FAO/ASTF Project: GCP/RAF/510/MUL:

Enhancing capacity/risk reduction of emerging Tilapia Lake Virus (TiLV) to African tilapia aquaculture: Intensive Training Course on TiLV

4-13 December 2018. Kisumu, Kenya

in cooperation with Kenya Marine Fisheries Research Institute (KMFRI) and Kenya Fisheries Service (KeFS)

Epidemiology Session

Principles of epidemiology and surveillance and their application to aquaculture

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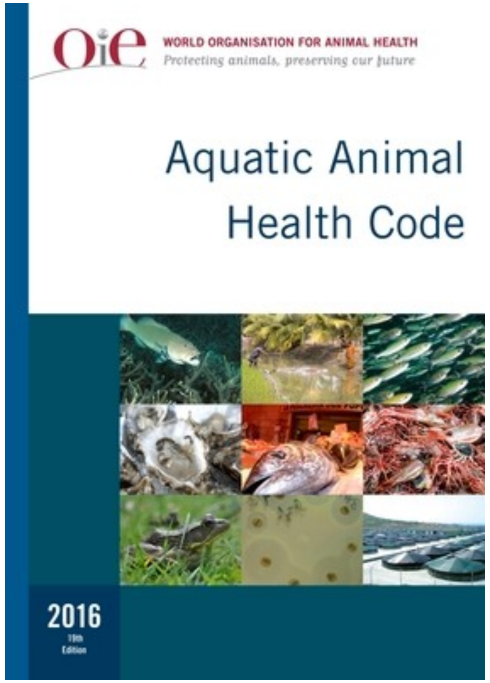
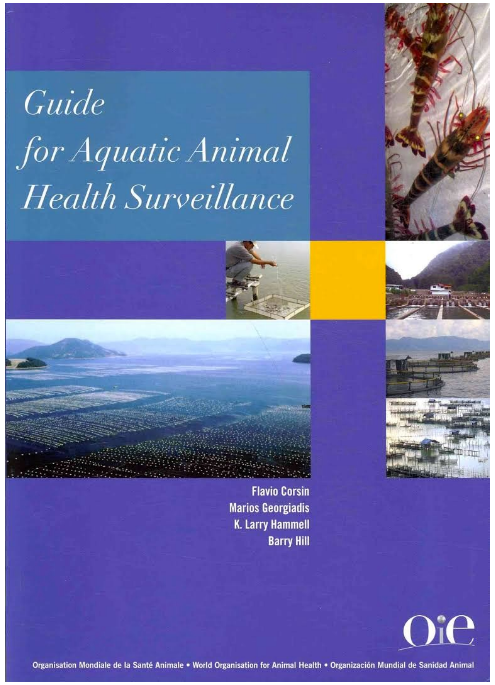
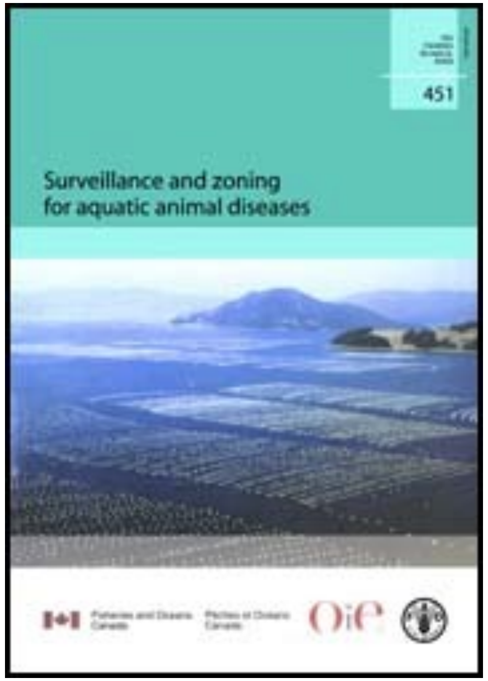
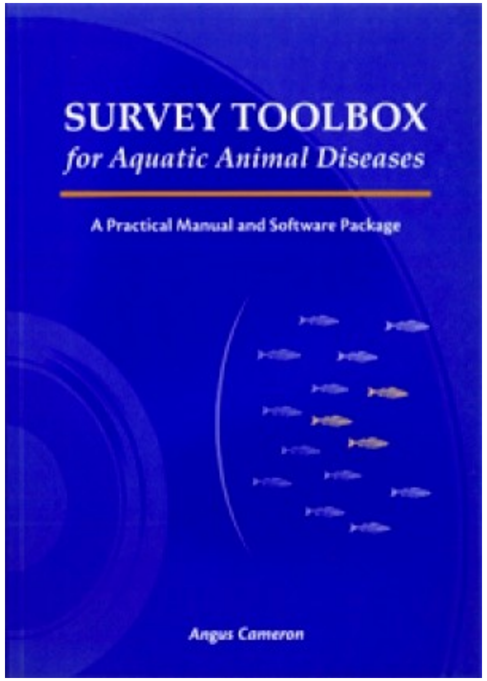
Food and Agriculture Organization of the United Nations

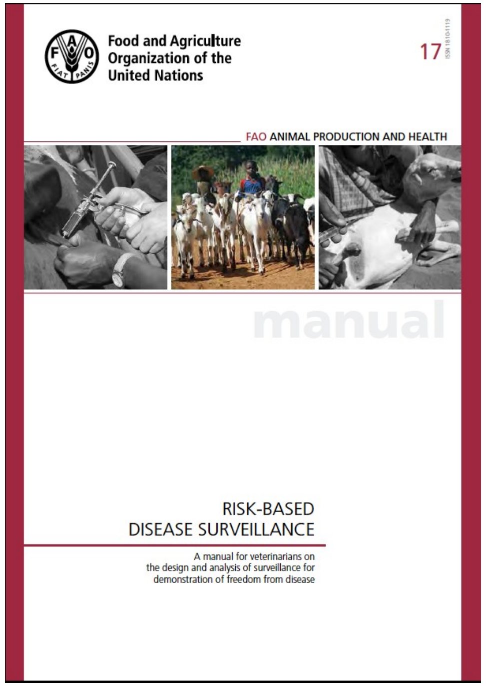
Available resources & useful references





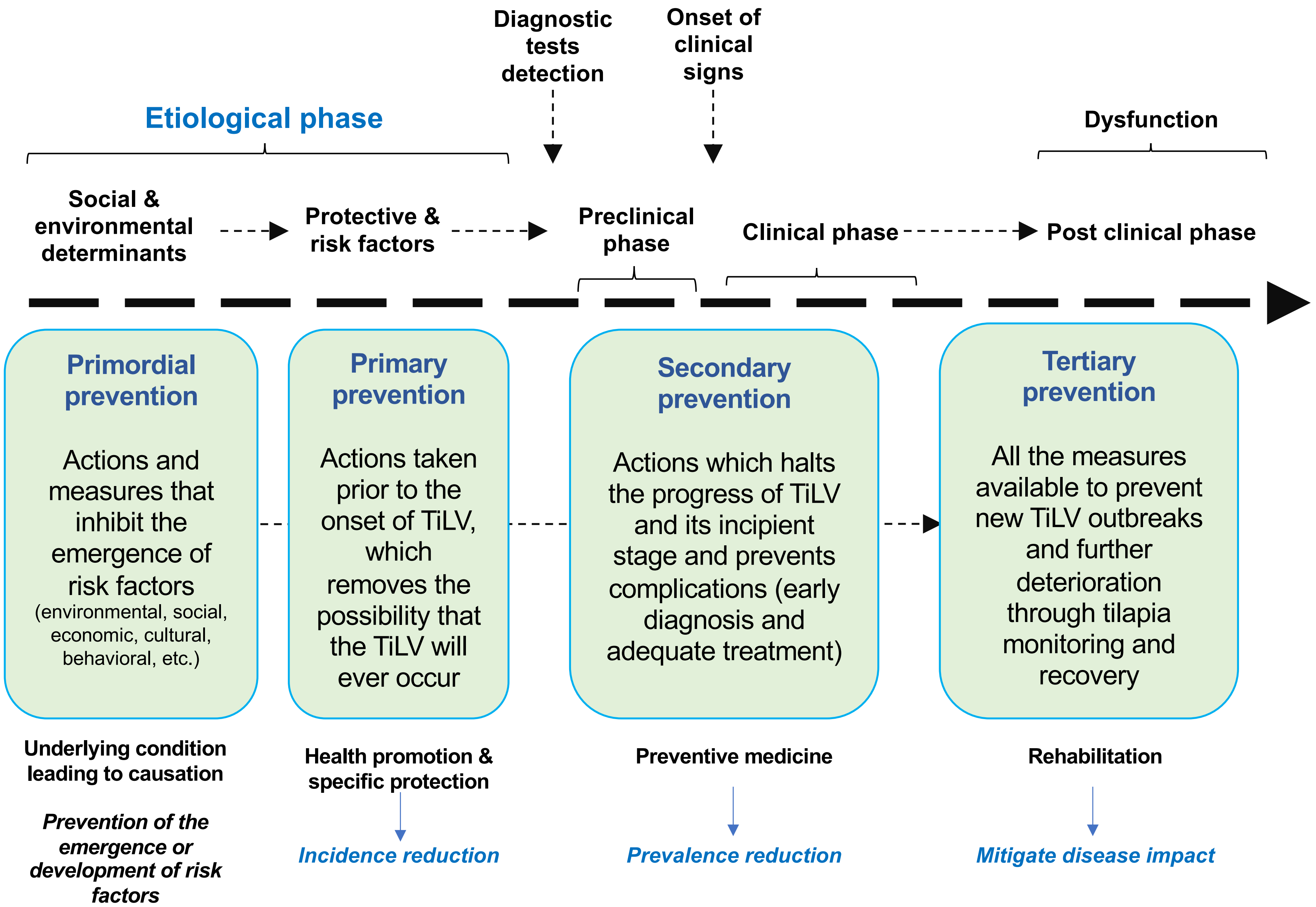






Overview

- What is epidemiology
- The epidemiological approach
- Investigating disease outbreaks
- Causality
- Patterns of disease
- Measuring disease frequency



Best management practices for Tilapia health

What is aquatic epidemiology?

- The study of disease in fish populations and of factors that determine its occurrence; the **keyword** being **fish populations**
- Additionally includes investigation and assessment of other health-related events, notably productivity
- All of these investigations involve observing fish populations and making inferences from the observations
- An integrating science with close links to clinical and laboratory medicine as well as biostatistics and health economics

Diseases in fish populations

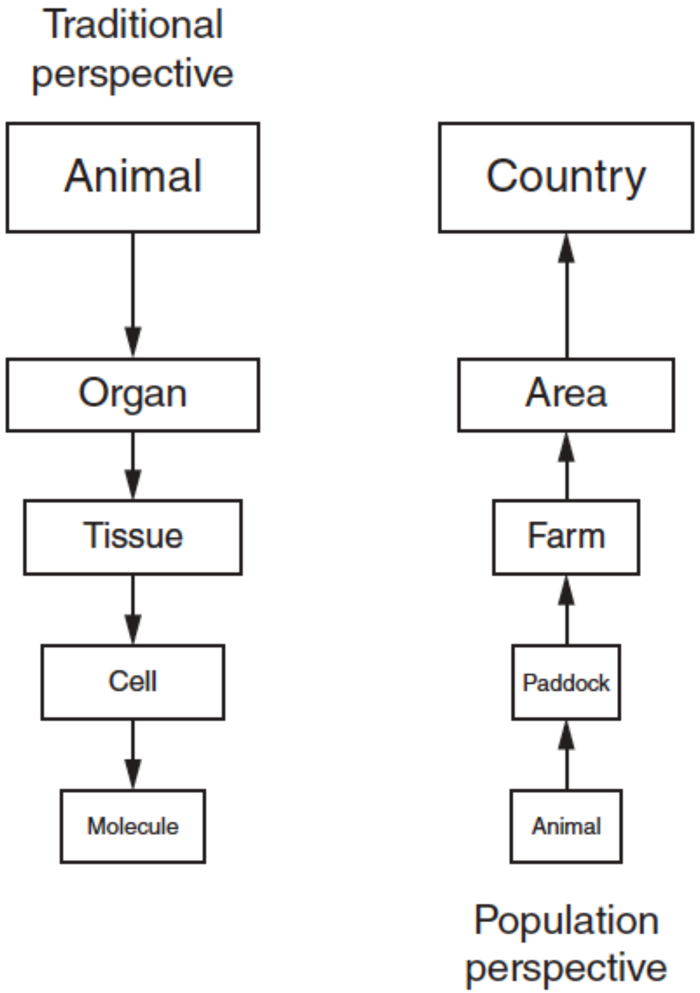
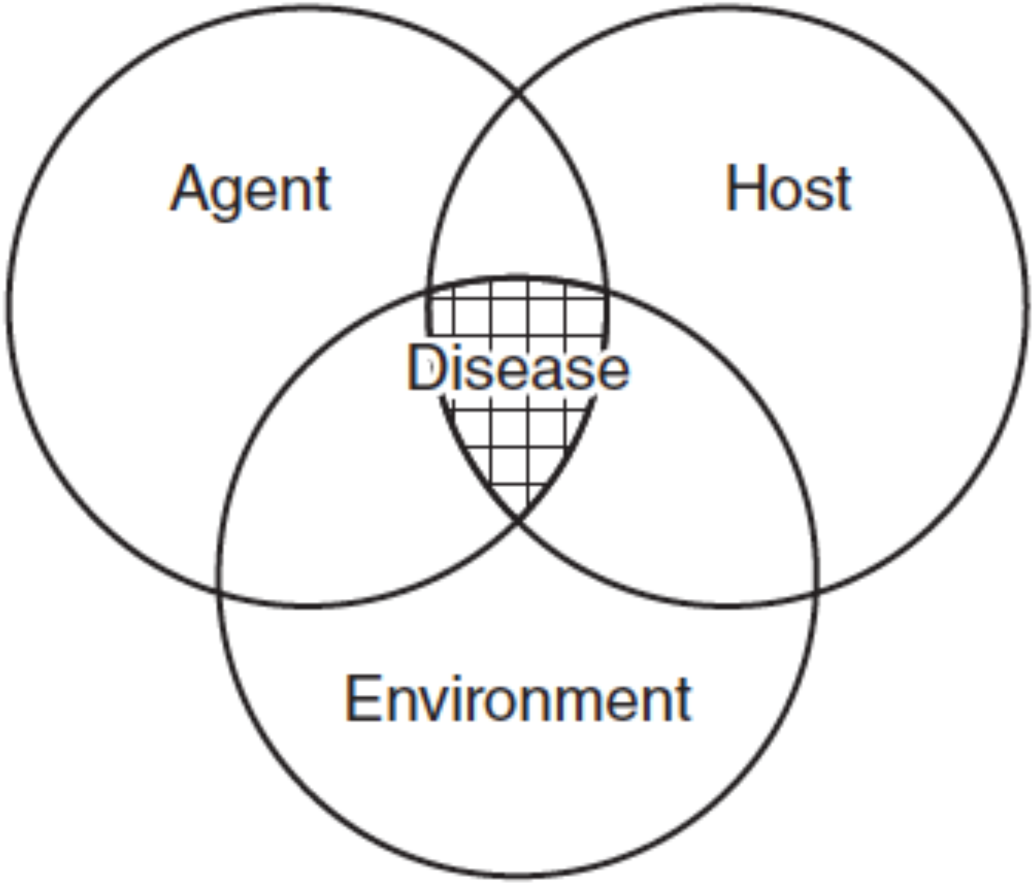


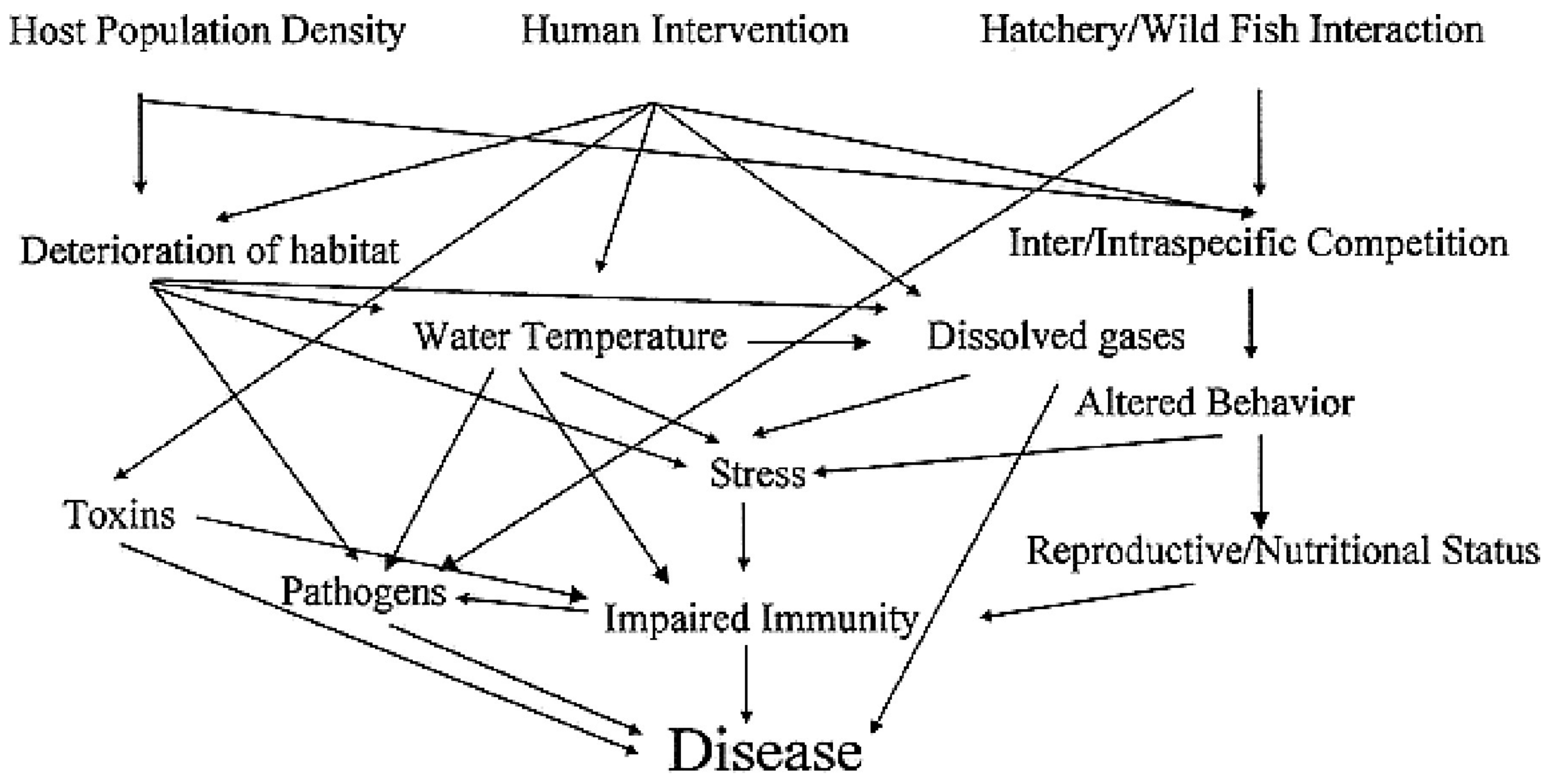
Fig. 1.1. Representation of the relationship between the traditional perspective of investigating disease and a population perspective.

Diseases in fish populations

- **Most diseases do not occur at random in a fish population** – they follow distinct patterns according to exposure of individuals in the population to various factors associated with the host, agent and environment



Web of causation for fish diseases



R.P. Hedrick, 1998. Relationships of the host, pathogen and environment: Implications for diseases of cultured and wild fish populations. Journal of Aquatic Animal Health 10:107-111.

Objectives of epidemiology

- Detecting the existence of a disease or other production problem
- Identifying the causes of disease
- Estimating the risk of becoming diseased
- Obtaining information on the ecology and natural history of the disease
- Defining and quantifying the impact and extent of the problem
- Planning and evaluating possible disease control strategies and biosecurity measures
- Monitoring and surveillance to prevent further disease episodes
- Assessing the economic impact of disease and control programs

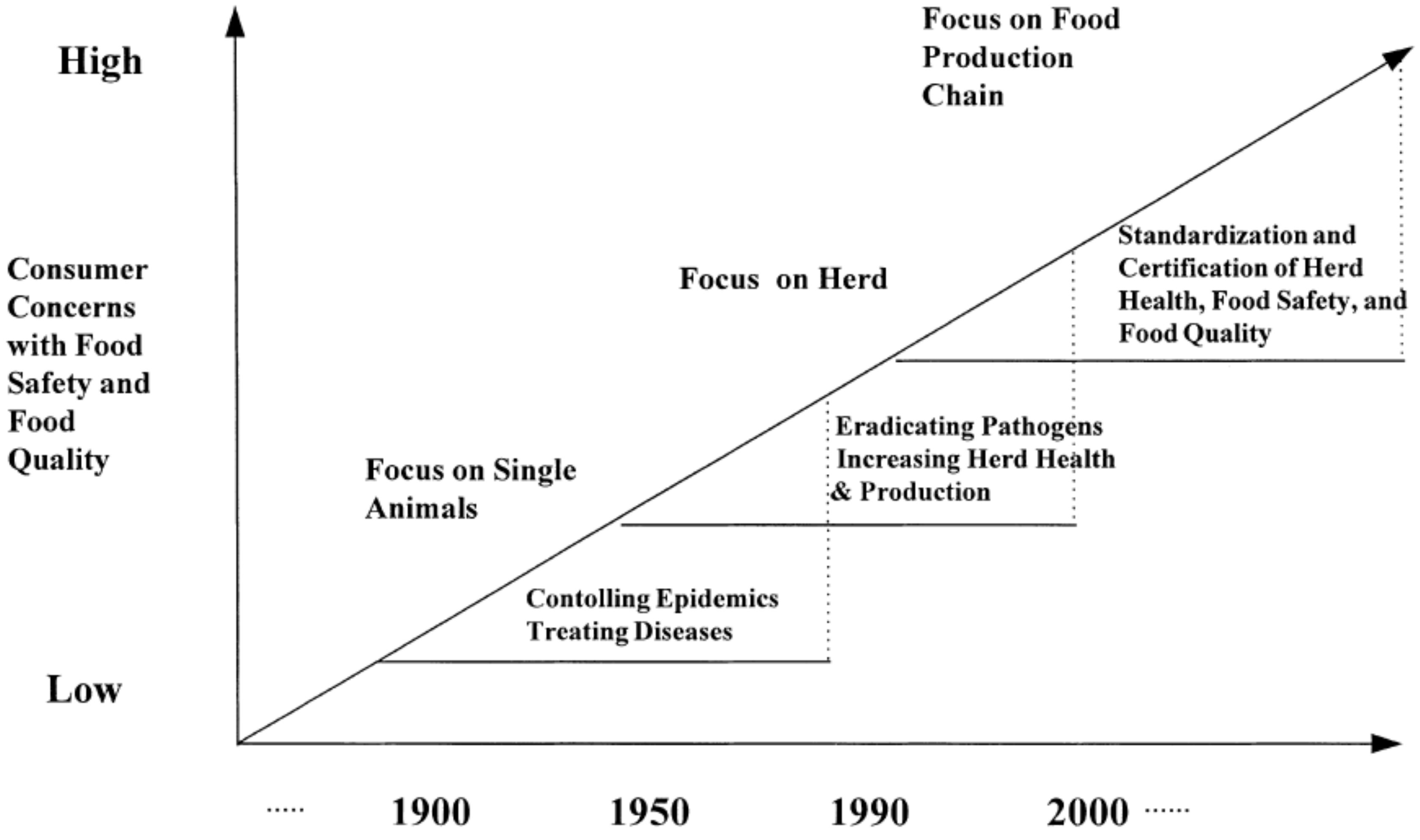
The Role of Epidemiology in Policy Development

Hueston, W.D. (2003) Science, politics and animal health policy: epidemiology in action. Preventive Veterinary Medicine 60, 3–13.

- Effective animal health policy development requires:
  - a sound scientific basis
  - clear understanding of social and political context in which policy is being made.

- Successful interventions need to be:
  - Politically, socially and economically acceptable

The Veterinarian's Role in Food Animal Practice Changing Over Time



Th. Blaha / Preventive Veterinary Medicine 39 (1999) 81-92

Components in epidemiology

- The first stage in any investigation is the collection of **relevant data**
- Investigations can be either **qualitative** or **quantitative** or a **combination** of these two approaches
- **Qualitative investigations**
  - The natural history of disease
  - Causal hypothesis testing
- **Quantitative investigations**
  - Surveys
  - Monitoring and surveillance
  - Epidemiological studies
  - Modeling
  - Risk assessments
  - Disease control

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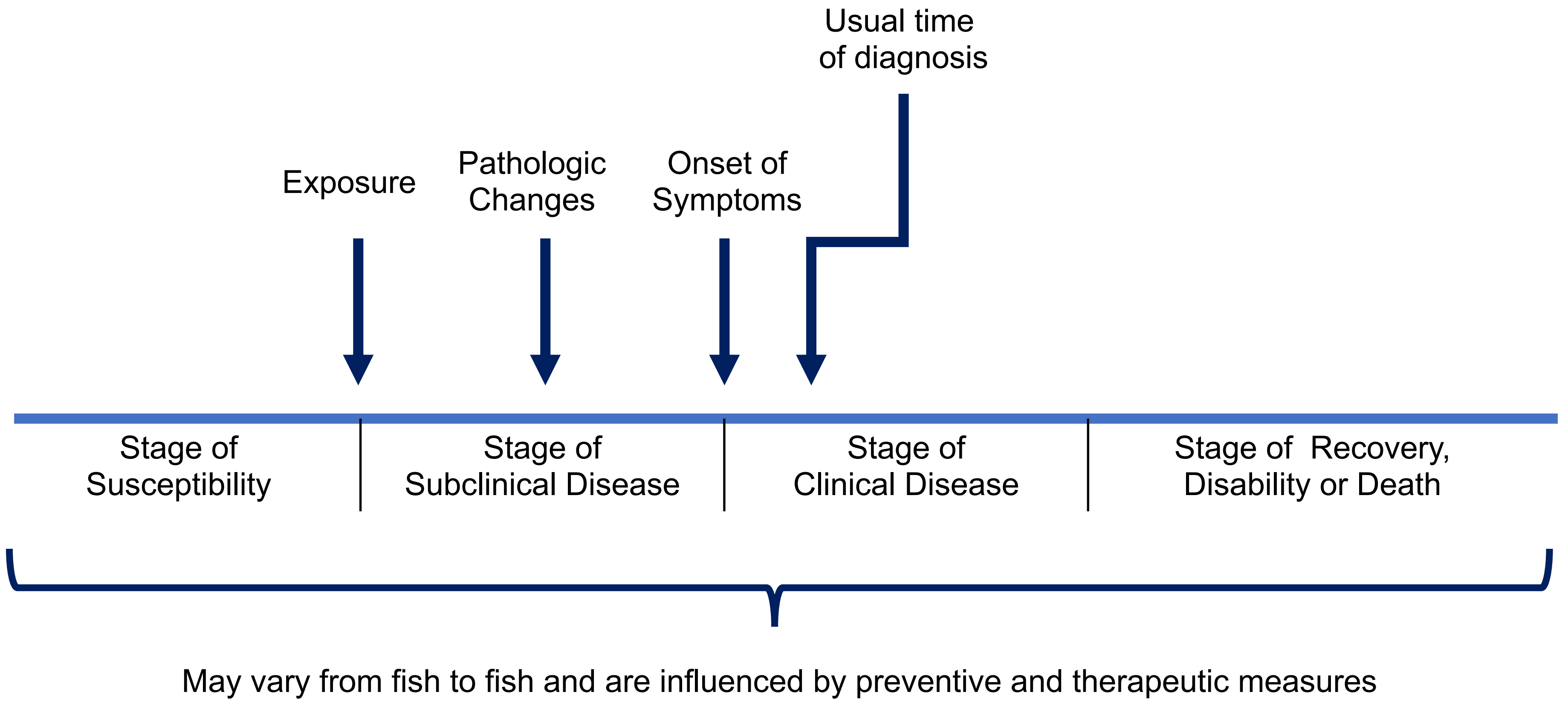
Natural history of disease

- Is the progression of a disease process in an individual over time, in the absence of treatment.

- The ecology of diseases, including the distribution, mode of transmission and maintenance of infectious diseases, is investigated by field observation.

Natural history of TiLV
(do we have drawn this?)



Causal hypothesis testing

- If field observations suggest that certain factors may be causally associated with a disease, then the association must be assessed by formulating a causal hypothesis.
- Causality (the relating of causes to effects) is described later
- Qualitative investigations were the mainstay of epidemiologists before the Second World War.

Components in epidemiology

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Surveys

- A survey is an examination of an aggregate of units (e.g., a group of fish)
- The examination usually involves counting members of the aggregate and characteristics of the members
- In epidemiological surveys, characteristics might include the presence of particular diseases, or production parameters such as harvest yield.
- Surveys can be undertaken on a **sample** of the population. Less commonly, a **census**, which examines the total fish population.

Monitoring

- Monitoring is the making of routine observations on health, productivity and environmental factors and the recording and transmission of these observations.
- Thus, the regular recording of harvest yields is monitoring, as is the routine recording of tilapia fillets inspection findings at processing plants.
- The identity of individual diseased fish usually is not recorded.

Surveillance

- Surveillance is a more intensive form of data recording than monitoring
- Includes all types of disease - *infectious and noninfectious* - and involves the collation and interpretation of data collected during monitoring programs, usually with the recording of the identity of diseased fish or farms, with a view to detecting changes in a fish population's health.
- It is normally part of control programs for specific diseases.

Types of Epidemiological Studies

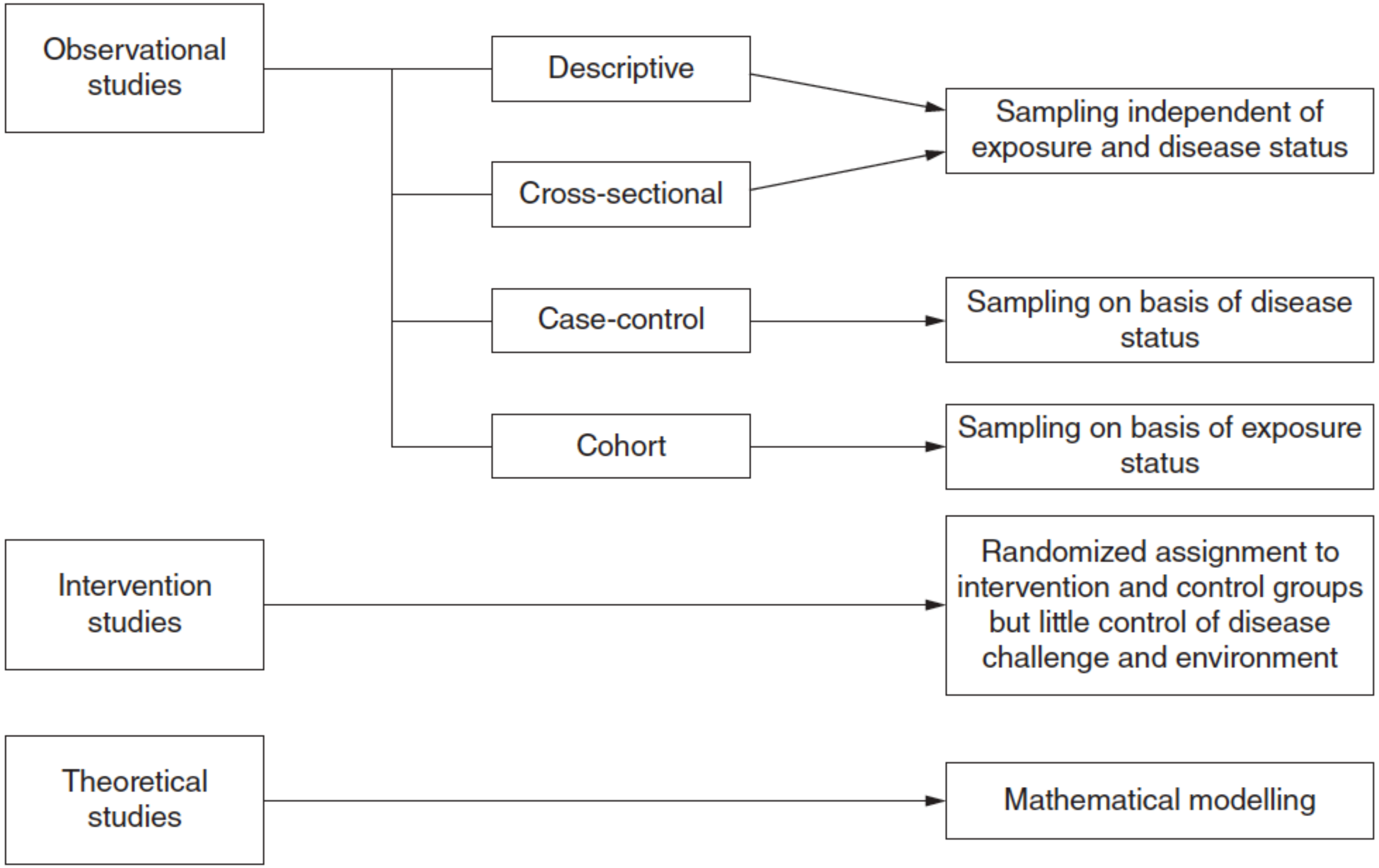

Fig. 1.3. Classification of quantitative epidemiological study types.

Epidemiological approach

- The key to any successful epidemiological investigation is to use a structured approach, being as systematic as possible and always ensuring that the current working hypothesis is that which is most consistent with available data and information.

- Use of a clear, objective and well-structured approach will ensure that your conclusions and recommendations are easily understood, and that the process of arriving at these conclusions is transparent.

Epidemiological approach

- Evaluate Patterns in fish populations!
- Describe
  - Current status (ill, not ill, recovered, dead, etc)
  - Changes over time
- Make comparisons
  - Between groups
  - Changes over time
- Establish cause
  - Initiate preventive or corrective measures

Epidemiological approach

- The Five W’s
  - Who ?
  - Where ?
  - When ?
  - What ?
  - Why ?
- Determining “Why” is the ultimate goal!

Epidemiological approach: first step

- To define clearly the problem and the scope, context and expected outcomes of the investigation.
- This might include determining if there is a disease problem and, if there is, to:
- determine the extent and impact of the problem;
- identify possible and probable cause(s) and source(s) of the problem;
- identify likely risk factors for the disease; and
- make recommendations for control and/or treatment and for future prevention.

SMART Objectives

- Specific;
- Measurable;
- Achievable;
- Relevant; and
- Time-limited.

Operational Issues

- Make sure that the terms of reference are clear and specific and understood.
- Are the project milestones and deadlines clearly defined and reasonable?
- If there are multiple people or organizations involved ensure that it is clear who is responsible for what, and particularly what your responsibilities are. For example, if you are expecting your client to provide data or assistance in some form be sure that this is clearly stated in your agreement with them, otherwise they might regard it as your responsibility to obtain the data.
- If there are costs associated with obtaining data, are these included in the budget?
- What resources will be available and who will provide them?
- Who will direct the project – who is in charge and what is the chain of command?
- How will data be shared and who will do the analysis?
- Who is responsible for project management (physical and financial), communication, collaboration, etc.?
- Who is responsible for collection, filing and collating of material?
- Who is responsible for writing the final report and in what format is it required?
- What other project outputs are required?
- Are the budget and payment schedule clear and appropriate?

Overview

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Causes of disease?

- Any “Exposure” that leads to new cases of disease
- Therefore, remove exposure and prevent some cases of disease

Causes of disease

- Examples:
  - Agent?
  - Host?
  - Environment?

Agent Factors

- Infectivity
- Pathogenicity
- Virulence
- Immunogenicity
- Host Range
- Life Cycle
- Reservoir
- Genetic Stability

Host Factors (exposures)

Intrinsic Factors

- Immunity
- Development stage or age
- Sex
- Strain

Host Factors (exposures)

Extrinsic Factors

- Use/occupation
- Nutritional
- Transportation
- Behavior

Host Factors (exposures)

Population Interactions

- Immunity ← most important factor
- Development stage or age
- Sex
- Strain
- Use / occupation
- Nutritional
- Behavior

Herd Immunity

Resistance of a group of fish to the invasion and spread of an infectious agent, because of the collective immunity of the group due to vaccination or prior exposure

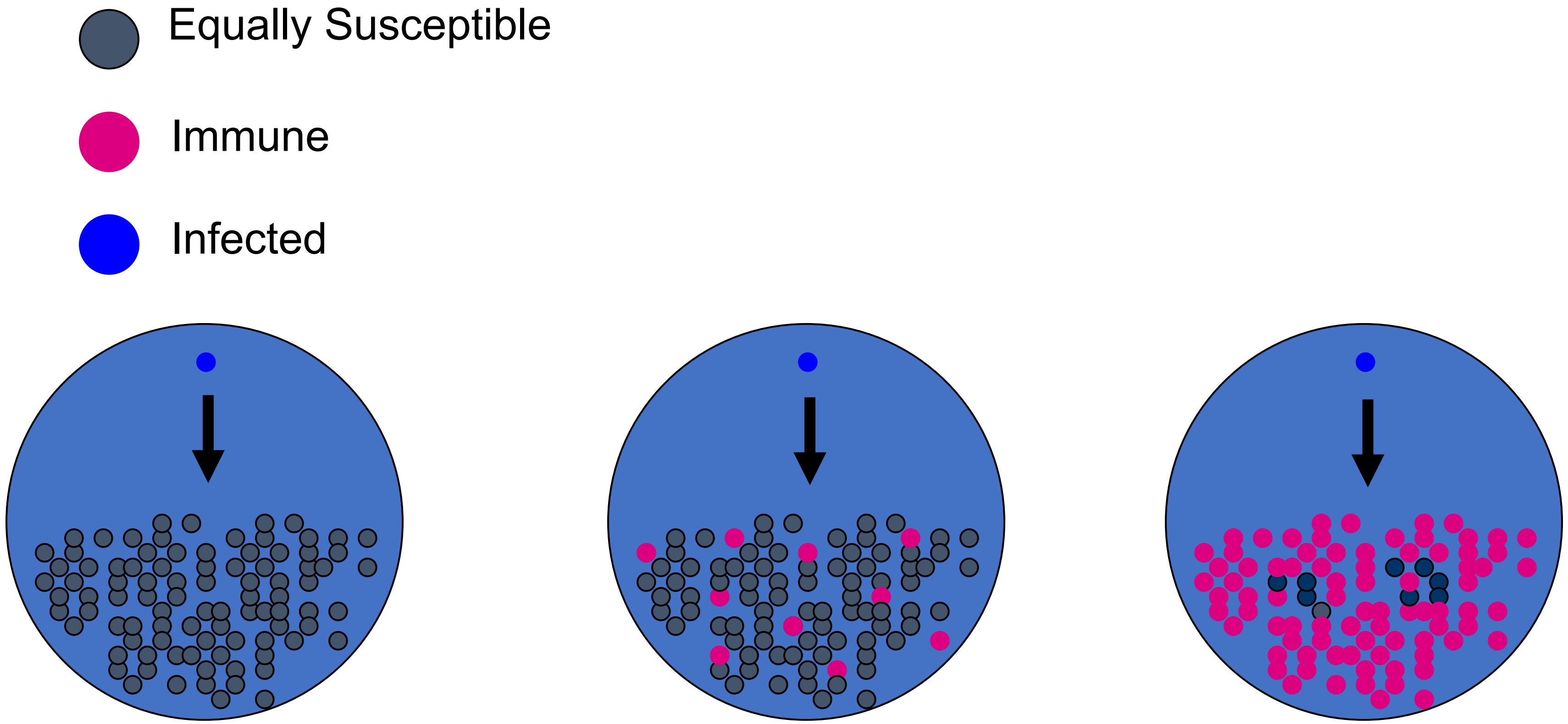
$$\text{Herd Immunity} = \frac{\text{No. resistant fish}}{\text{Total number in farm}}$$

Herd Immunity

Underlying principle: transmission of infectious disease within a farm is primarily affected by

- Proportion of resistant/susceptible fish
- Effective contact rate between fish

Herd Immunity



- Individuals can have equal “biological” susceptibility but differ in likelihood of exposure

Environmental Factors (exposures)

- Climate
- Landscape and geography
- Flora and fauna
- Geology
- Hygiene
- Housing
- Noise
- Water (temperature, salinity, oxygen, etc.)
- Currents
- Vector exposure

Infectious Disease Concepts

- Exposed
- Contaminated
- Colonized
- Infested
- Infected
- Infectious
- Infectivity
- Contagious
- Pathogenicity
- Virulence

Infectious Disease Concepts

- Pathogenicity
  - the ability to produce clinical disease
  - refers to the proportion of infections that result in disease, and does not take into account the severity of the disease

$$= \frac{(\text{mild signs + mod. signs + severe signs + deaths})}{\text{All infected fish}}$$

Infectious Disease Concepts

Virulence

severity of a disease

the ability of the agent to produce severe disease

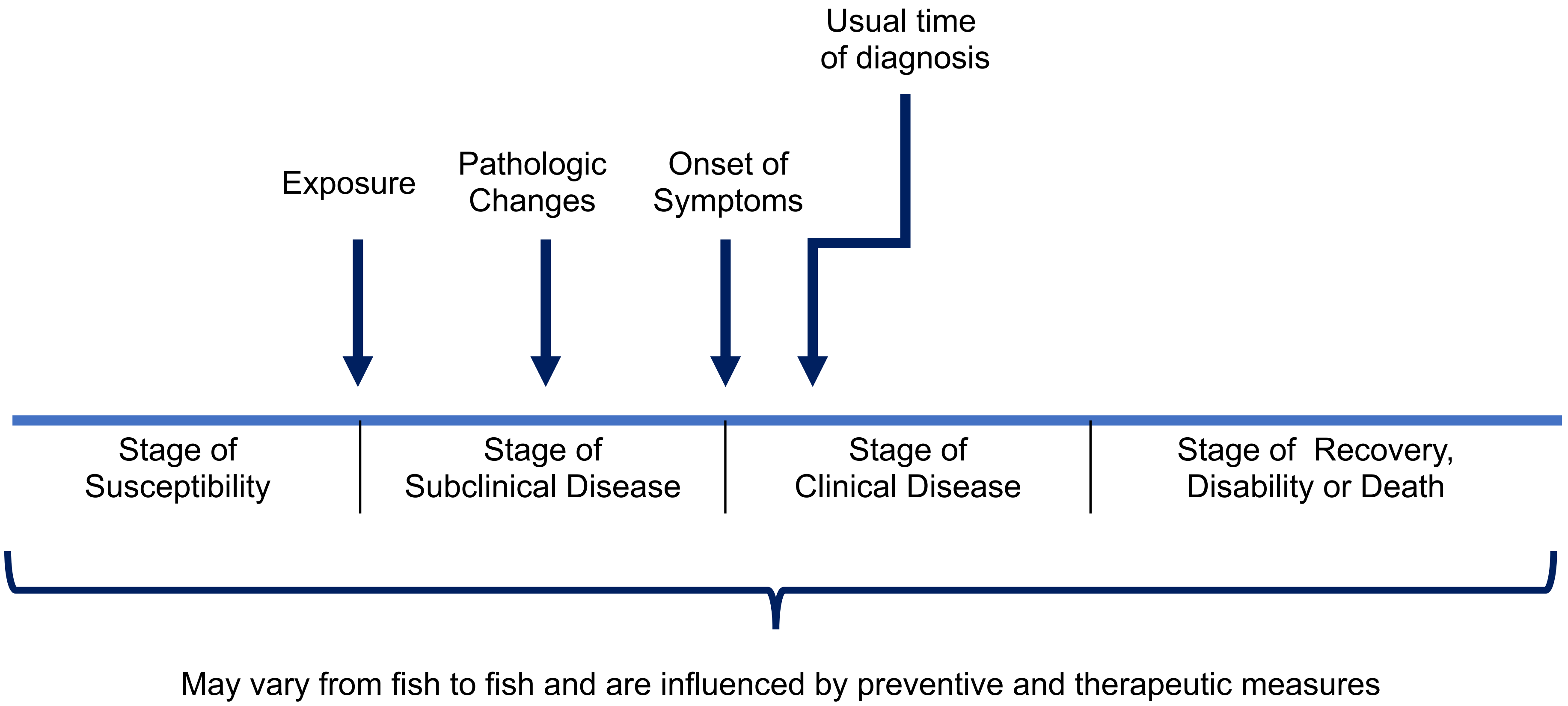
$$= \frac{(\text{severe signs + deaths})}{\text{all infected fish}}$$

Infectious Disease Concepts

- Phenotype/Genotype
- Antigen
- Antigenic
- Incubation period
- Subclinical disease
- Clinical disease
- Carrier
- Persistent infection
- Latency
- Persistence in environment

Natural history of TiLV

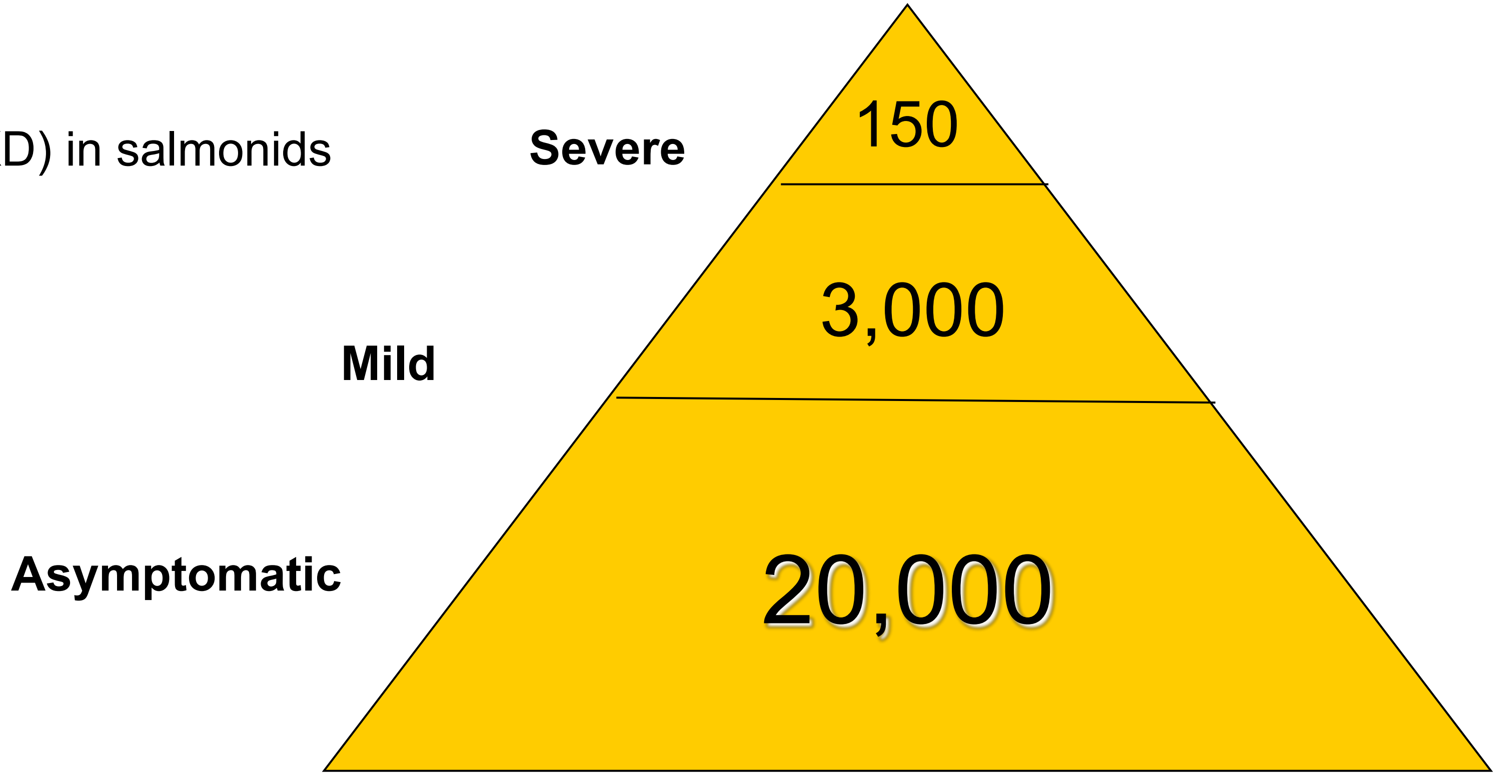
Spectrum of disease



Infectious Disease Concepts

- Clinical disease as the tip of the iceberg

Bacterial Kidney Disease (BKD) in salmonids



Infectious Disease Concepts

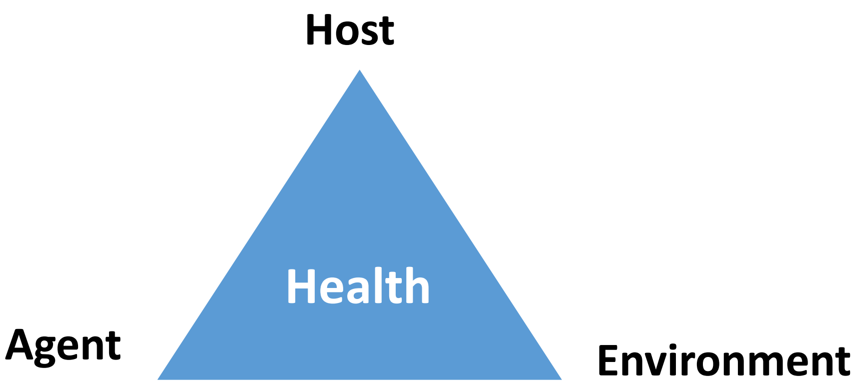
- Contact & Transmission
  - Direct
  - Indirect
  - Fomites or vehicles
  - Vectors

Infectious Disease Concepts

- Evidence of Exposure
  - Direct: Identification of agents (antigen)
    - Culture (incl. biochemical reactions)
    - Polymerase chain reaction (and sequencing of products)
    - Other antigen detection methods e.g. ELISA
  - Indirect: Biological response to agents
    - Pathology on tissues from animal
    - Serum antibody
      - Seronegative vs seropositive (-/+)
      - Seroconversion (change from negative to positive)
      - “Concentration” or a “score” for tests such as ELISA

Forces Influencing Infectious Disease Occurrence

- Agent characteristics
  - Pathogenicity, virulence, infectivity, survival, life cycle, etc.
- Likelihood of exposure
- Host's ability to mount an immune response against the agent

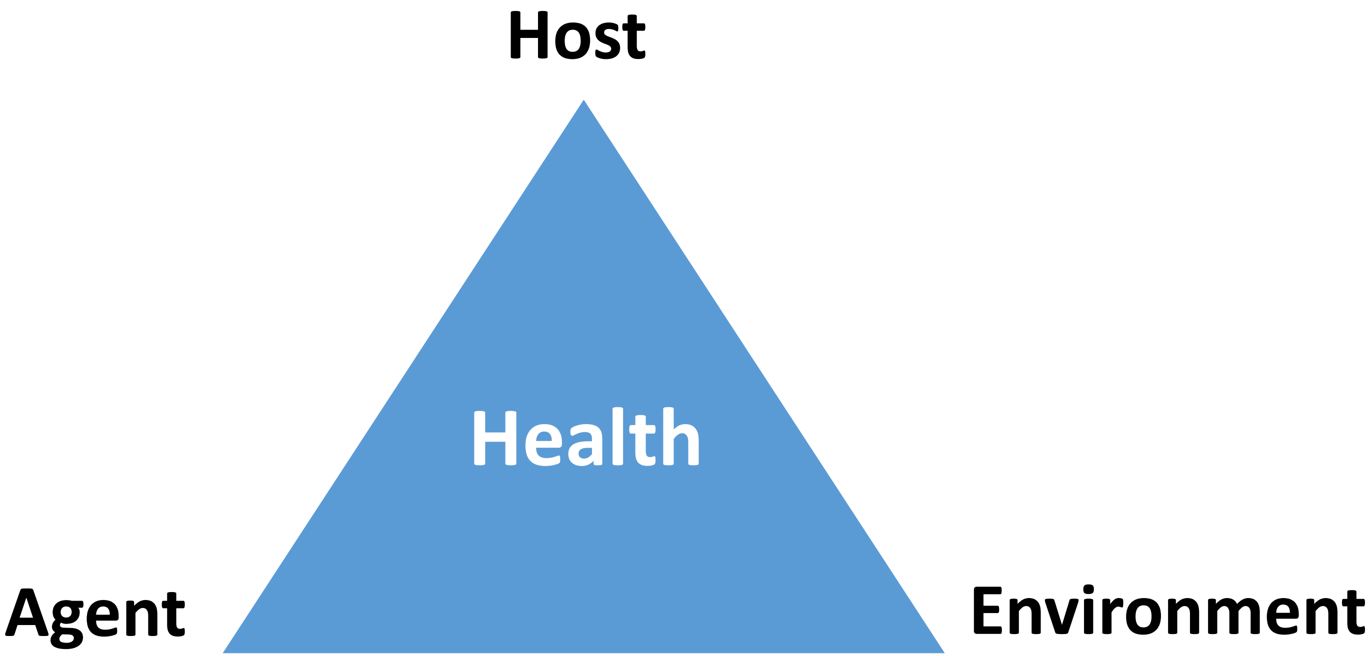


Environmental Factors

- Micro-environment
  - Proximity or local environment
- Macro-environment
  - General or regional environment
- Social factors
  - Social and political influences

Multiple Causes

- Bovine Respiratory Disease
- Classic veterinary example of multifactorial disease



Risk of Disease Is Not Equal: Host

- Age affects risk
  - Fresh calves vs. yearlings
- Immunity
  - Exposure
  - Vaccination
- Stress
  - Weaning
  - Transport
  - Processing
  - Mixing

Risk of Disease Is Not Equal: **Agent**

- Variability in agents
  - *Manheimia hemolytica* biotypes
  - *Haemophilus somnus*
  - Virus strains (Bovine herpes virus (BHV), bovine respiratory synctial virus (BRSV), and bovine viral diarrhea (BVD))
- Different agents
  - Bacterial
    - *Pasteurella*, *Haemophilus, Actinobacillus*
  - Viral
    - BHV, BRSV, Parainfluenza, Coronavirus, BVD?

Risk of Disease Is Not Equal: Environment

- Season
- Transport
- Pasture vs. Background vs. Feedlot

Multiple Levels of Causation

- *e.g.*, Vector borne-diseases
  - Virus or bacteria
  - Mosquitoes, ticks
  - Environment

Remove Exposure ➔ Prevent Disease

Why Worry about Causation?

- We can only prevent disease by removing exposure to causal factors

Causal Factors?

- Two basic philosophies about causation of infectious diseases
  - Presence of an agent -> disease
  - Agent alone is not sufficient to produce disease

Henle-Koch Postulates

- First recognized criteria for establishing cause:
  - The organism is found in all disease cases.
  - The organism is not found in other individuals as a non-pathogenic parasite.
  - It must be possible to produce a pure, sustainable culture of the organism.
  - It must be possible to experimentally reproduce the same disease in a susceptible host.

One Agent ➔ One Disease

Robert Koch

Louis Pasteur

Problems with Koch's Postulates

- Doesn't directly relate to non-infectious diseases
- Not every exposed individual becomes infected.
- Not all infected individuals develop disease.
- Not possible to recovery of infectious agents from all infected individuals or even all disease cases.
- Did Koch identify THE cause?

Multiple Causes - Models

- Agent, host, and environment all contribute to the occurrence of disease
- Causal relationships are not always simple
- Models assist with in understanding and describing complex causal relationships
  - Necessary, sufficient, and component causes
  - Web of causation
  - Path models
  - Venn Diagrams

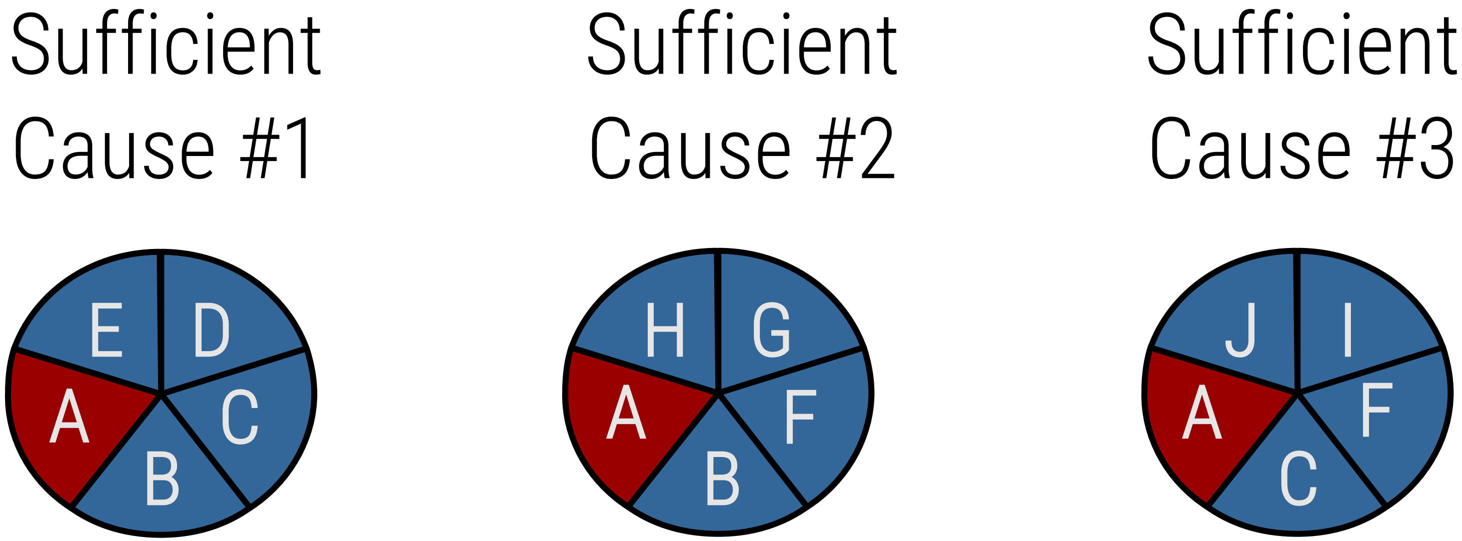
Necessary and Sufficient Causes

- Component cause
  - Any causal factor (Host, Agent, Env.)
- Sufficient cause
  - Set of component causes that is capable of causing disease
  - Once all of the sufficient causes are present, disease <u>WILL</u> occur
- Necessary cause
  - Component cause that is REQUIRED for disease to occur

Modern concepts of disease
Bradford–Hill criteria

Criteria	Description
Strength of association	Strong associations with higher risk ratios are more likely to be causal than a weak association
Consistency	Consistently finding an association between a putative cause and a disease outcome in multiple studies by different investigators
Specificity	If a factor is only associated with a specific disease it was said to be specific and considered more likely to be causal
Temporality	The causal factor should precede the outcome it is proposed to be causing
Biological gradient	A dose-response association is supportive of a causal relationship
Plausibility	Is the association biologically plausible?
Coherence	The proposed causal association should not contradict current scientific knowledge
Experiment	A causal association is more likely if it is supported by results from controlled, randomized trials
Analogy	A causal association may be more likely if there are other examples of causal associations for analogous exposures and outcomes

Necessary and Sufficient Causes



- 10 Component Causes (A, B,C, D, E, . . . J)
- 3 Sufficient Causes (1, 2, 3)
- 1 Necessary Cause (A)

AMERICAN
Journal of Epidemiology
Formerly AMERICAN JOURNAL OF HYGIENE

VOL. 104 DECEMBER, 1976 NO. 6

Reviews and Commentary

CAUSES

KENNETH J. ROTHMAN

PUBLIC HEALTH MATTERS

Causation and Causal Inference in Epidemiology

Kenneth J. Rothman, DrPH, Sander Greenland, MA, MS, DrPH, C Stat

Total factors = 10
5 sufficient causes to disease
One necessary factor

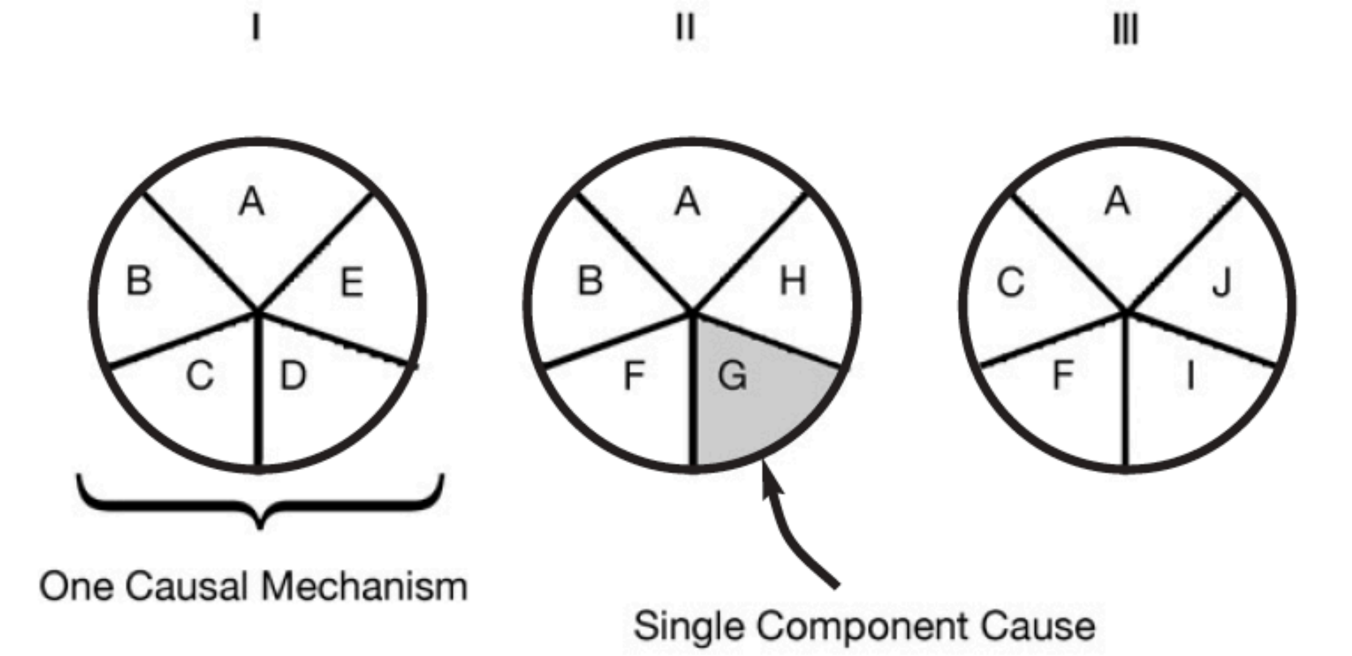


FIGURE 1—Three sufficient causes of disease.

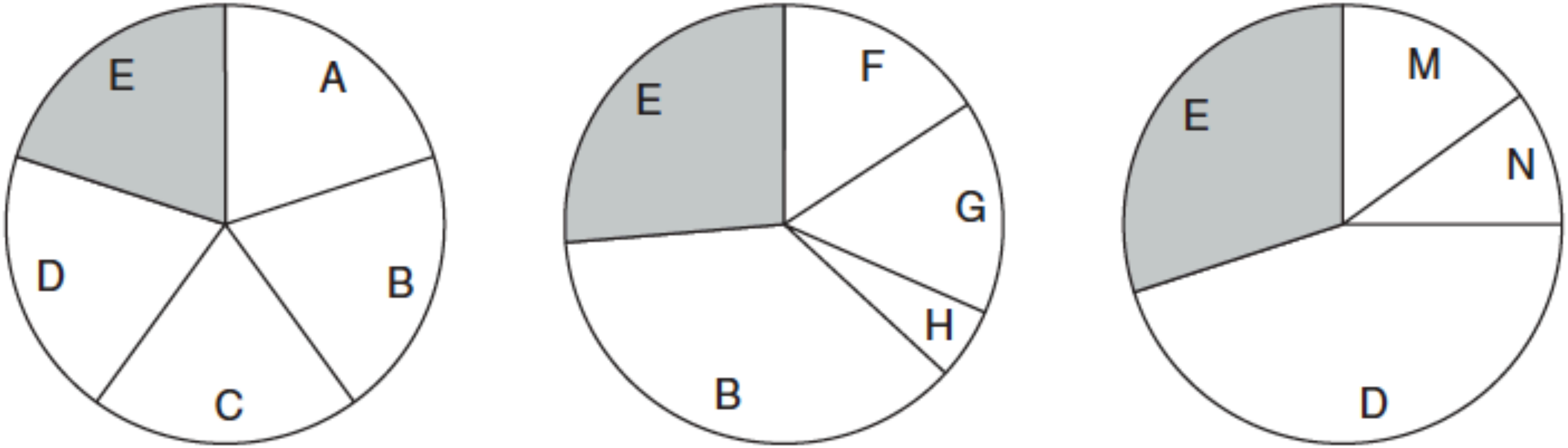


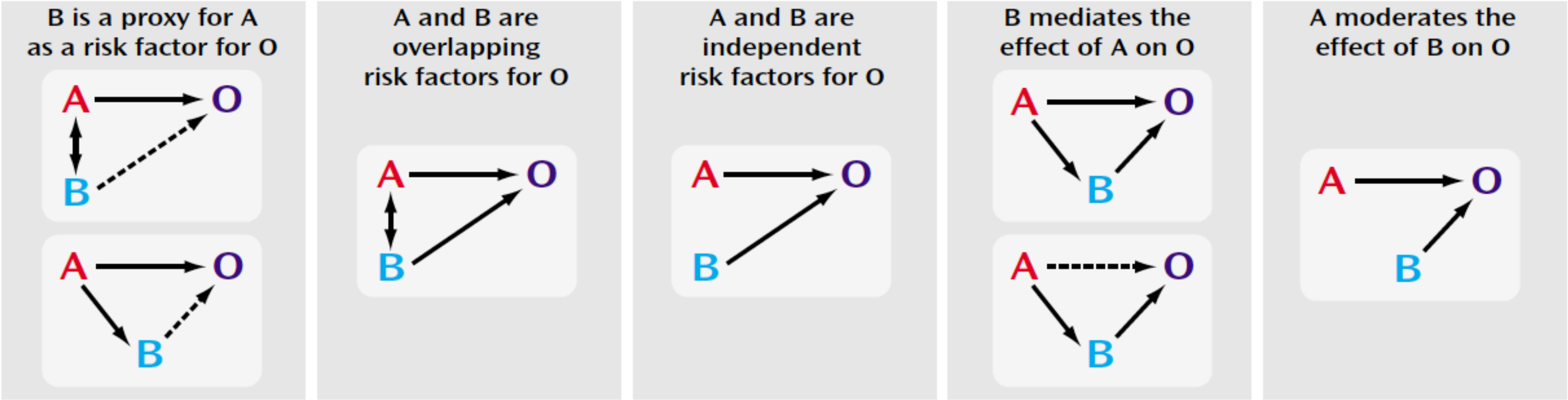
Fig. 4.1. Use of pie charts to demonstrate three separate sufficient causal mechanisms, each made up of multiple component causes identified by letters. There is one candidate necessary cause (E) that is the only component cause found in every sufficient causal mechanism (adapted from Rothman and Greenland, 2005).

Reviews and Overviews

How Do Risk Factors Work Together? Mediators, Moderators, and Independent, Overlapping, and Proxy Risk Factors

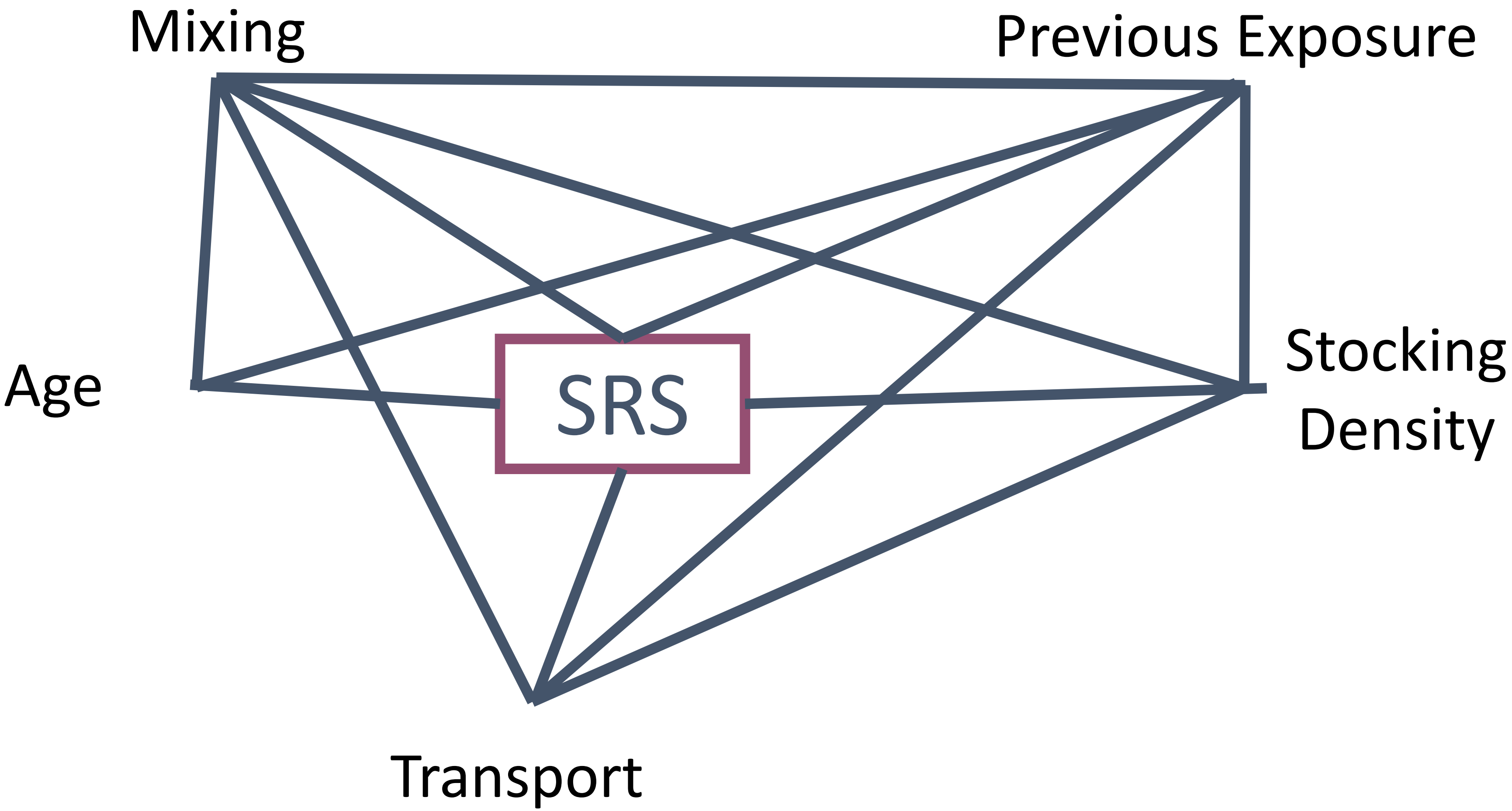
Kraemer, Stice, Kazdin et al. Am J Psychiatry 2001; 158:848–856

FIGURE 1. Five Ways Risk Factors A and B Can Work Together to Affect Outcome O[a]

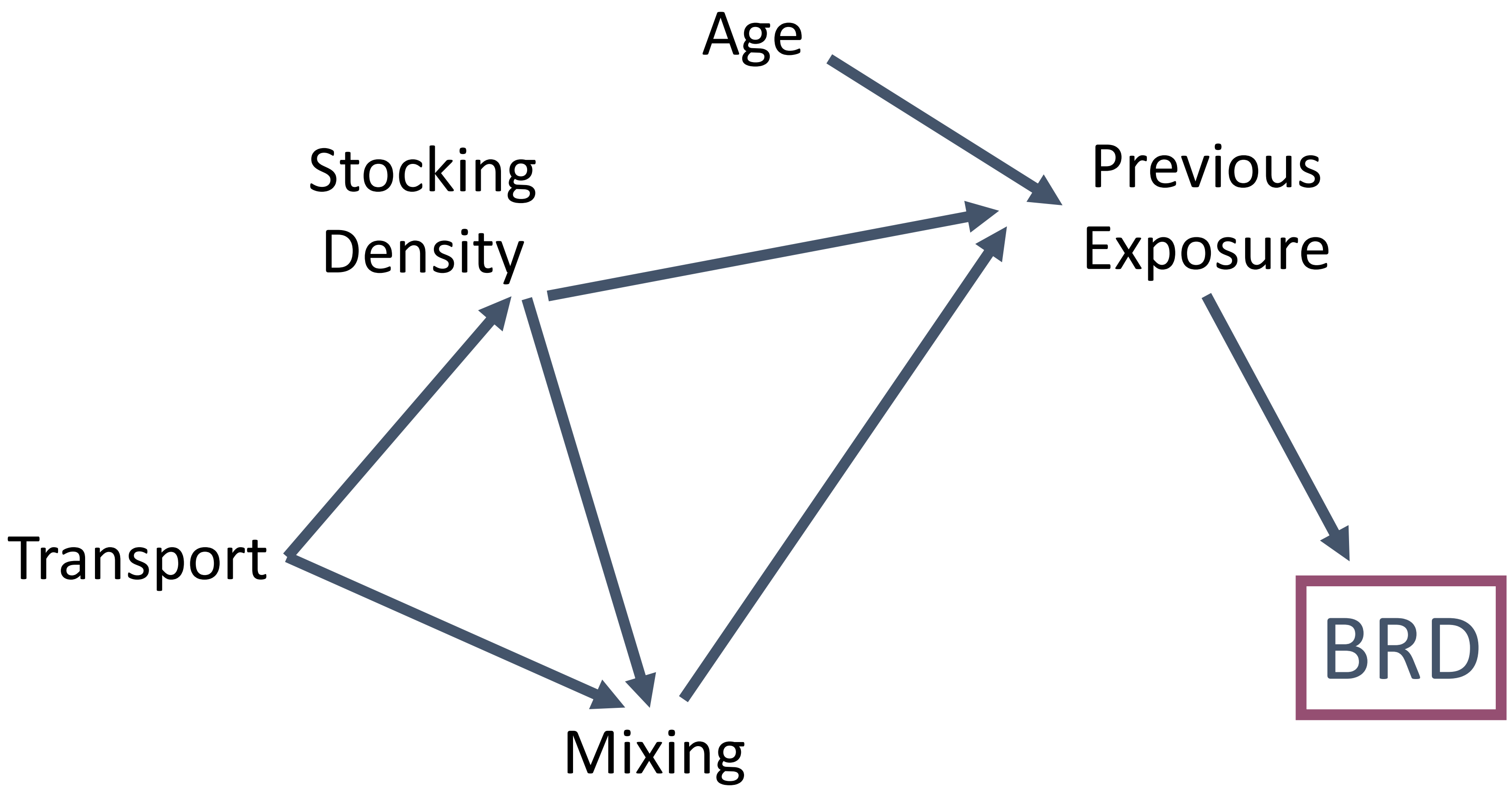


[a] Left to right positioning indicates temporal order. A solid arrow indicates a correlation. A dotted arrow indicates a correlation that weakens or disappears when the other risk factor is considered.

Web of Causation

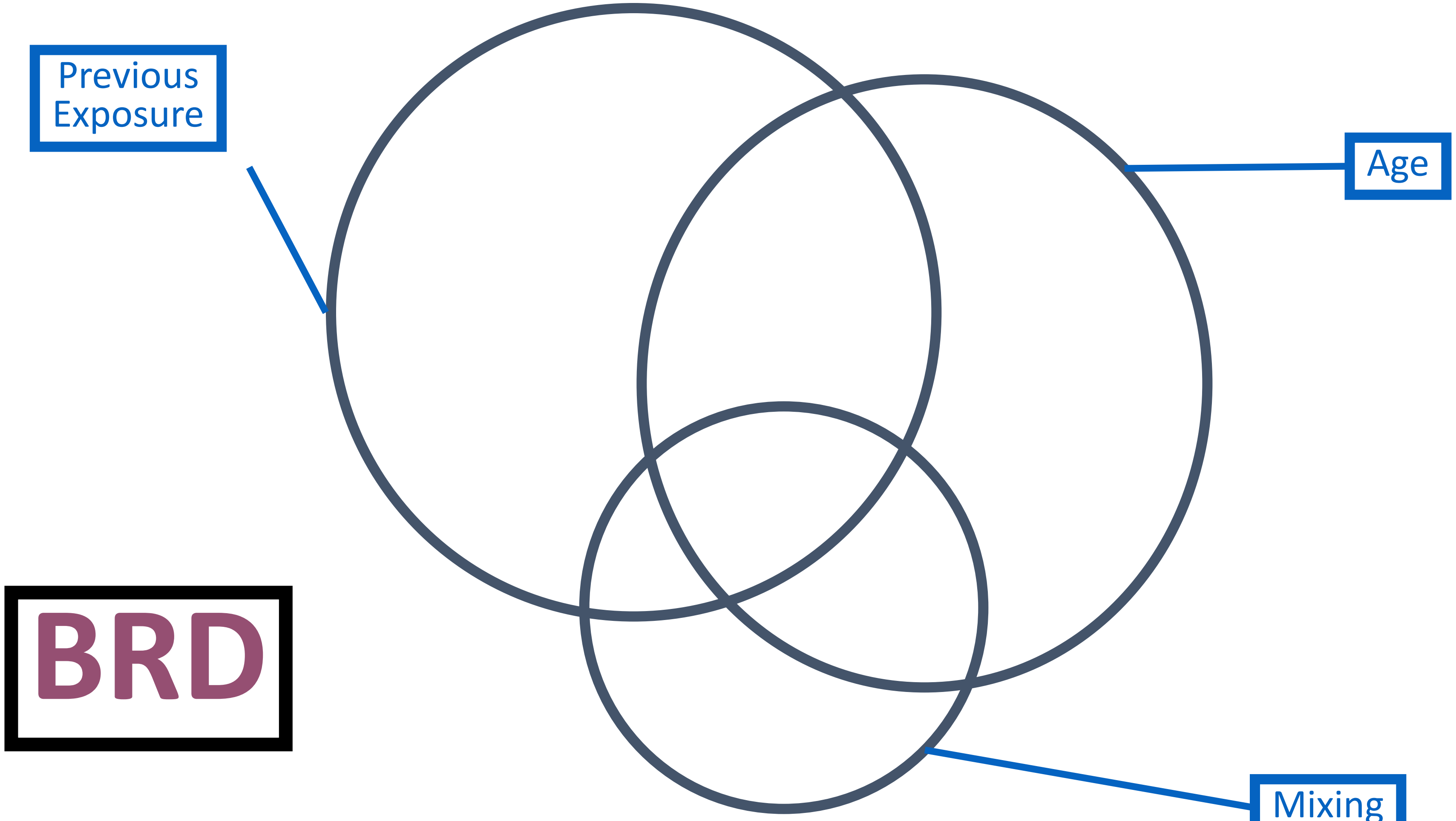


Path Model:
Causal Sequence



Venn Diagram

Magnitude and Interaction of Causes

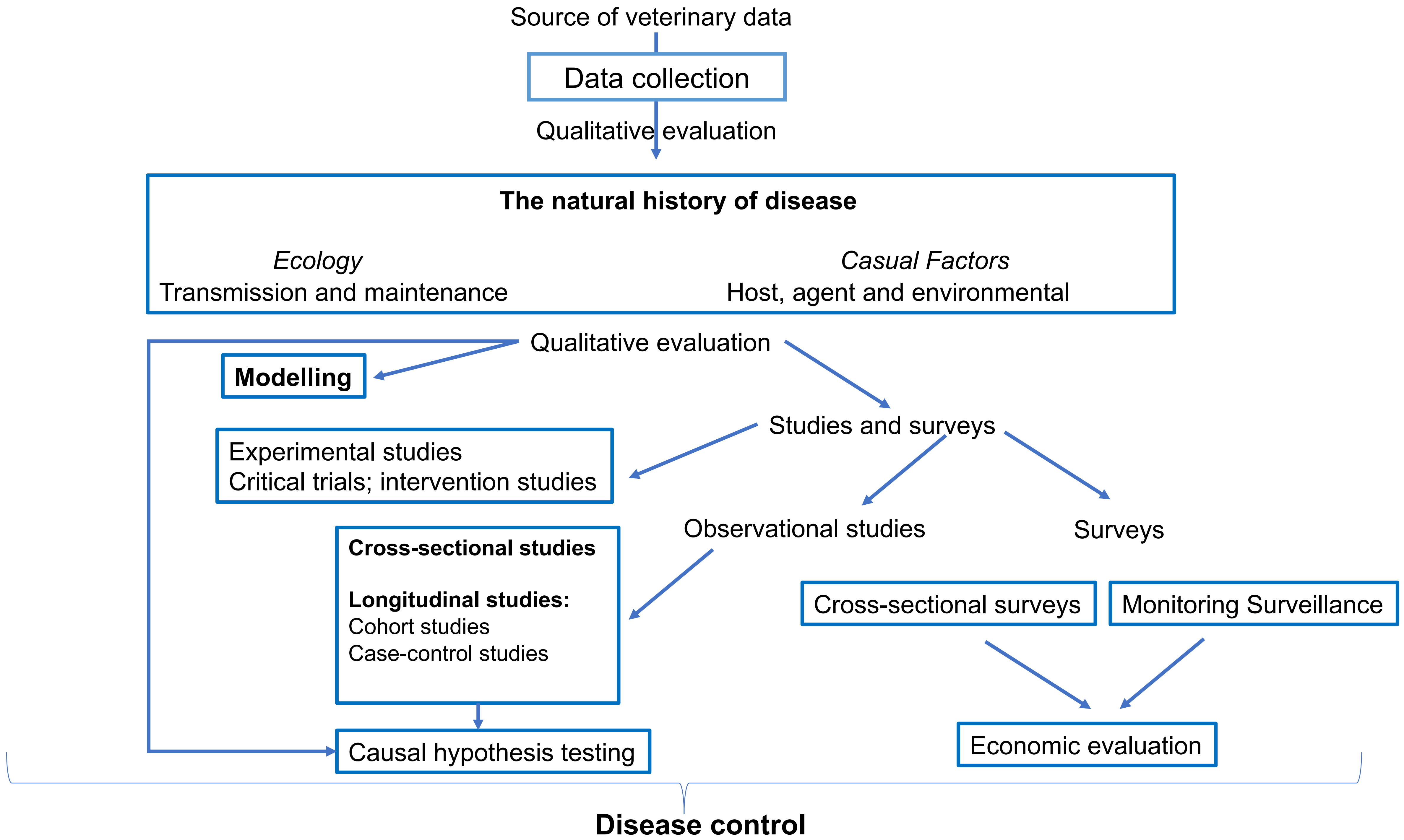


How Do We Identify Important Risk Factors?

- Summarize disease occurrence in population.
- Compare risk of disease among animals with different exposures.
- Measure associations with disease occurrence.

Why Characterize Populations

- Look for Patterns!
- Describe populations
  - Current status
  - Changes over time
- Make comparisons
  - Between groups
  - Changes over time
  - Establish “cause”
  - Establish preventive measures


Source of veterinary data
Data collection
Qualitative evaluation
The natural history of disease
Ecology
Transmission and maintenance
Casual Factors
Host, agent and environmental
Qualitative evaluation
Modelling
Studies and surveys
Experimental studies
Critical trials; intervention studies
Observational studies
Surveys
Cross-sectional studies
Longitudinal studies:
Cohort studies
Case-control studies
Cross-sectional surveys
Monitoring Surveillance
Causal hypothesis testing
Economic evaluation
Disease control

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Epidemiology Session

Principles of epidemiology and surveillance and their application to aquaculture

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