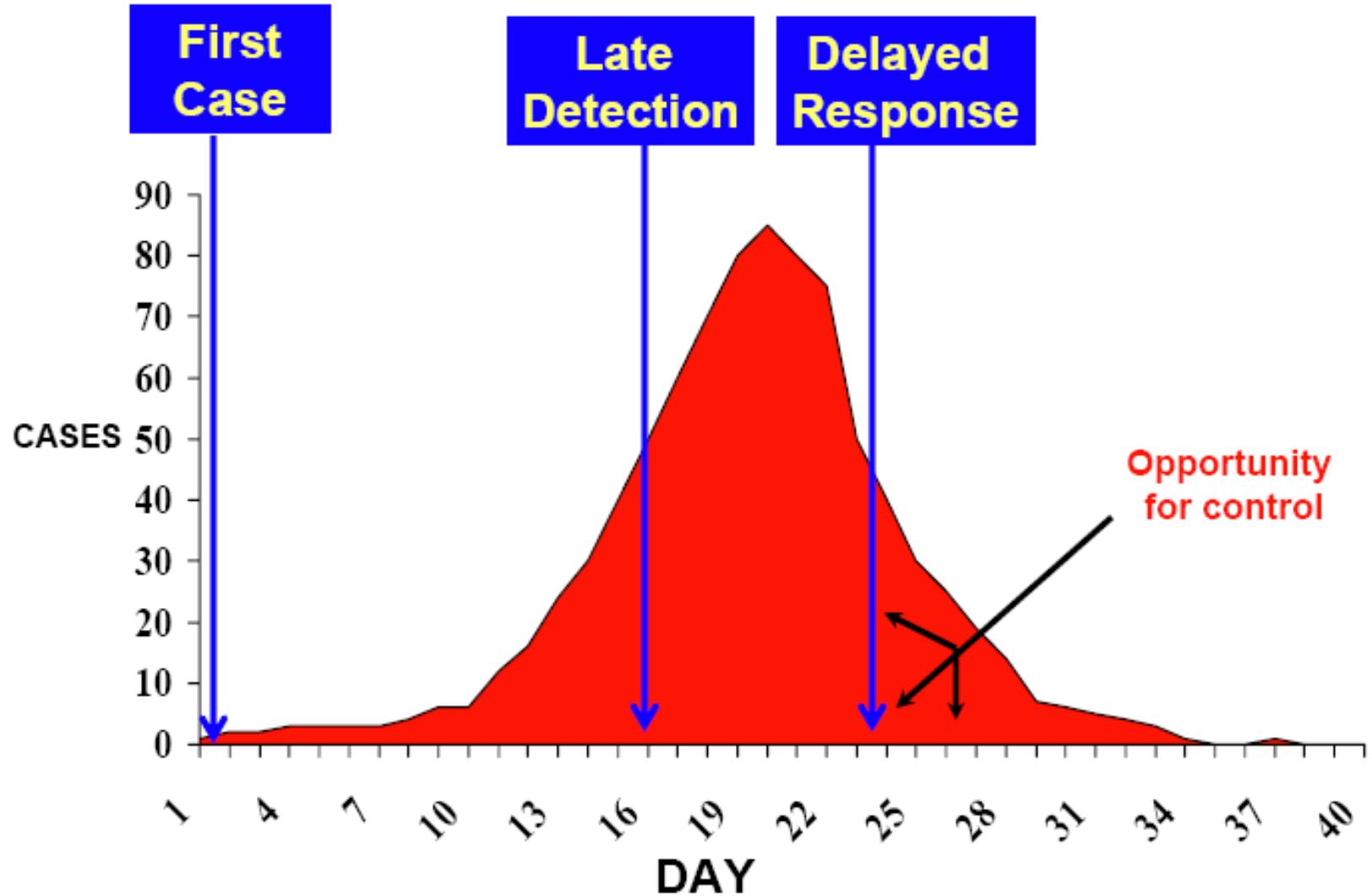




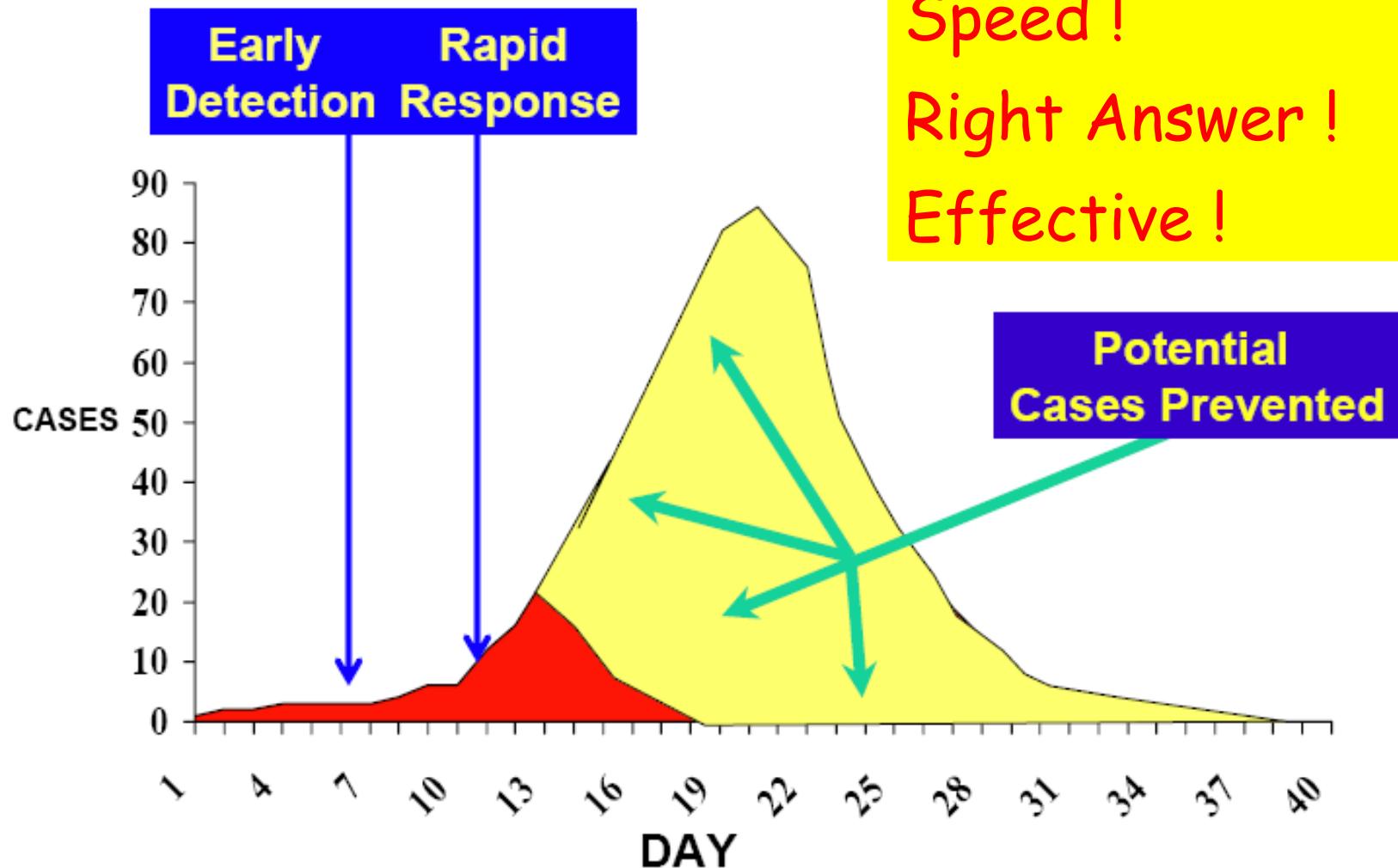
Rapid and coordinated response



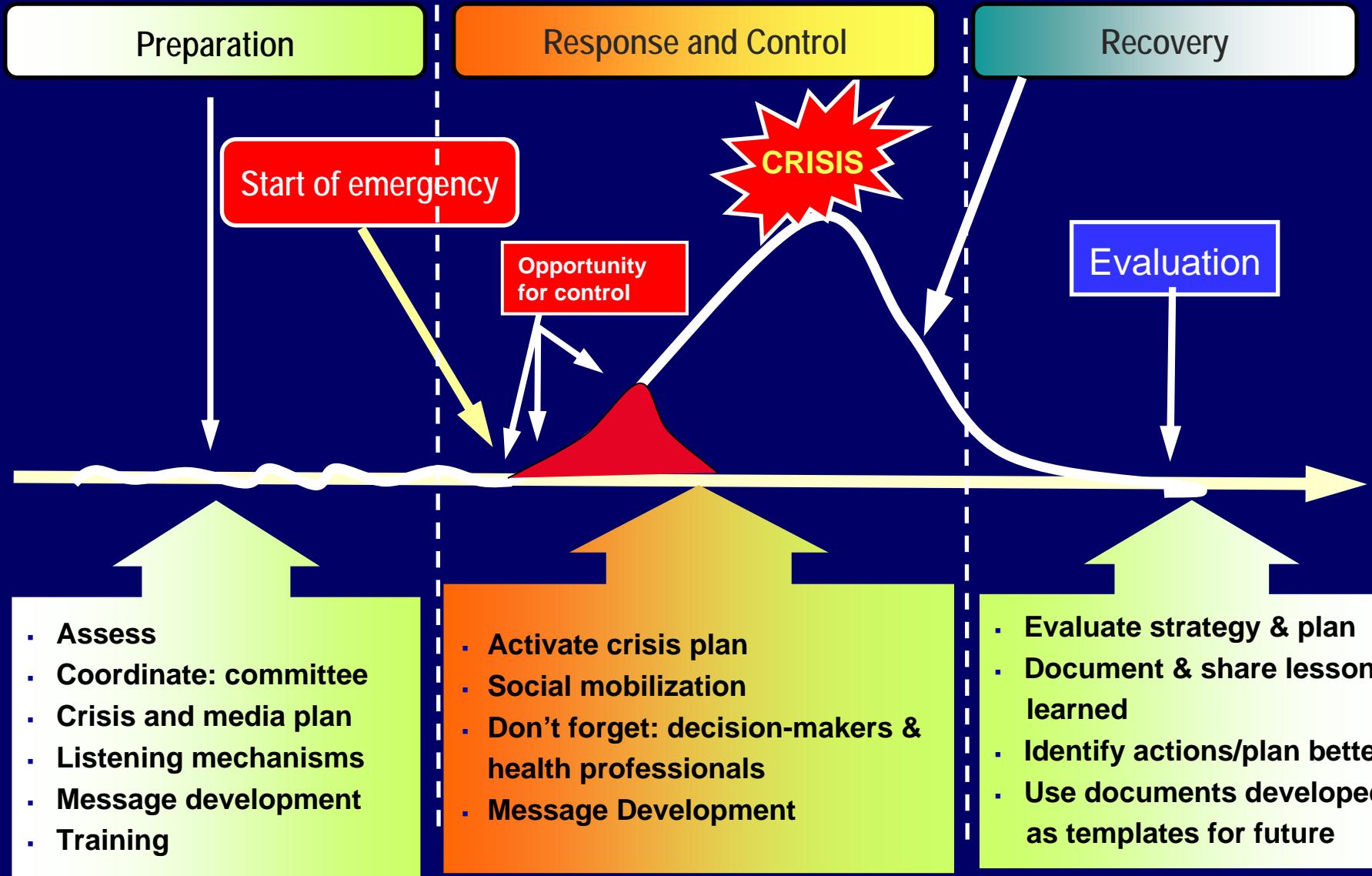
Outbreak Detection and Response Without Preparedness



Outbreak Detection and Response With Preparedness



Risk Communication for PHEs



Since the early 1950s, approximately 3,200 EIS officers have responded to requests for epidemiologic assistance (Epi-Aid) within the United States and throughout the world. Requests to assist with emergency responses, investigate infectious and environmental disease outbreaks, and quantify the impact of chronic diseases are examples of Epi-Aid responses.

1950s

- Contamination of killed poliovirus vaccine with live virus
- Childhood lead poisoning from peeling paint

1960s

- Smallpox epidemics through 1977
- Hong Kong influenza epidemics

1970s

- Legionnaires disease
- Ebola virus in Zaire and Sudan
- Aspirin-associated Reye syndrome

1980s

- Toxic shock syndrome
- HIV/AIDS
- Accutane-associated birth defects

1990s

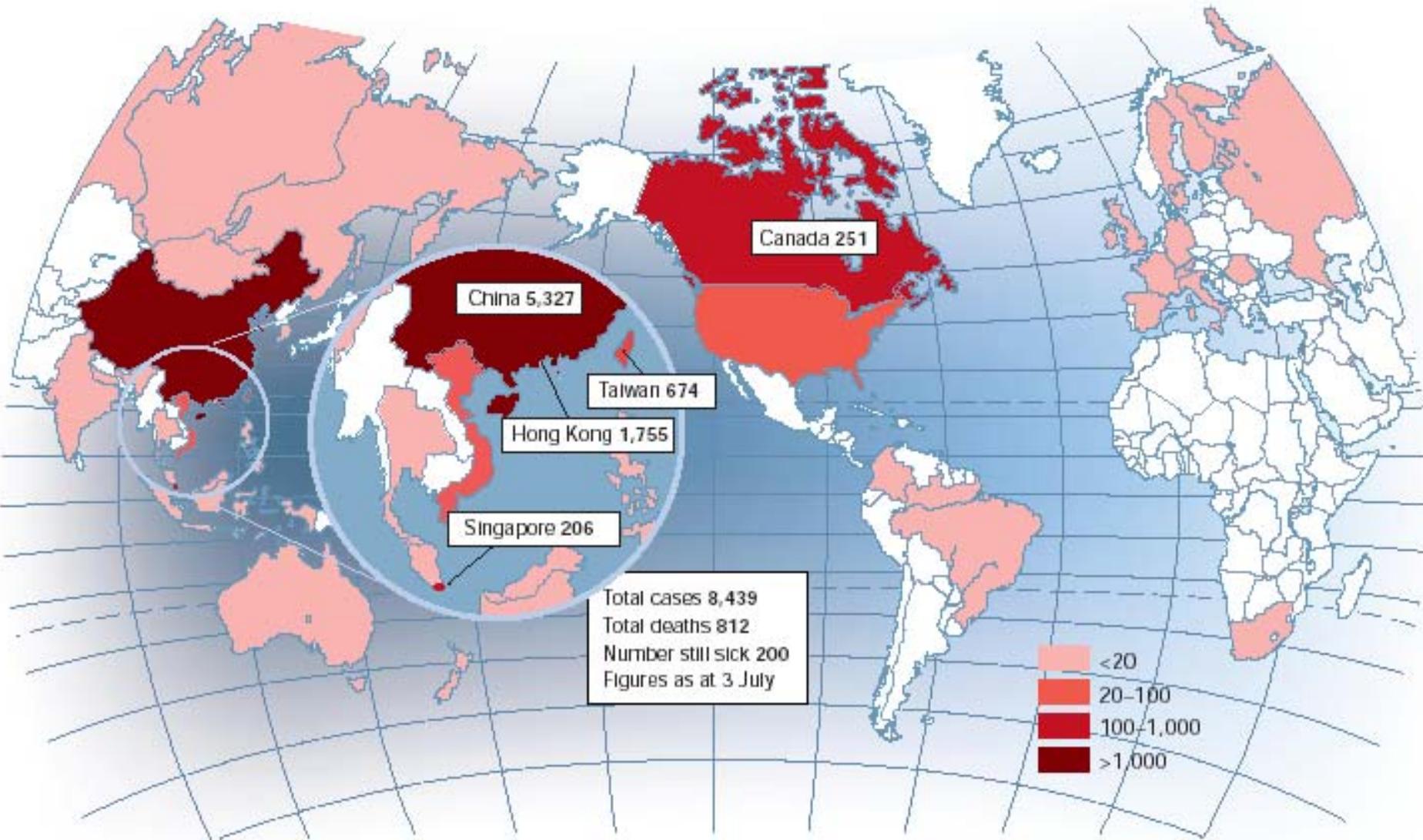
- Health effects of Hurricane Andrew
- West Nile virus epidemic
- Cardiac valvulopathy associated with fenfluramine (fen-phen)

2000s

- 9/11 terrorist attacks
- Anthrax terrorist attacks
- Hurricane Katrina
- Nationwide salmonellosis outbreaks
- Pandemic H1N1 influenza

SARS

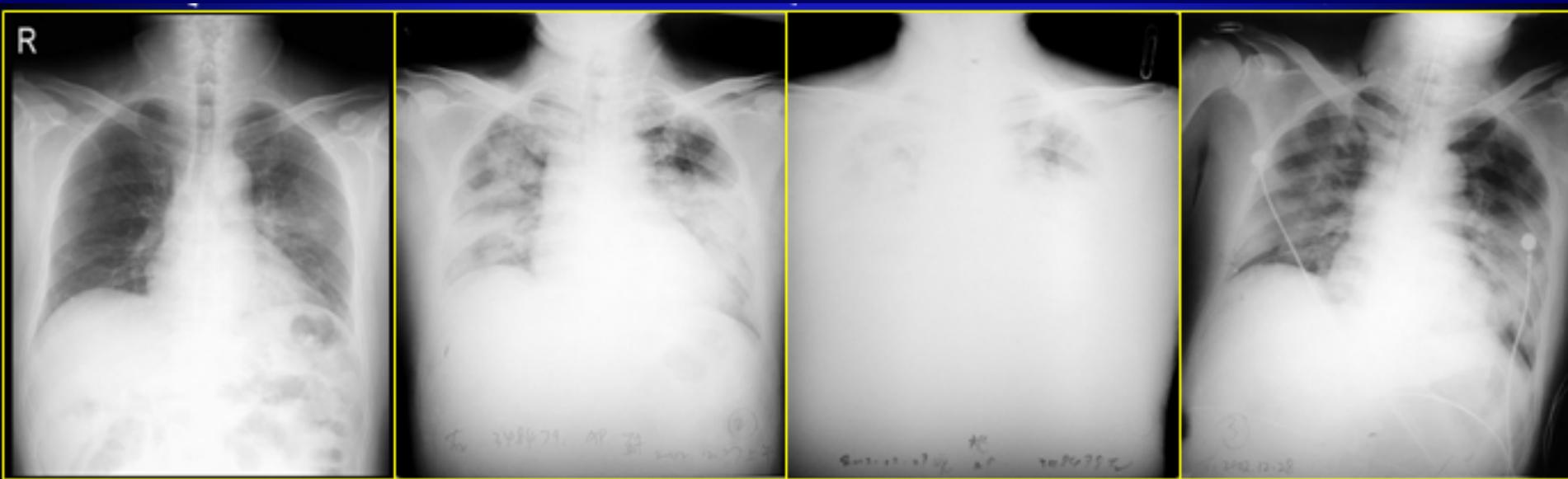
(Severe Acute Respiratory Syndrome)



Pattern of an epidemic: the total number of SARS cases worldwide (above) was contained thanks to global alerts and patient quarantine; and the number of new cases (right) has now tailed off.

1,000

SARS is the first deadly infectious disease of the 21st Century. It started in Guangdong of China in November 2002. An epidemic of SARS affected 26 countries and resulted in more than 800²³¹ cases in 2003.



Source: Dr. Zhong, Nan shan

Spread from Hotel M

Reported as of March 28, 2003

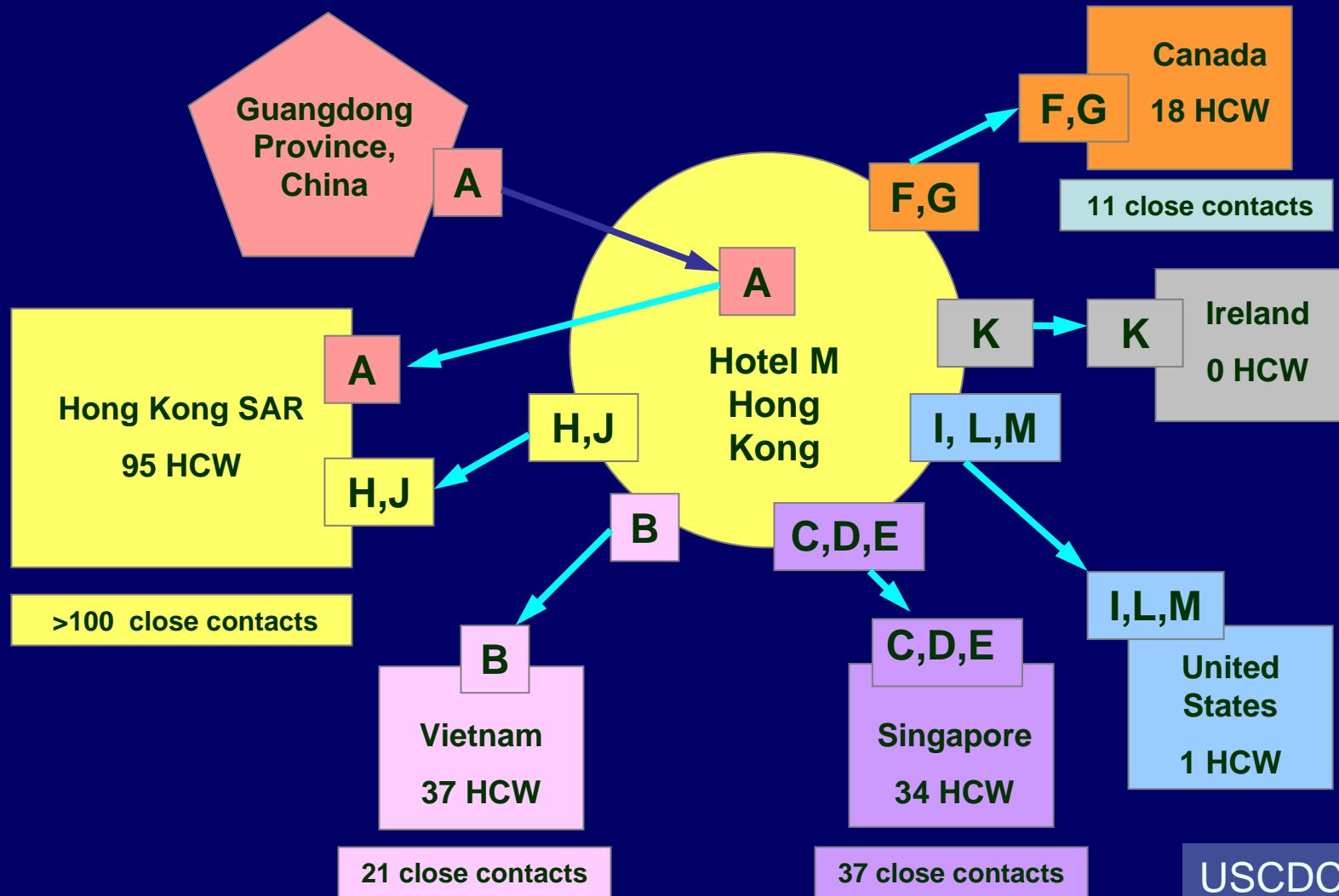
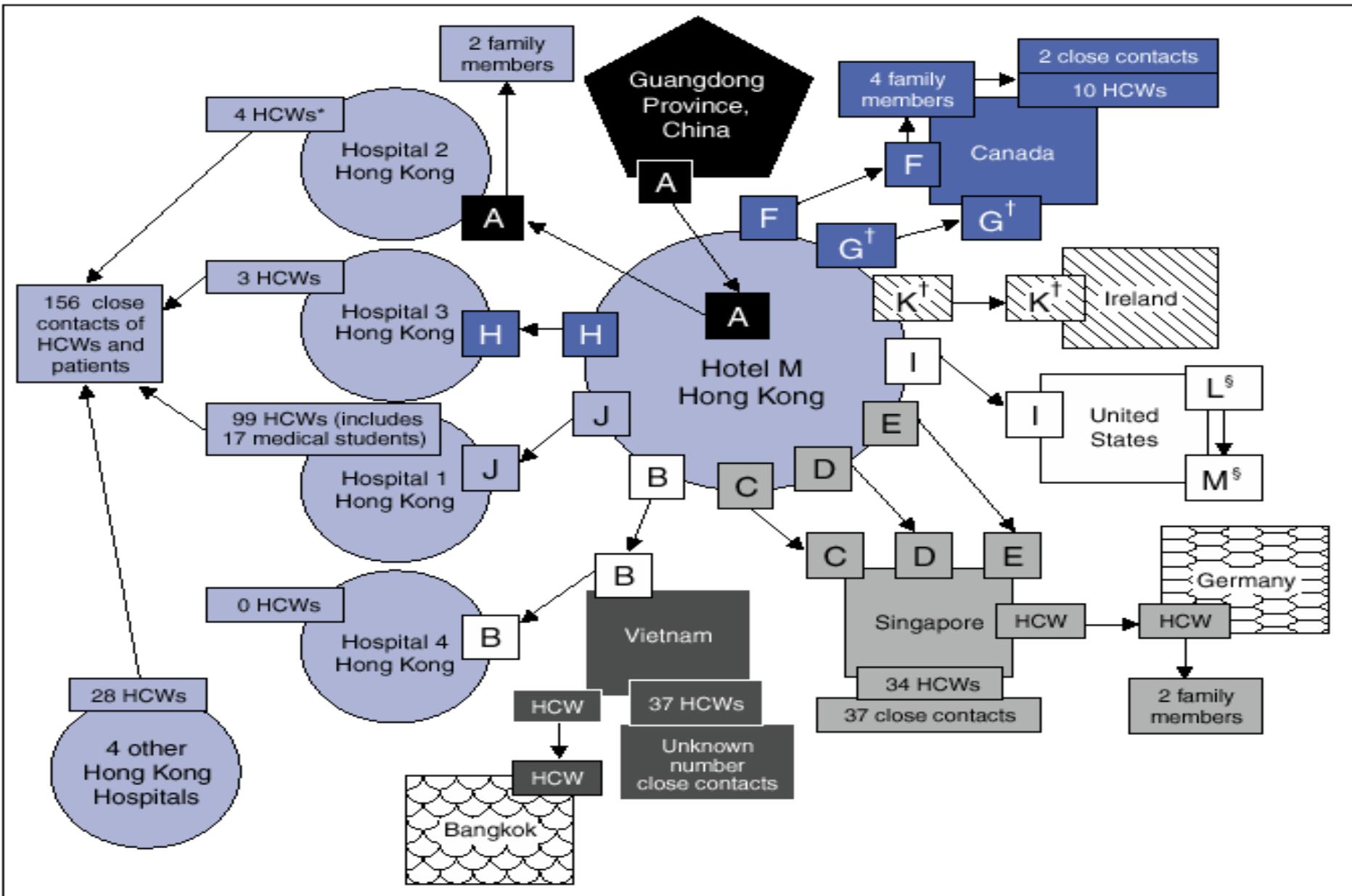


FIGURE 1. Chain of transmission among guests at Hotel M — Hong Kong, 2003



* Health-care workers.

† All guests except G and K stayed on the 9th floor of the hotel. Guest G stayed on the 14th floor, and Guest K stayed on the 11th floor.

§ Guests L and M (spouses) were not at Hotel M during the same time as index Guest A but were at the hotel during the same times as Guests G, H, and I, who were ill during this period.

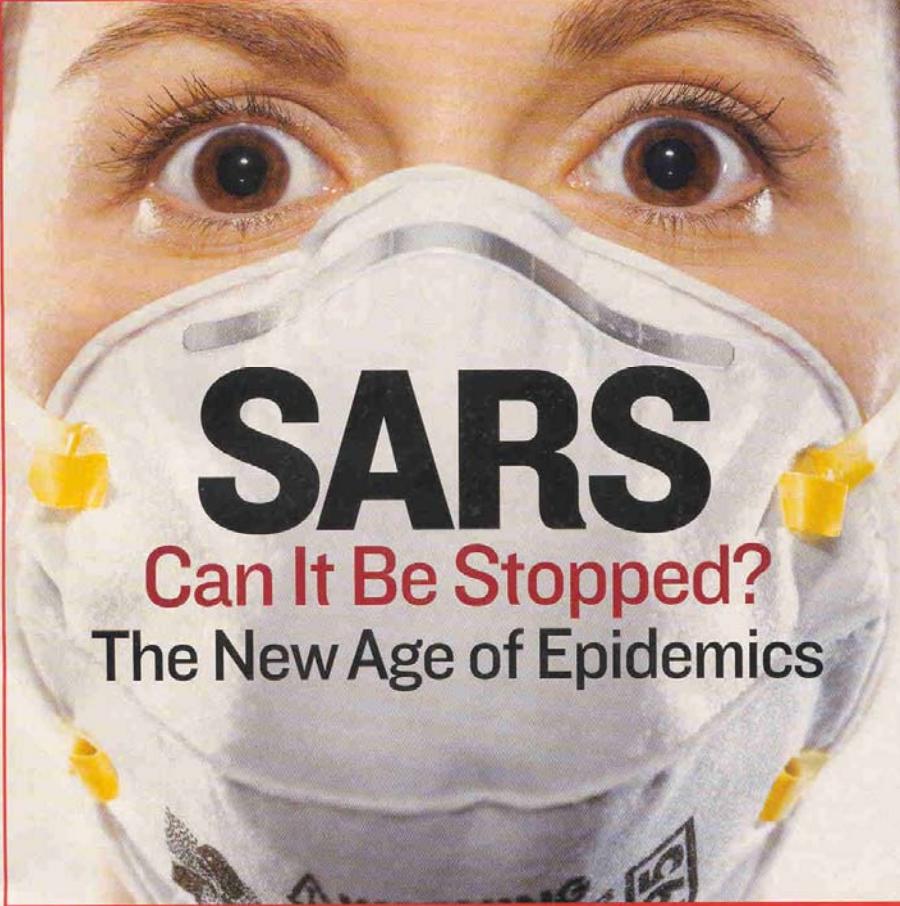
PYONGYANG'S BOMB • HOT SUMMER MOVIES

Newsweek

THE INTERNATIONAL NEWSMAGAZINE

newsweek-int.com

May 5, 2003



SARS

Can It Be Stopped?
The New Age of Epidemics

9 770163 706002



18

Australia	A\$13.95	China	US\$13.95	Malaysia	RM8.00	Philippines	P12.50	Sri Lanka	Rs.100.00
Bangladesh	BDT22.00	Hong Kong	HK\$25.00	Maldives	R15.00	Palestine	NIS 10.00	Turkey	TRY 10.00
Burma	K27.00	India	Rs 19.00	Myanmar	K1.15	Papua New Guinea	P10.00	U.S. Territories	US\$13.95
China	Rs 46.75	Indonesia	Rs 15.00	Nepal	NR 7.00	Peru	US\$7.00	Taiwan	NT\$13.95
			(PST 10.00)	New Zealand	NZ\$ 10.00	Thailand	B120.00	U.S. Forces	US\$17.00

The Economist

APRIL 26TH-MAY 2ND 2003

www.economist.com

Talking to North Korea

PAGE 10

Talking about talks on Kashmir

PAGE 21

The scourge of spam

PAGE 56

America's foreign-policy clique

PAGE 27

The SARS virus

Could it become China's Chernobyl?



Australia... AED 9.95/£10.00
Bulgaria... 19.75/£
Brazil... 16.80/£10.00
Canada... 16.80/£10.00
China... 14.95/£8.75
Fiji... 16.80/£10.00
Hong Kong... 16.80/£
India... 16.80/£10.00
Indonesia... 16.80/£10.00
Japan... 16.80/£10.00
Korea... 16.80/£10.00
Malta... 16.80/£
Myanmar... 16.80/£10.00
Nepal... 16.80/£
New Zealand... 16.80/£10.00
Pakistan... 16.80/£
Philippines... 16.80/£10.00
Singapore... 16.80/£10.00
Tunisia... 16.80/£10.00
Uganda... 16.80/£10.00
Uzbekistan... 16.80/£10.00
Vietnam... 16.80/£10.00
Yemen... 16.80/£10.00

Figure 3. Probable SARS cases in selected sites¹⁶

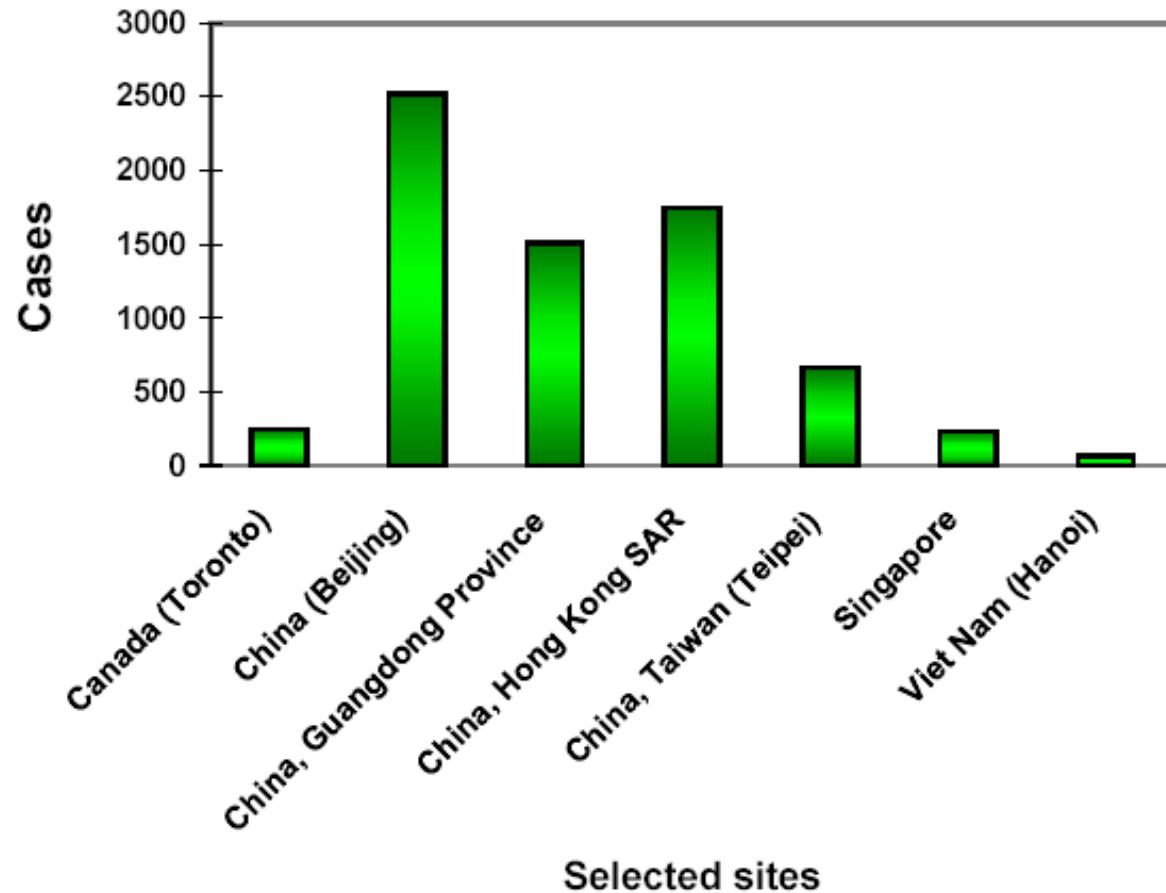
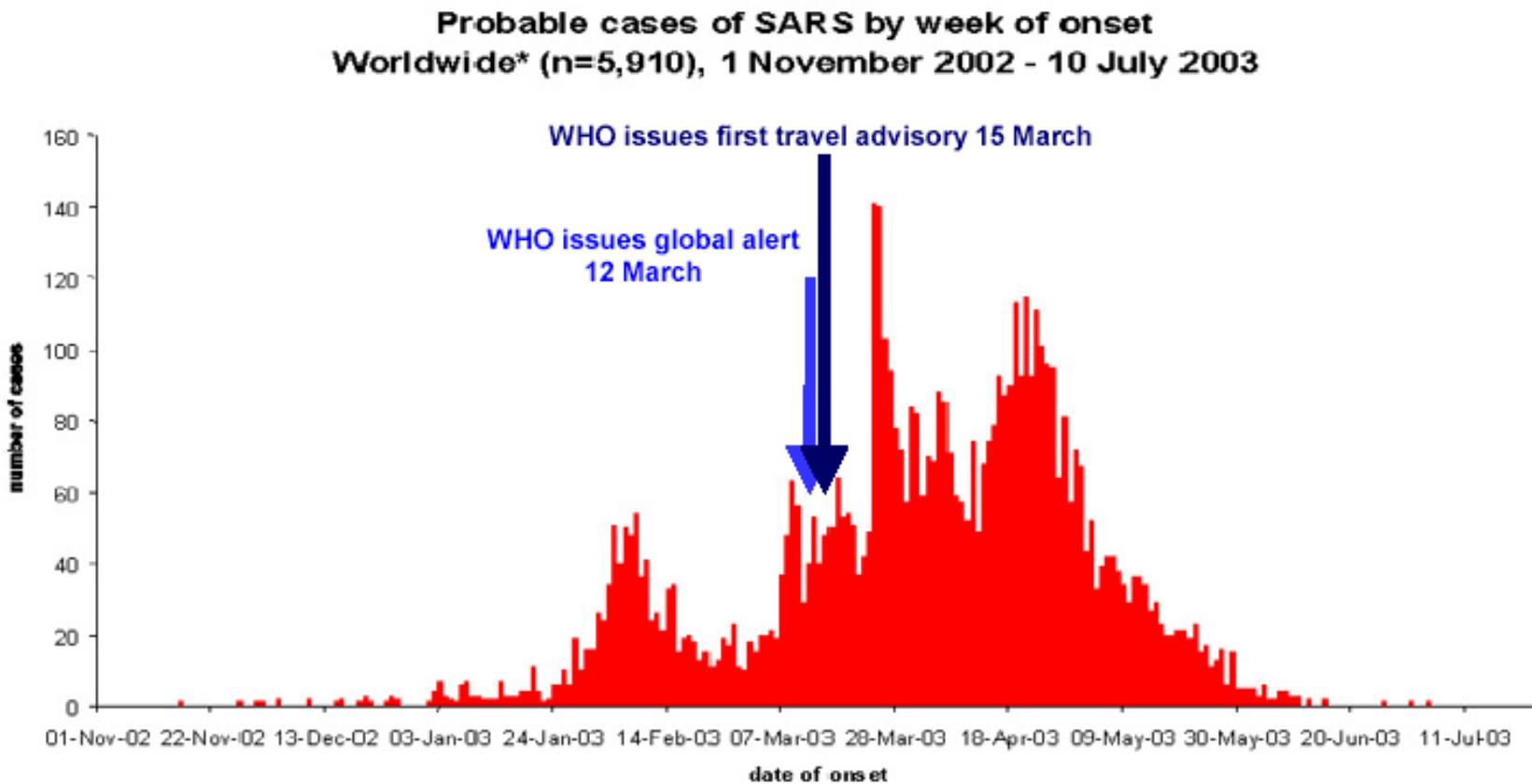
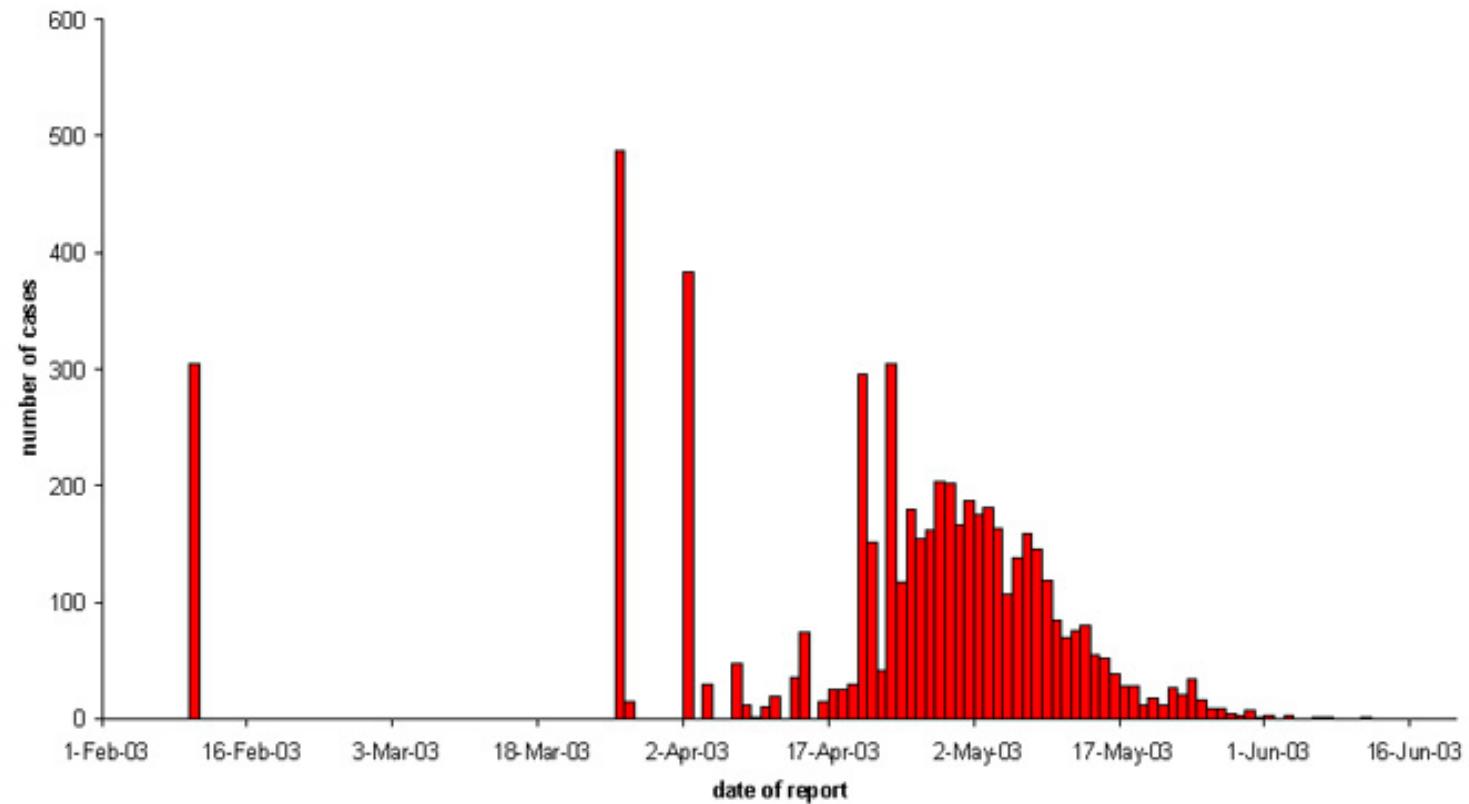


Figure 2.



* This graph does not include 2,527 probable cases of SARS (2,521 from Beijing, China), for whom no dates of onset are currently available.
Adapted from World Health Organization. Epidemic curves – Severe Acute Respiratory Disease (SARS) <http://www.who.int/csr/sars/epicurve/epiindex/en/index1.html>

**Probable cases of SARS by date of report
China, 1 February - 16 June 2003 (n=5,549*)**

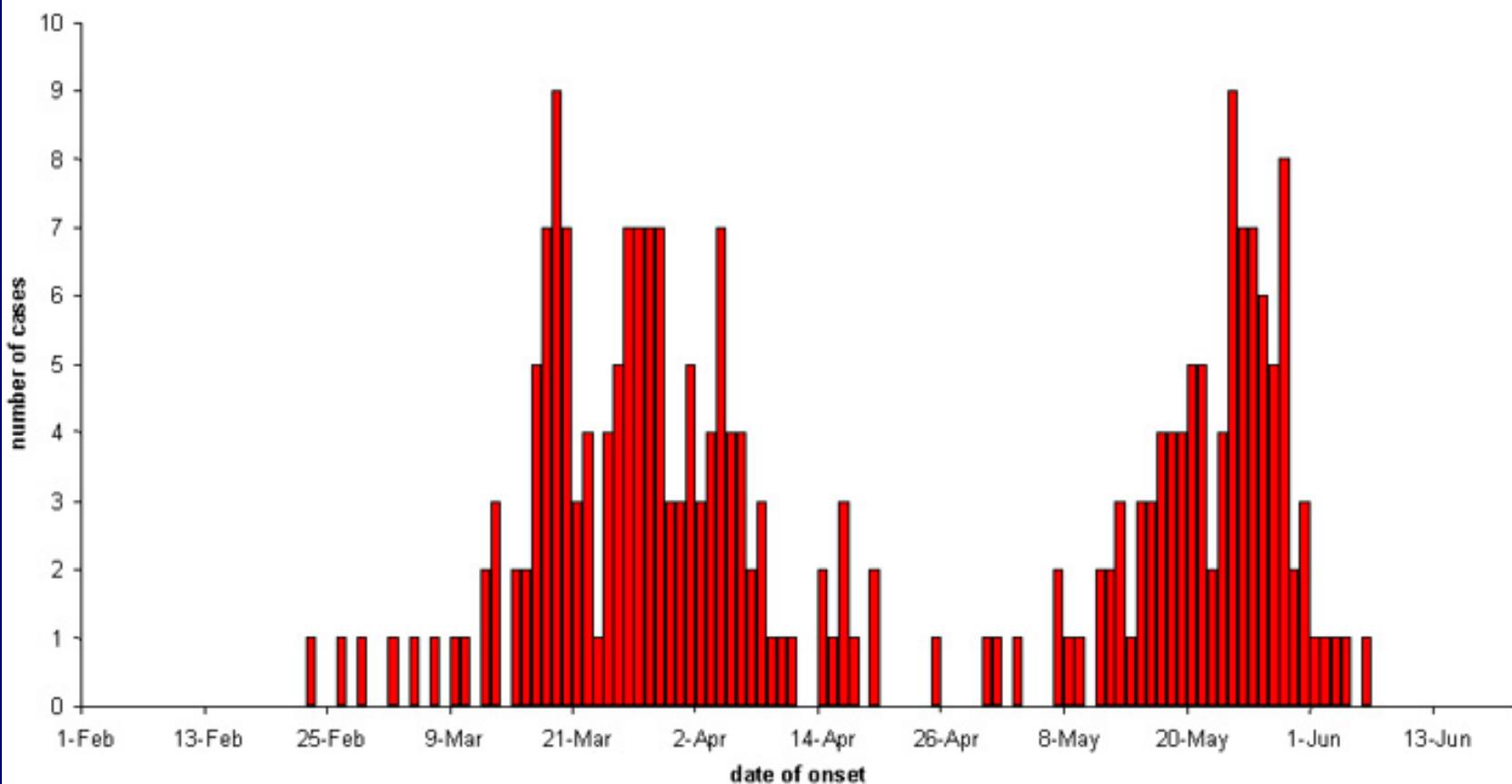


* As of 16 June 2003, 5,326 probable cases of SARS have been reported from China.

This graph includes 223 probable cases of SARS who had been discarded and for whom dates of report could not be identified.

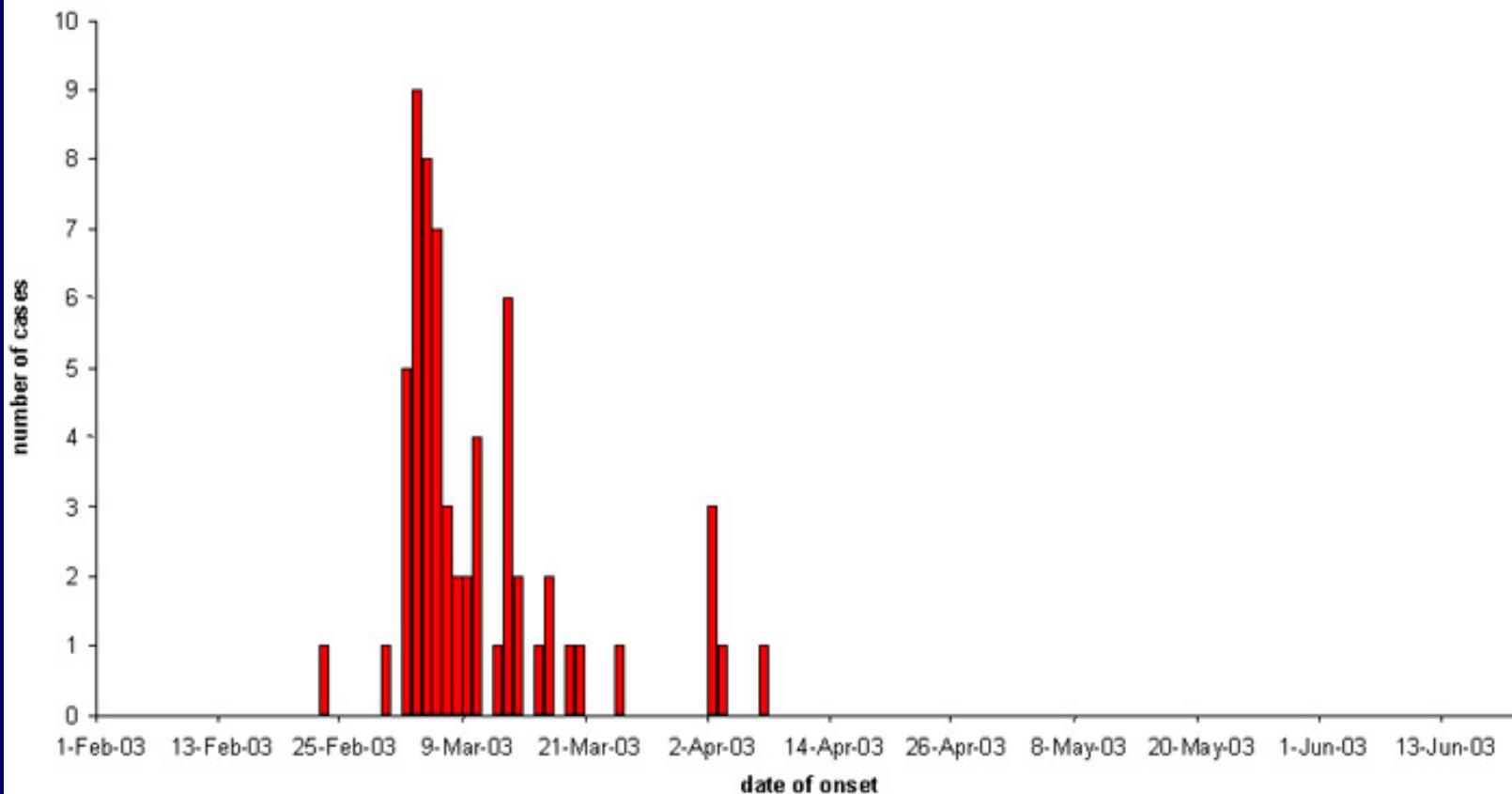
Source: Ministry of Health, China, WHO

**Probable cases of SARS by date of onset
Canada, 1 February - 13 June 2003 (n=242*)**



* As of 16 June 2003, 1 additional probable case of SARS has been reported from Canada for whom no date of onset is available.
Source: Health Canada

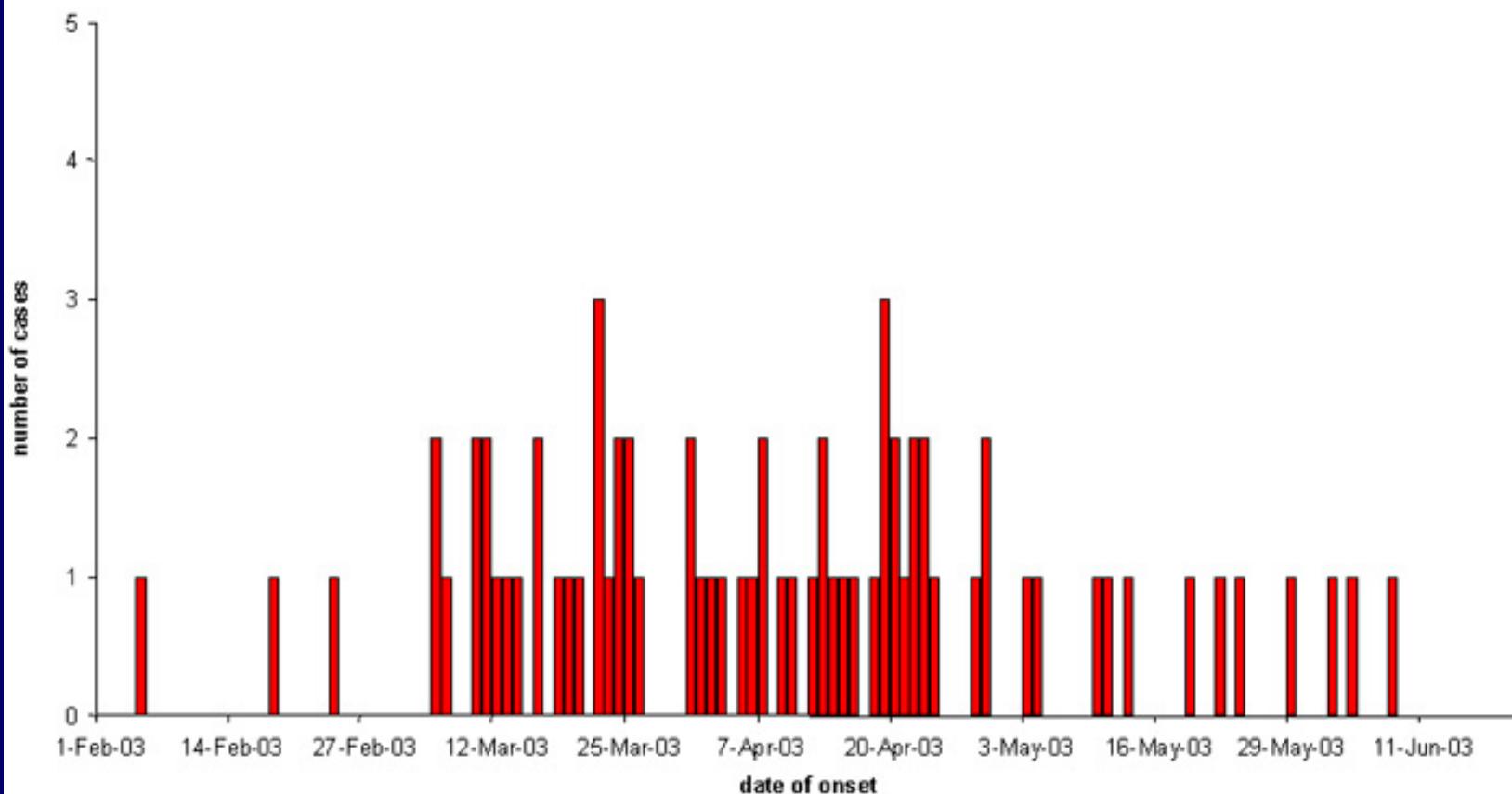
**Probable cases of SARS by date of onset
Viet Nam, 1 February - 16 June 2003 (n=62*)**



* As of 16 June 2003 an additional probable case of SARS has been reported from Viet Nam for whom no date of onset is currently available.

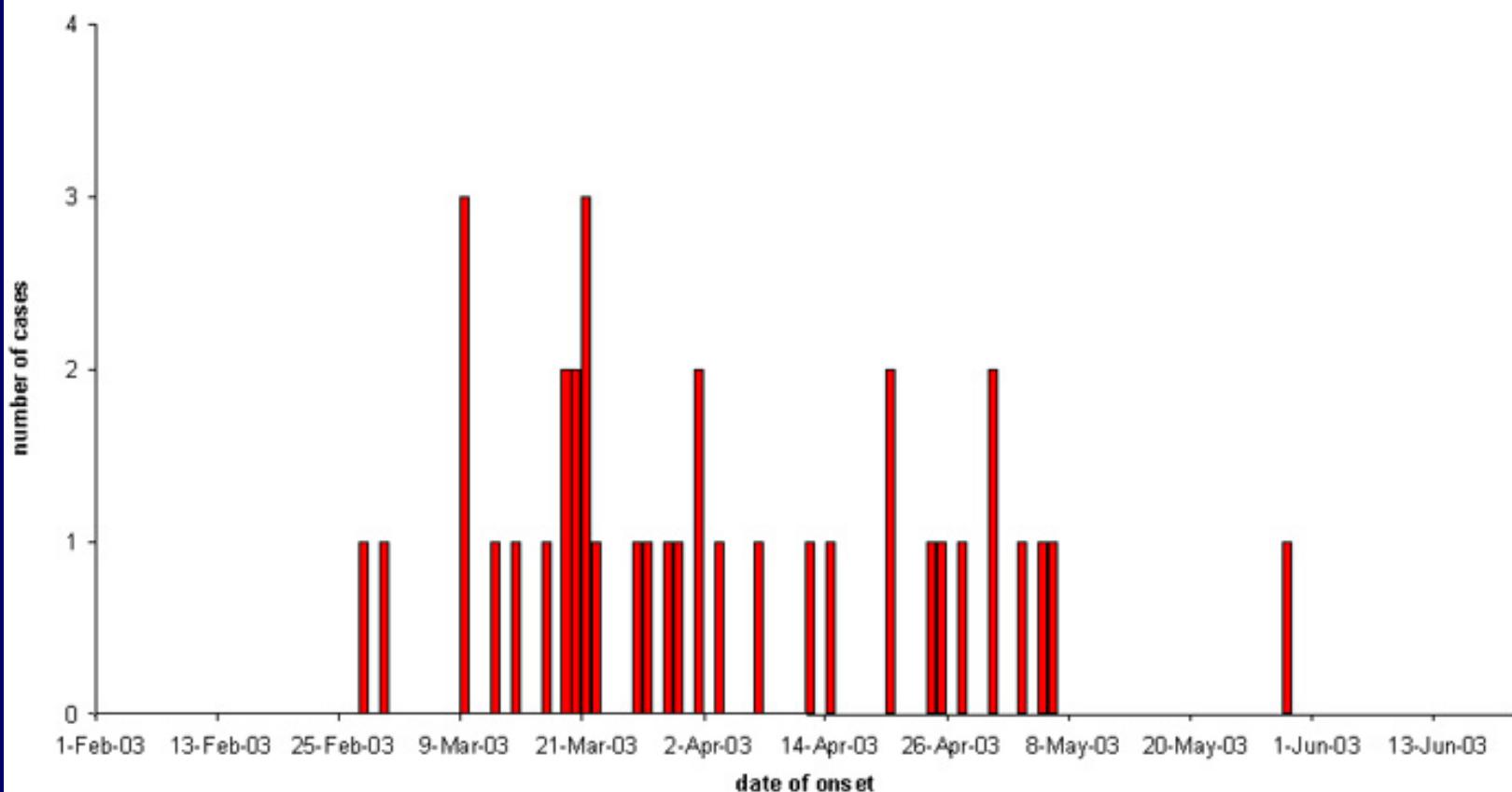
Source: Ministry of Health, Viet Nam, WHO

Probable cases of SARS by date of onset
United States of America, 1 February - 13 June 2003 (n=71*)



*As of 16 June 2003, 1 additional probable case of SARS has been reported from USA for whom no date of onset is available.
Source: CDC United States of America

Probable cases of SARS by date of onset
WHO European Region, 1 February - 16 June 2003 (n=37*)

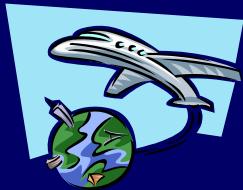


* As of 16 June 2003, an additional 2 probable cases of SARS have been reported from countries in the WHO European Region for whom no dates of onset are available.

Source: WHO EURO

1st Line of Response: Astute Clinician

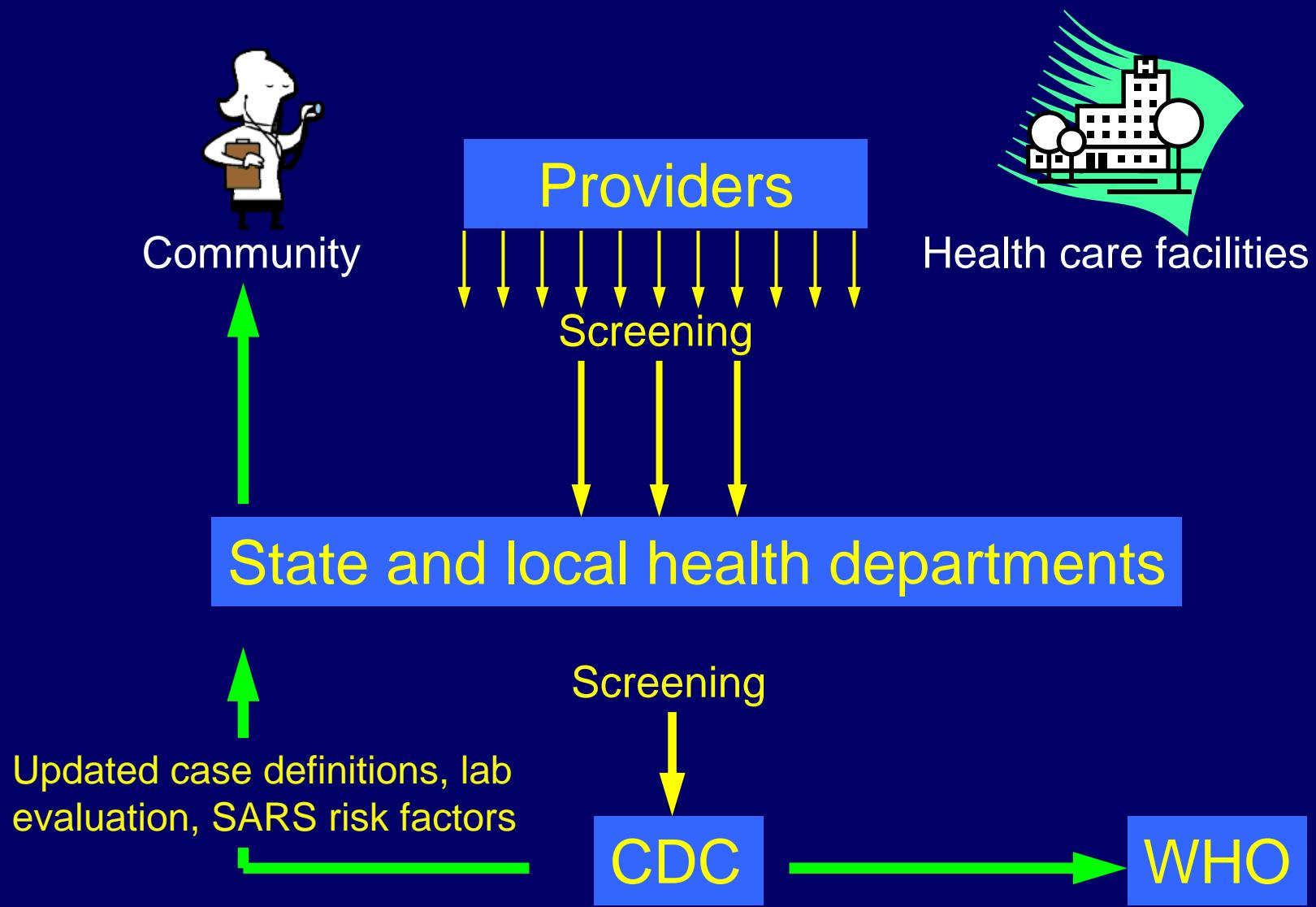
Screen all persons being hospitalized
for CXR-confirmed pneumonia:



1. In the last 10 days, have you **traveled** to mainland China, Hong Kong or Taiwan*, or been in close contact with other ill persons who have?
2. “Are you employed as a **healthcare worker** with direct patient contact?”
3. “Do you have **close contacts** who have been told they have pneumonia?”



Approach to surveillance and reporting





WHO Team in GDCDC, 2003.04.04

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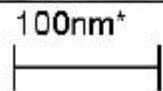


University of Hong Kong first to announce the discovery of SARS coronavirus
March 27, 2003

Electron Micrograph of the Coronavirus

Copyright of the University of Hong Kong

Magnification = 100.00 K X

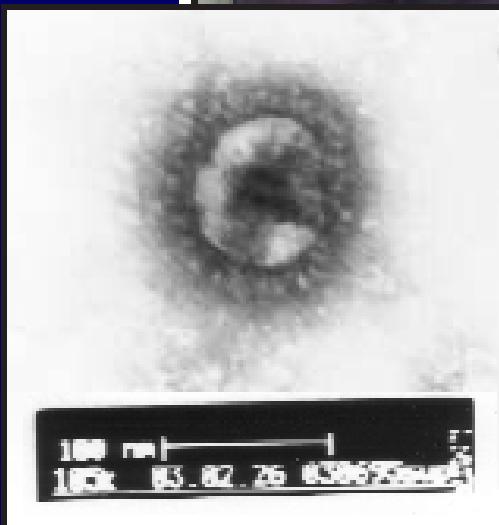


EHT = 20.00 kV
WD = 3 mm

Signal A = SE2
Photo No. = 519

Date : 25 Mar 20
Time : 17:06:07

China's Missed Chance



They saw it first. Yang Ruifu (left) and Zhu Qingyu had pictures of the new coronavirus (*inset*) on 26 February—but they kept quiet about it.

The microbiologists at the Academy of Military Medical Sciences had discovered the new coronavirus on 26 Feb, but kept quiet about it

SCIENCE VOL 301 18 JULY 2003



WHO team collected samples at Guangzhou animal market, 2004.01.14 **250**

Isolation and Characterization of Viruses Related to the SARS Coronavirus from Animals in Southern China

Y. Guan, B.J. Zheng, Y.Q. He, X. L. Liu, Z.X. Zhuang,

A novel coronavirus (SCoV) is the etiological agent of the Severe Acute Respiratory Syndrome. SCoV-like viruses were isolated from Himalayan palm civets found in a live animal market in Guangdong, China. Evidence of virus infection was also detected in other animal, including a raccoon-dog, and in humans working at the same market. All the animal isolates retain a 29-nucleotide sequence, which is not found in most human isolates. The detection of SCoV-like viruses in small wild mammals in live retail market indicates a route of interspecies transmission, although the natural reservoir is not known.



Science 4 September 2003

Y. Guan



Under suspicion. Civets were found to have the SARS virus, but they may not be the primary animal reservoir.

Control Measures in Guangdong

Break the chain of transmission
from infected to healthy persons

1. Early case identification

Efficient surveillance and reporting system

Public information and education to encourage prompt reporting of symptoms

2. Promptly and effectively patient isolation

Strict hospital infection control

3. Timely contact tracing

Management of close contacts by home confinement or quarantine

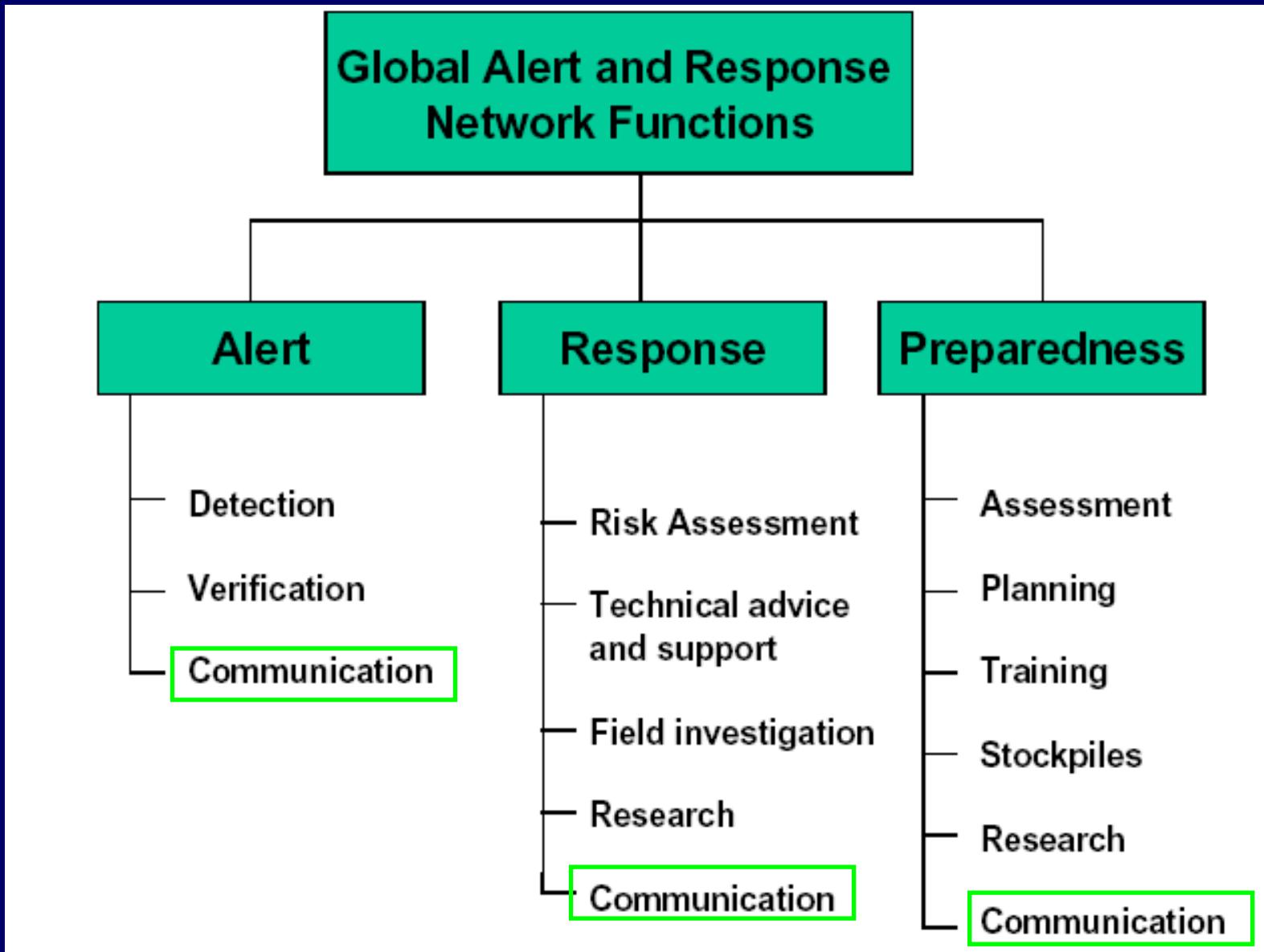
4. Wild animal administration

Farm Market Restaurant

Disease prevention messages are slowly integrated into life activities



*"We're thinking of moving to another part of the country—
somewhere between Lyme disease and killer bees."*



Quality Communications

- Accurate / Science based
- Timely and Relevant
- Comprehensible
- Appropriately Targeted
- Credible
- Coordinated

Preparing Messages

STARCC Principle

- Simple
- Timely
- Accurate
- Relevant
- Credible
- Consistent

Health Communication

Health communication focuses on choosing

the **right channel** to reach
the **right audience** with
the **right message** at
the **right time**

- Share the **information** about disease outbreaks nationally / globally **as soon as they occur**
- Share successful **strategies** to contain the disease
- **Panic is fuelled** when information is concealed or only partially disclosed

Best practices for effective communication

1. Build trust

The foundation for effective outbreak communication

Trust in the honesty of authorities reduces public anxiety
during the uncertainties of an outbreak

2. Announce early

Early announcement contributes to early containment
in a situation where every day counts

3. Be transparent

Candid easily understood complete accurate

4. Respect public concerns

Today, effective risk communication is viewed as
a dialogue between technical experts and the public

5. Plan in advance

Costly errors can be avoided when the issues and principles of risk
communication are considered in advance

广东省人民政府新闻办公室

Information Office, the People's Government of Guangdong Province



Prevention and treatment condition on SARS presentation in Guangdong
2003.05.16.



WHO team leader at main gate of GDCDC, 2004.01.12



GDCDC communicated with the reporters from main news paper in Guangdong
on flu pandemic(H1N1), 2009.05.28

Media communication



Provide information → Control information

Serve the media → Media cooperate

6. Screening Test

Medicine screening

Mass examination of the population to detect the existence of a particular disease, as diabetes or tuberculosis.

Health screening

A guideline that recommends interventions performed for the **early detection of disease** or disease precursors in apparently **well** individuals so that health care can be provided early in the disease or before the disease manifests (e.g., screening for prostate cancer).

Webster's Online Dictionary

Medicine screening

- Screening is a strategy used in a population to detect a disease in individuals without signs or symptoms of that disease
- Unlike what generally happens in medicine screening tests are performed on persons without any clinical sign of disease

[http://en.wikipedia.org/wiki/Screening_\(medicine\)](http://en.wikipedia.org/wiki/Screening_(medicine))

Medicine screening

The intention of screening is
to identify disease in a community early,
thus enabling earlier intervention and management
in the hope
to reduce mortality and suffering from a disease.

Principles of Screening

WHO 1968

1. The condition should be an **important** health problem.
2. There should be a **treatment** for the condition.
3. **Facilities** for diagnosis and treatment should be **available**.
4. There should be a **latent stage** of the disease.
5. There should be a **test** or examination for the condition.
6. The test should be **acceptable** to the population.
7. The **natural history** of the disease should be adequately **understood**.
8. There should be an **agreed** policy on whom to treat.
9. The total cost of finding a case should be **economically** balanced in relation to medical expenditure as a whole.
10. Case-finding should be a **continuous** process, not just a "once and for all" project.

Health Screening (Screening tests)

Screening refers to a test or exam done to find a condition before symptoms begin.

Screening tests may help find diseases or conditions early, when they are easier to treat.

Some conditions that doctors commonly screen for include

- Breast cancer and cervical cancer in women
- Prostate cancer in men
- Colorectal cancer
- Diabetes
- High blood pressure
- High cholesterol
- Osteoporosis
- Hearing and vision loss
- Sexually transmitted diseases (STDs)
- Newborn screening
- Genetic screening

Screening Test

		Disease Status		Total
		+	-	
Test Results	+	A True +	B False +	A + B
	-	C False -	D True -	C + D
Total		A + C	B + D	

Sensitivity = $A / (A + C)$; the probability of testing positive if disease is truly present

Specificity = $D / (B + D)$; the probability of testing negative if the disease is truly absent

Positive predictive value = $A / (A + B)$; the probability that a person who tests positive actually has the disease

Negative predictive value = $D / (C + D)$; the probability that a person who tests negative actually is free of the disease **271**

7. OR and RR

Basic Presentation of Results

		Disease		Total
		Yes	No	
Exposed	Yes	A	B	A+B
	No	C	D	C+D
Total		A+C	B+D	A+B+C+D

- Epidemiologists use **two-by-two tables** to study the association between an exposure and disease.
- Any rates needed for epidemiologic analysis can be **calculated from this basic table**.

Odds Ratio (OR)

- Calculated to identify the likelihood of exposure to a risk when comparing two groups, one with and one without disease.
- Exposure odds in the disease group divided by exposure odds in non-disease group.

Ratio = 1, no association

Ratio > 1, association between exposure and disease

For example

If the prevalence of smoking among lung cancer patients is 95/100
the prevalence of smoking among people without lung cancer is 25 /100

$$\text{Odds Ratio} = 95 / 25 = 3.8$$

Thus, there is an association between lung cancer and smoking.

Case-control study

	Cases	Controls	Total
Exposed	a	b	a+b
Unexposed	c	d	c+d
Total	a+c	b+d	T

We cannot calculate rates or a relative risk from a case-control study, but we can calculate an odds ratio as an estimate of the relative risk.

$$\text{Odds ratio} = a \cdot d / b \cdot c$$

Case-control study

Exposure to Grocery Store A among cases and controls
Legionellosis outbreak, Louisiana, 1990

		Cases	Controls	Total
Shopped at Grocery Store A?	Yes	25	28	53
	No	2	26	28
Total		27	54	81

$$\text{Odds ratio} = a d / b c$$

$$= 25 \times 26 / 28 \times 2 = 11.6$$

Relative risk (RR)

- Calculated to identify differences in disease rate between exposed and unexposed (to a risk) groups.
- Risk of disease among exposed divided by the risk of disease among unexposed
 - RR = 1, no difference between two groups.
 - RR > 1, association between exposure and disease.

For example,

If lung cancer mortality rate among smokers is 131 per 100,000, and the lung cancer rate among non-smokers is 11 per 100,000, then

$$R R = 131/11 = 11.9$$

Thus, there is an association between smoking and lung cancer

Attack rate by consumption of vanilla ice cream

Oswego, New York, April 1940

Ate vanilla ice cream?	Yes	III	Well	Total	Attack Rate (%)
		43	11	54	79.6
	No	3	18	21	14.3
Total		46	29	75	61.3

Relative risk = $79.6 / 14.3 = 5.6$

$$\text{Attack rate} = \frac{\text{Number of new cases among the population during the period}}{\text{Population at risk at the beginning of the period}} \times 100$$

Attributable risk

Calculate to identify the proportion of disease among exposed people that actually results from the exposure

- Individual attributable risk = $RR - 1 / RR$
- Population attributable risk = $Pe (RR - 1) / 1 + Pe (RR - 1)$

Pe = proportion of population exposed

For example

If RR of lung cancer due to smoking is 15
and that 30% of the population are smokers.

$$\text{Population attributable risk} = \frac{(.30)(15 - 1)}{1 + (.30)(15 - 1)} = .81$$

Thus, 81% of lung cancer would be Attributed to smoking

81% of lung cancer would be eliminated if smoking were eliminated

8. Four Types of Causal Relation

From Association to Causation

1. We determine whether there is an association between an exposure or characteristic and the risk of a disease.

To do so, we use:

- a. Studies of group characteristics:
ecologic studies
 - b. Studies of individual characteristics:
case - control and *cohort studies*
2. If an association is demonstrated, we determine whether the observed association is likely to be a causal one.

From Association to Causation

Types of Association

- **Real** association
(causal)
- **Spurious** association
(non causal, due to confounding)

Interpreting Associations- Causal and Non-Causal

Causal

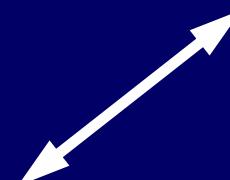
Characteristic Under Study



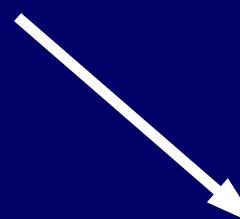
Disease

Non-Causal
(due to confounding)

Characteristic Under Study



Factor X



Disease

Interpreting Associations- Causal and Non-Causal

Causal

Non-Causal
(due to confounding)

Coffee Consumption

Coffee Consumption

Pancreatic Cancer

Pancreatic Cancer
284



Real Association

Smoking

Real Association



Spurious Association

Pancreatic Cancer
284

Types of Causal Relationships: Direct vs Indirect

Direct

Factor



Disease

Indirect

Factor 1



Factor 2



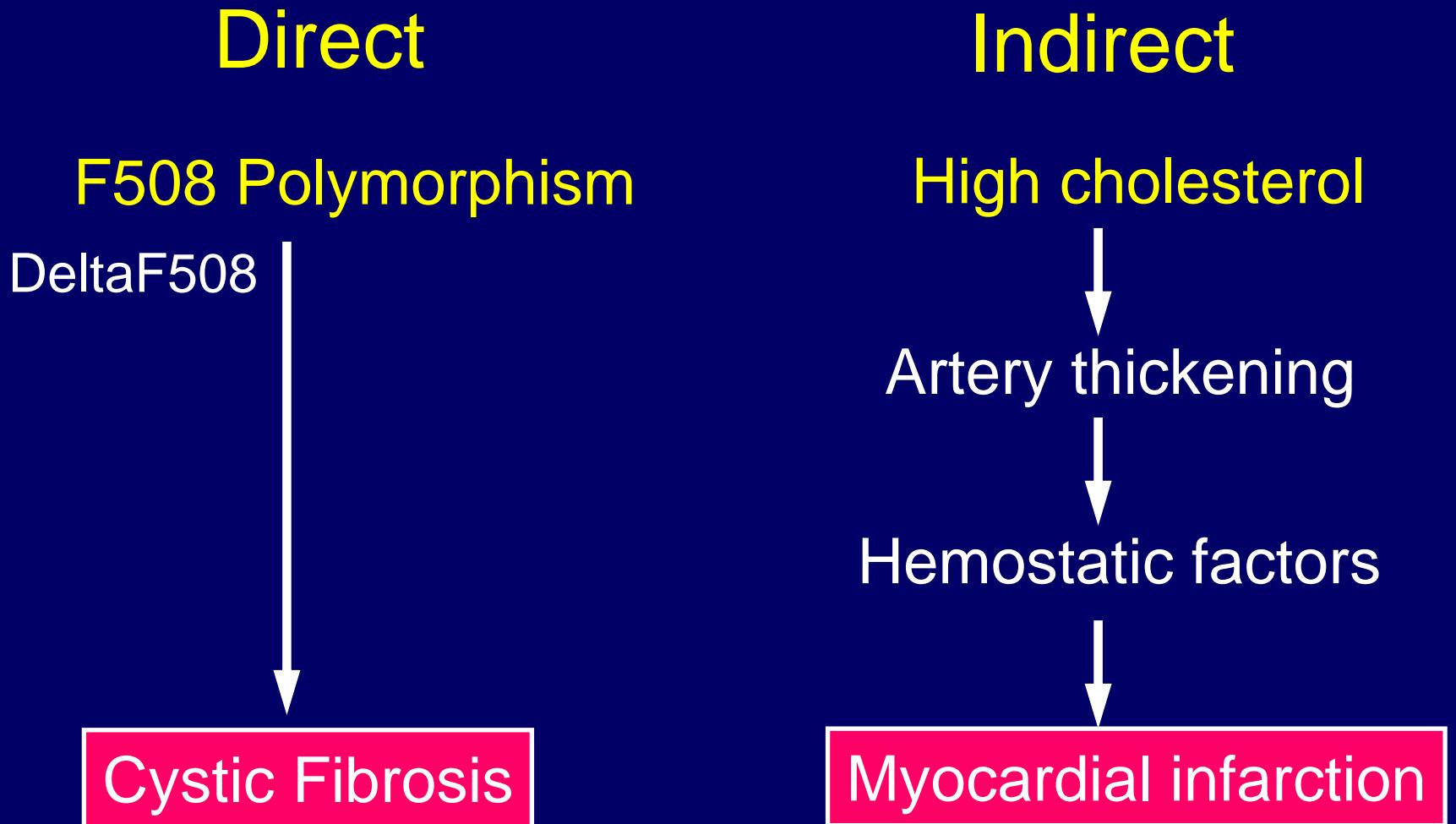
Factor 3

Factor 4



Disease

Types of Causal Relationships: Direct vs Indirect



What Causes an myocardial infarction (MI)

Epidemiological studies combined with laboratory study identify risk factors

- Cigarette smoking
- Cholesterol
- Elevated blood pressure
- Stress
- Family history
- Obesity
- Etc

Which of the above contribute the most risk

What are the relationship between risk factors

Two Components of Causation

- **Necessary Factor**

Without that factor, the disease never develops

- **Sufficient Factor**

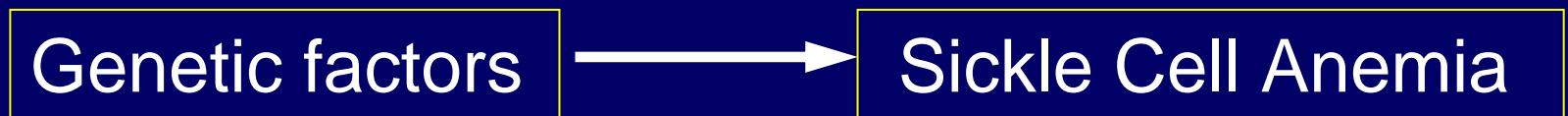
In the presence of that factor, the disease always develops

Using these 2 components of Causation,
we can produce a unified frame work of causation
that will encompass all Disease Processes

Four Types of Causal Relation

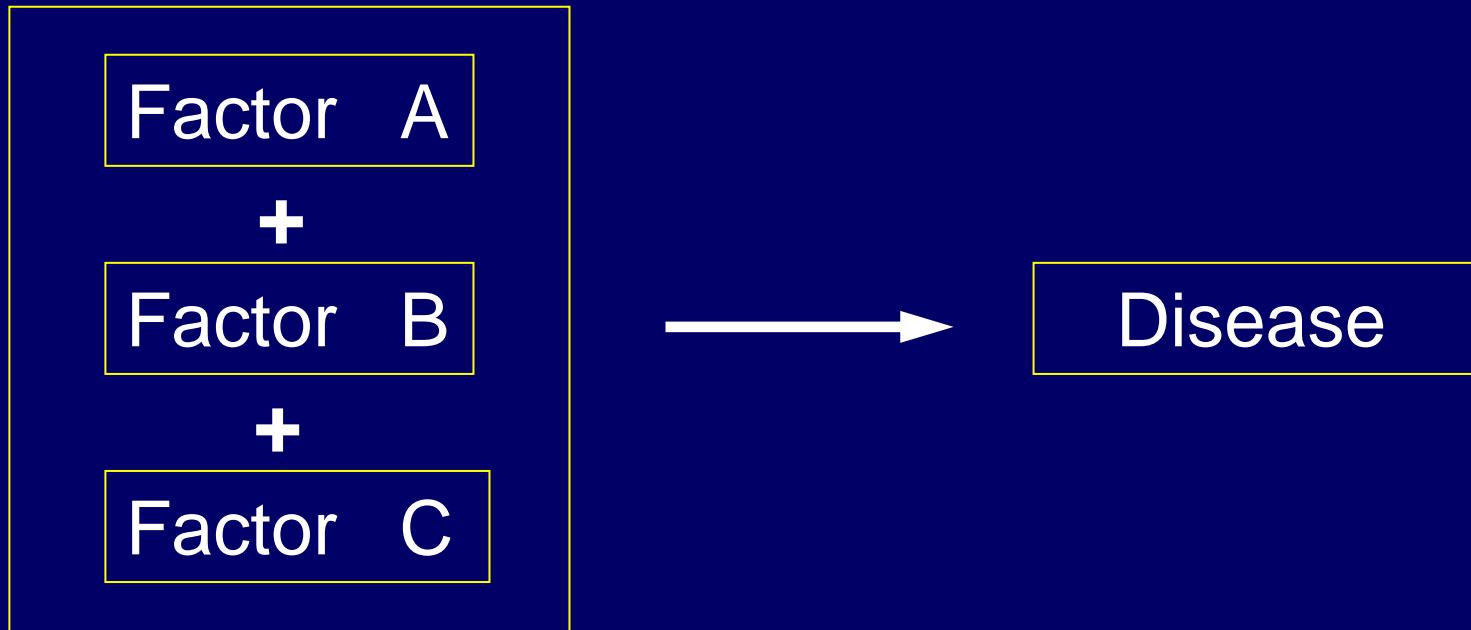
1. Necessary and sufficient
2. Necessary but Not Sufficient
3. Sufficient but Not Necessary
4. Neither sufficient Nor Necessary

1. Necessary and Sufficient



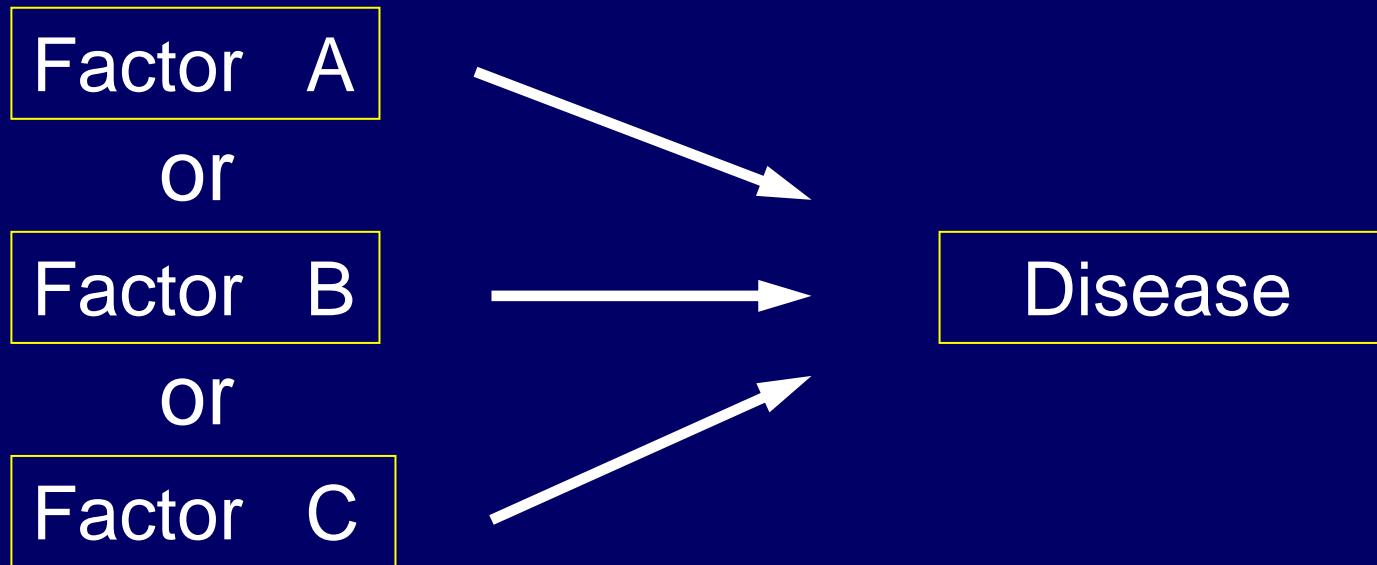
- Factor A is both Necessary and sufficient
- Most infectious disease will not cause illness in everyone, and not all heavy smokers develop lung cancer
- Rarely occur

2. Necessary but Not Sufficient



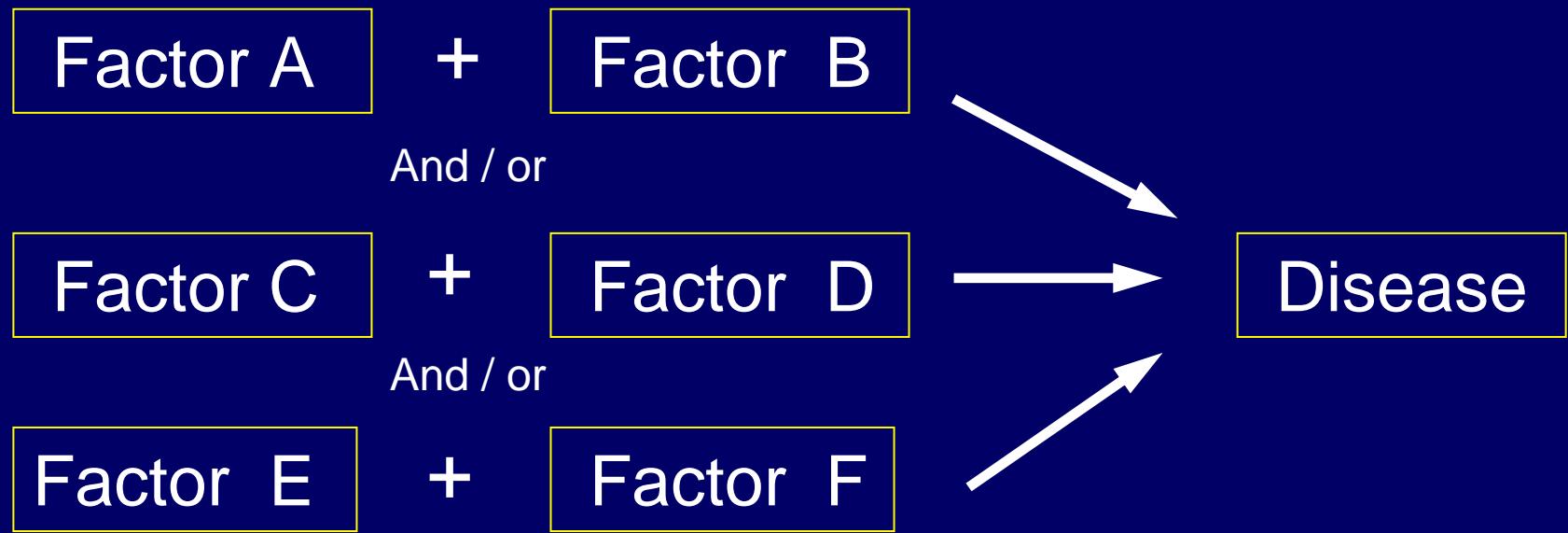
- Each factor is a necessary but not a sufficient cause
- All are necessary to cause disease
but each factor alone cannot cause disease
- Thus multiple factors are required often in a specified temporal sequence.
For cancer to result, a promoter must act after an initiator has acted.

3. Sufficient but Not Necessary



- Each factor is sufficient but not necessary
- Each factor can produce the disease without the other factors being present
- For example ,**radiation exposure or benzene exposure** can each produce leukemia without the presence of the other. However, not really sufficient because other co-factors either known or unknown are in the causal process

4. Neither Sufficient Nor Necessary



- Each factor is neither sufficient Nor Necessary
- Risk factors combine in ways we know little about to produce disease which probably most accurately represent the causal relationships that operate in **most chronic diseases**

Biological

Psychological

Social

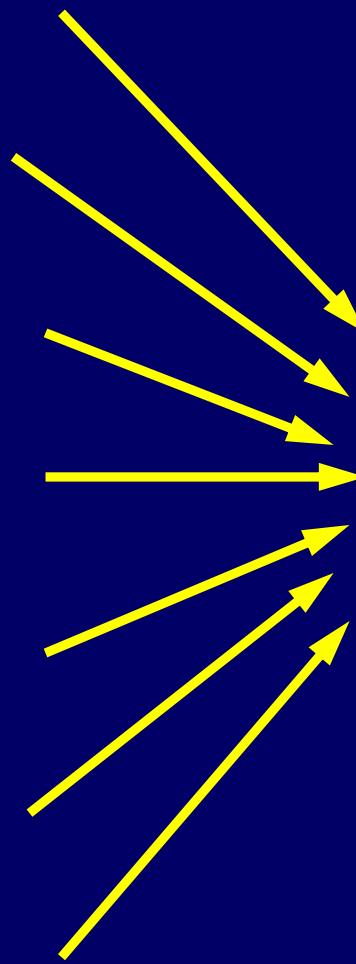
Genetic

Neurological

Spiritual

Family

Addiction



What causes tuberculosis?

Particular microorganism
Crowded living conditions
Silicosis

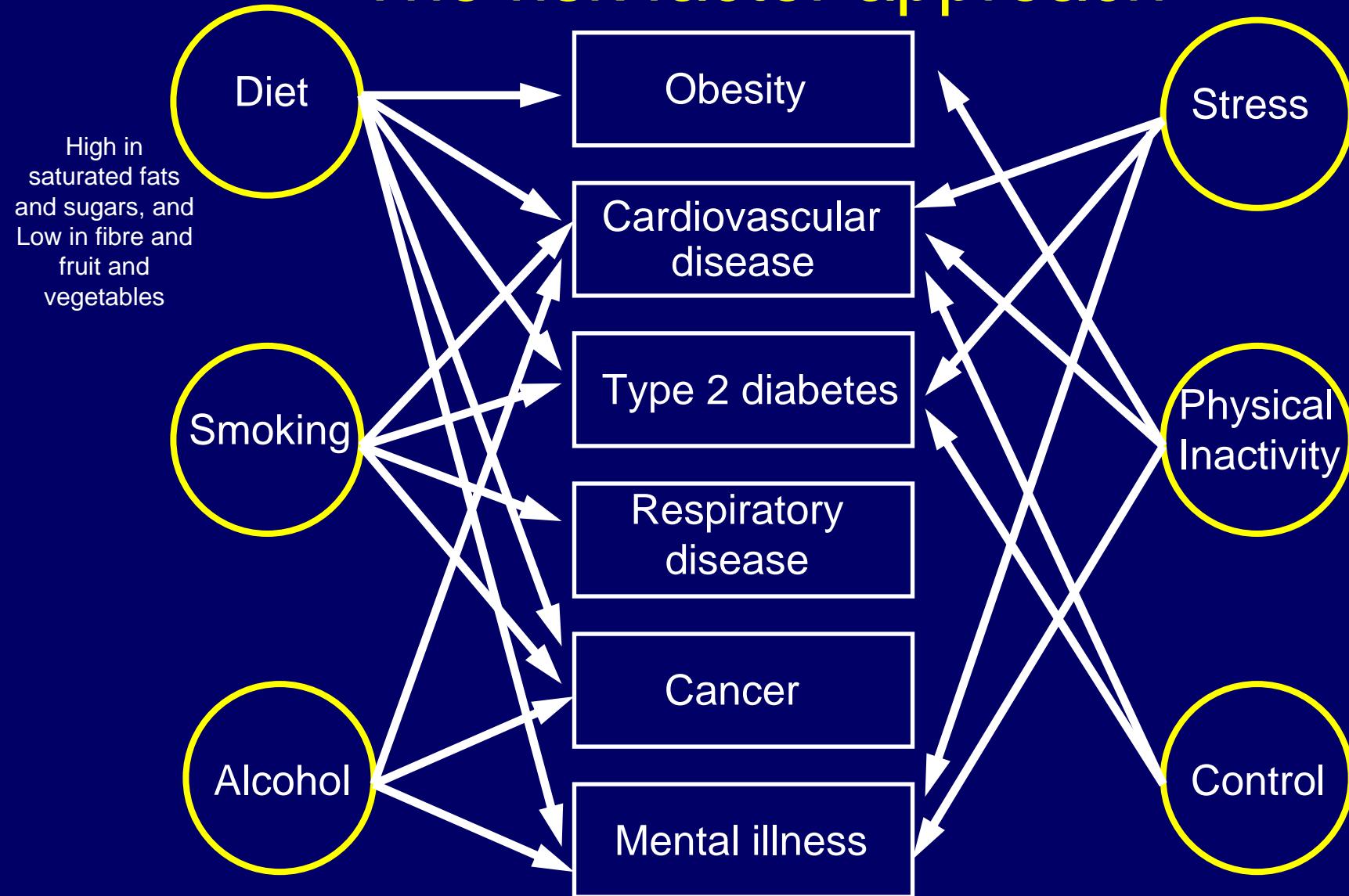
Immune deficiency
Malnutrition
Some genetic factors

Case 1: the mycobacterium + immune deficiency
may operate to cause a case of TB.

Case 2: the mycobacterium + silicosis + malnutrition
may operate.

- One cause, the mycobacterium is **necessary**
- Various combinations that include the mycobacterium
may be **sufficient**.

The risk factor approach



A more complex view of causation

Jim has a bad day at work

stops at the bar for a couple of drinks on the way home

He gets into his car, drives too fast

slips on an icy patch as he rounds a curve

collides with Mary's car.

Mary is pregnant

Jim's car did not have anti-lock brakes?

Mary's car did not have air bags?

Mary was not wearing her seat belt? ?

Mary suffers an abdominal injury, and loses the baby

Association & Causation

- A principal aim of epidemiology is to assess the **cause of disease**
- However, since most epidemiological studies are by **nature observational** rather than experimental, a number of **possible explanations** for an observed association **need to be considered** before we can infer a cause-effect relationship exists.
- That is the observed association **may** in fact be **due to** the effects of one or more of the **following**:

1. Chance (random error)
2. Bias (systematic error)
3. Confounding

9. Guidelines for assessing causation

The Henle-Koch postulates

In the mid-19th century, as the germ theory of disease arose, Henle and his pupil Koch formulated postulates from which the inference could be made that a specific living organism caused a particular disease. In simplified form there were three:

1. The organism is always found with the disease.
2. The organism is not found with any other disease.
3. The organism, cultured from one with the disease and cultured through several generations, produces the disease.

Koch's postulates

An example of deterministic causality.

To prove that an organism causes a disease,
he required that

1. The organism must be isolated in every case of the disease (i.e. be necessary)
2. The organism must be grown in pure culture.
3. The organism must always cause the disease when inoculated in to an experimental animal (i.e. be sufficient)
4. The organism must then be recovered from the experimental animal and identified

The Henle-Koch postulates

In 1876 Koch demonstrated that anthrax met these criteria, and many other infectious diseases followed.

The idea that a specific, identifiable agent could cause a specific disease was revolutionary, and paved the way for interventions such as vaccines.



Robert Koch
1843 - 1910 Germany

Discovered the **tuberculosis bacillus** and also a method of growing it in pure culture (1882)

Led a German expedition to Egypt and India, where he discovered the **cholera bacillus** (1883)

1905 Nobel Laureate in Medicine
for his investigations and discoveries in relation to tuberculosis.

Hills Criteria of Causation

Almost a century later, in 1964, the Surgeon General's report on smoking implicated tobacco as a cause of lung cancer.

This ignited a tremendous controversy about whether such causal thinking could be applied to chronic diseases.

The Surgeon General's report, and a soon published paper by Sir Austin Bradford Hill, advanced standards that could be used to judge when an association might be causal.



Austin Bradford Hill
1897 - 1991 English

English epidemiologist and statistician. He pioneered rigorous statistical study of patterns of disease and, together with William Richard Doll was **the first** to demonstrate the connection between cigarette smoking and lung cancer.

His work on smoking and lung cancer, which involved collecting data on the smoking habits and health of over 30,000 British doctors for several years, in the precomputer age, is considered to be among the great medical achievements of the century.

Hills Criteria of Causation

Hill's Criteria form
the basis of modern epidemiological research,
which attempts to establish
scientifically valid causal connections
between potential disease agents and
the many diseases that afflict humankind.

Hills Criteria of Causation

1. Temporal Relationship
2. Strength.
3. Dose-Response Relationship Biological Gradient
4. Consistency
5. Plausibility Biological Plausibility
6. Consideration of Alternate Explanations
7. Experiment Cessation of Exposure
8. Specificity
9. Coherence

1. Temporal Relationship

Exposure always precedes the outcome.

If factor "A" is believed to cause a disease,
then it is clear that factor "A" must necessarily always
precede the occurrence of the disease.

This is the only absolutely essential criterion.

A cause must precede an effect in time.
This one is true!

1. Temporal Relationship

- Exposure to the factor must have occurred before the disease developed
- Easiest to establish in a cohort study
- Sometimes this is hard to know, especially in cross-sectional studies.
- Time-order can also be uncertain when disease has a long latent period, and when the exposure may also represent a long duration of effect.
(Low serum cholesterol and colon cancer)

1. Temporal Relationship

- Length of interval between exposure and disease very important
- If the disease develops in a period of time too soon after exposure, the causal relationship is called into question



In this case, the latent period is not long enough for disease to develop if caused by this exposure

1. Temporal Relationship

Asbestos and Lung Cancer

Well - established temporal relationship



New Study



In this case, the latent period is not long enough for lung cancer to develop if caused by exposure.

2. Strength

- This is defined by the size of the association as measured by appropriate statistical tests.
- The stronger the association, the more likely it is that the relation is causal.
- Usually measured by relative risk.
Higher the relative risk, more likely causal.

2. Strength

- The larger the relative risk or odds ratio, the higher the likelihood that the relationship is causal
- However, care must be taken to examine confidence intervals and sample size

If the confidence interval is wide (e.g., 1.8 - 22.6), an OR of 12.0 is less strong because we are less confident of the strength of the odds ratio

2. Strength

Which odds ratio would you be more likely to infer causation from ?

- | | | |
|----|------------|--------------------------|
| 1. | $OR = 1.4$ | $95\% CI = (1.2 - 1.7)$ |
| 2. | $OR = 9.8$ | $95\% CI = (1.8 - 12.3)$ |
| 3. | $OR = 6.6$ | $95\% CI = (5.9 - 8.1)$ |

2. Strength

- A **strong association**, such as a five- or tenfold increase in risk, is more likely to be causal than a **weak association**, such as a 10% increase in risk, because a weak association is more likely to be **spurious**, arising from bias, confounding, or **chance**.
- However, a weak association does not rule out causality ! In epidemiology, most causes have much weaker relationship to effects.

For example, high cholesterol may lead to heart disease, but it need not (**insufficient**) and heart disease does not require a high cholesterol (**unnecessary**).

3. Dose-Response Relationship

- As the dose of exposure increases the risk of disease also increases
- This is not considered necessary for a causal relationship, but does provide additional evidence that a causal relationship exists
- Cessation of Exposure
If exposure is reduced or eliminated risk will decline
HOWEVER, in certain cases, the damage may be irreversible. Emphysema is not reversed with the cessation of smoking, but its progression is reduced

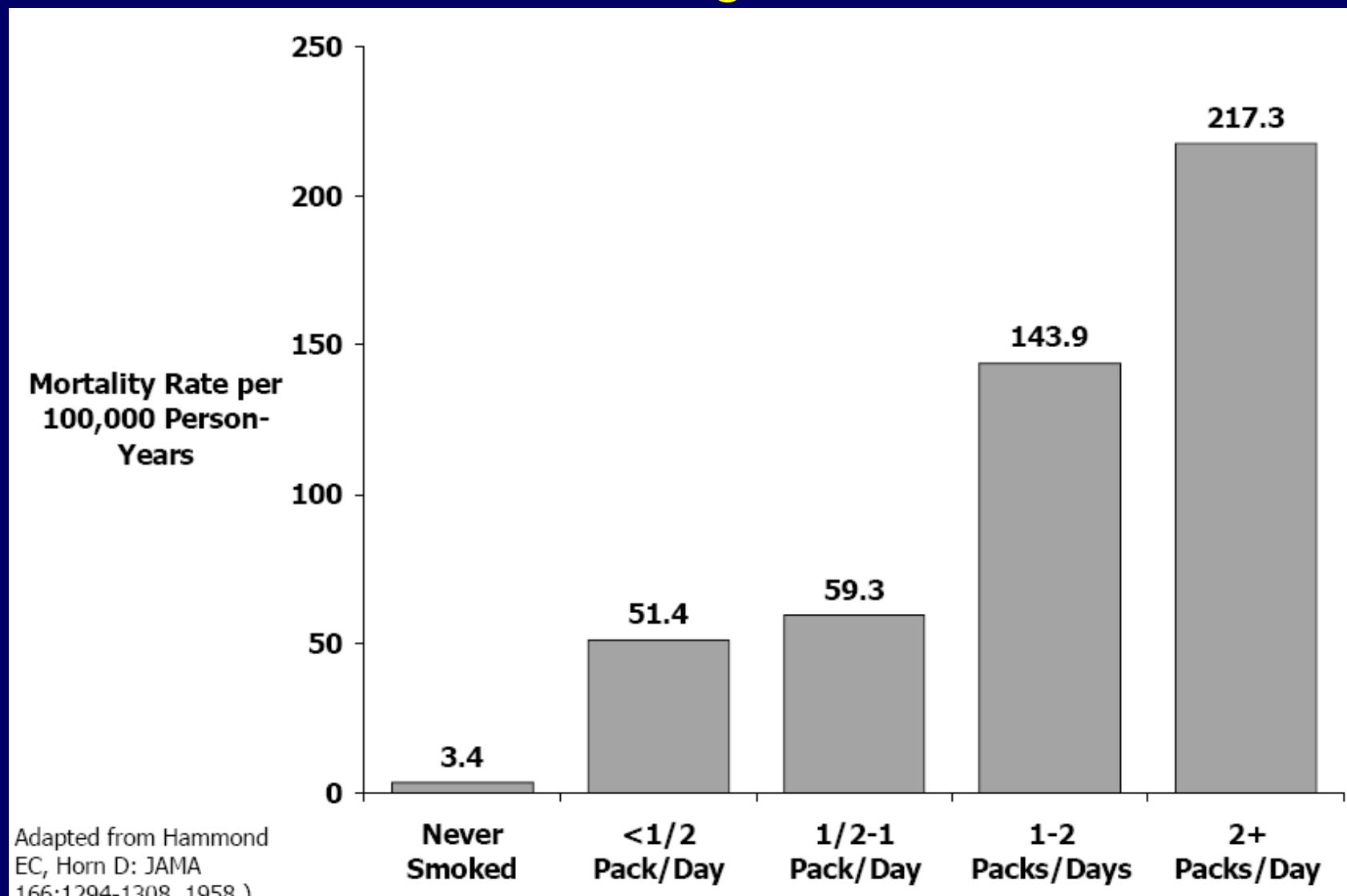
3. Dose-Response Relationship

- However, as with specificity, the **absence** of a dose-response relationship does not rule out a causal relationship.
- Dose-response is **not relevant** to all exposure-disease relationships, because disease sometimes only occurs above a **fixed threshold of exposure**, and thus a dose-response relationship need not be seen.

3. Dose-Response Relationship

- There is a strong dose response relationship between number of cigarettes smoked per day and mortality from lung cancer
- A dose-response gradient is helpful, but its absence doesn't rule out causation (Diethylstilbestrol (DES) and vaginal adenocarcinoma, asbestos and mesothelioma) and
- Its presence doesn't prove causation (since it may result from confounding or bias).

Age- standardized death rates due to well- established cases of bronchogenic carcinoma



Adapted from Hammond
EC, Horn D: JAMA
166:1294-1308, 1958.)

4. Consistency

- Results **replicated** in other studies.

CONSISTENCY AND UNBIASEDNESS OF FINDINGS

Confirmation of the association by **different investigators**,
in **different populations**, using **different methods**

- This is why **numerous experiments** have to be done before meaningful statements can be made about the causal relationship between two or more items.

For example

it has taken thousands of highly technical studies of the relationship between **cigarette smoking** and **cancer** before a definitive conclusion can be made that cigarette smoking **increases the risk of** (but does not cause) cancer.

4. Consistency

- If the association is repeatedly observed in different populations in different settings, it is more likely to be causal than an isolated observation.
- However, lack of consistency does not rule out a causal connection; some causes only work in certain circumstances, say in the presence of cofactors.

4. Consistency

Consistency can mean either:

- Exact replication, as in the laboratory sciences, or
- Replication in different studies and in different populations
(under many different circumstances) .

In epidemiology, exact replication is impossible !

Meta-analysis

is a formal method to assess the consistency of the measure of association across many studies.

5. Plausibility

- The association agrees with currently accepted understanding of pathological processes.

However, studies that disagree with established understanding of biological processes may force a reevaluation of accepted beliefs.

- The idea of causation must be biologically plausible.
This may be elusive because we hold many fixed ideas;
many people doubted for years that peptic ulcer disease could be infectious in origin!
(H. pylori bacteria)

5. Plausibility

- Does the association fit with what we know about the underlying biology
- Sometimes we know little or nothing about the underlying biology
(“ Black Box ” epidemiology)

6. Consideration of Alternate Explanations

- Make sure studies have taken other possible explanations into account and effectively ruled out such alternate explanations
- Requires a knowledge of the literature and known risk factors for the disease

6. Consideration of Alternate Explanations

- Consider the example of coffee consumption, smoking and pancreatic cancer.
 - Did the investigators consider the associations between smoking, coffee consumption and pancreatic cancer?
 - If the investigators did not consider possible confounders and effect modifiers, the association is less likely to be causal!

7. Experimental evidence

- Supporting data from human or animals experiments, such as lung cancer in animals exposed to cigarette smoke, helps establish a causal relationship.
- The condition can be altered (prevented or ameliorated) by an appropriate experimental regimen.

8. Specificity

- A specific exposure is associated with only one disease
This may be OK for infectious agents
but clearly wrong in many other circumstances
(chronic diseases)
- This is used by tobacco companies
to argue that smoking is not causal in lung cancer
 - Smoking is associated with many diseases
 - such as lung cancer, bladder cancer, emphysema, and heart disease.
- The weakest of the criteria
(should probably be eliminated)

8. Specificity

- When specificity of an association is found, it provides additional support for a causal relationship.
However, absence of specificity in no way negates a causal relationship
- Causality is most often multiple.
Therefore, it is necessary to examine specific causal relationships within a larger systemic perspective.

9. Coherence

- The association should be compatible with existing theory (biological background) and knowledge.
- The evidence must fit the facts that are thought to be related,
e.g., the rising incidence of dental fluorosis and the rising consumption of fluoride are coherent.

9. Coherence

The idea of causation must **accord with other observations.**

For example, as Hill wrote, a causal relationship between **smoking and lung cancer** was coherent with the observations that **smokers had dysplasia of the bronchial epithelium**, or that lung cancer was a predominantly male disease.

However, the absence of coherent information does not rule out a causal relationship.

Guidelines for Assessing Causation

1. Temporal relationship

Exposure to risk factor occurred before disease onset

2. Strength of Association

Usually measured by relative risk.

Higher the relative risk, more likely causal

3. Dose-response Relationship

As the dose of exposure increases
the risk of disease also increases

4. Replication of the Findings

Results replicated in other studies

5. Biologic Plausibility

- Does the association fit with what we know about the underlying biology
- Sometimes we know little or nothing about the underlying biology ("Black Box" epidemiology)

Guidelines for Assessing Causation

6. Consideration on Alternate Explanations

Make sure studies have taken other possible explanations into account and ruled out such explanations

7. Cessation of Exposure

If exposure is reduced or eliminated risk will decline

8. Specificity of the Association

A specific agent is associated with only one disease

Ok for infectious agents

but falls apart with many risk factors for chronic diseases
(cigarette smoking associated with several diseases)

9. Consistency with Other knowledge

Guidelines for Assessing Causation

In general, 5 criteria must be met
to establish a cause-and-effect relationship:

1. **Strength of association**
the relationship must be clear
2. **Consistency**
observation of the association must be repeatable
in different populations at different times
3. **Temporality**
the cause must precede the effect
4. **Plausibility**
the explanation must make sense biologically
5. **Biological gradient**
there must be a dose-response relationship

Summary

Health-related states **detective**

Detection

Problem

Intelligence

Cause

Reasoning

Control

Effective

Speed ! Timely !

Right answer !

Effective and efficient !

Coordination !

Communication !

Improve population health !



谢谢 Thanks