

EPIDEMIOLOGY: SYSTEMATIC APPROACH TO DISEASE OUTBREAK INVESTIGATION

Outbreak investigation is uncovering and interpreting clues for how to control a problem and how to prevent a recurrence. With problems in herds, comparing affected with unaffected animals, both in cross-section (at one time point) and over time to identify the differences provides the clues.

Disease response in a herd is a continuum, with herd members experiencing differing exposure and expressing differing severity ranging from unexposed to inapparent to subclinical to clinical to fatal. This range occurs because herd members have differing intrinsic characteristics (e.g., age, genetics, immune status) and differing exposures (e.g., feed amounts, infectious doses, social order stresses, exposure timing differences). During disease progression through a herd, individuals exposed at different time points are at different points in the **disease natural history**. The performance of diagnostic tests are strongly affected by an animal's position in this spectrum, often being better on animals with greater severity. This range in responses provides the clues for solving the problem.

Clinical cases are “red flag” evidence of a herd problem but rarely are they the full extent of the problem. For every animal expressing clinical signs, often ten or more are subclinical, being detectable only by laboratory testing. Concentrating only on the observably ill animals is a serious mistake, particularly if concluding from their absence that the problem is over. Many infectious agents enter a herd, such as by importation of a subclinical carrier, and spread for weeks to years before being diagnosed in a clinical case. Although an infectious agent may be found in clinical animals, unless the agent always causes clinical disease or other evidence shows that this agent is present only in the affected animals, one cannot conclude that the agent alone is responsible for the problem. Co-infections with ubiquitous agents are common and clinical disease outbreaks often occur in groups in which the agent is circulating far more widely than the clinically affected animals. A decline is the typical “natural history” or progression of infectious disease outbreaks even without any interventions as the animals respond to the infection and the pool of susceptible animals shrinks. Clinical cases may disappear altogether even though the infection is still widespread in the herd.

The logic for determining cause is based on **Mill's Five Methods of Induction** (System of Logic, 1843). Stated as Bradford Hill's **Criteria of Causation** (1965) or **Evan's Postulates** (1976), they provide the logical basis for screening risk factors. For a risk factor to be causal, it should meet the following conditions:

- The problem prevalence is higher in those exposed to the risk factor than those not
- Risk factor exposure is more frequent among those with the problem than those without
- The likelihood of having the problem and the severity of the host response increases with increasing risk factor dose
- Risk factor exposure either coincides with problem onset or precedes it by a bell-shaped or log-normal incubation period distribution
- A host response (e.g., culture, serological titer or clinical chemistry result) either follows the risk factor exposure in those lacking it before exposure or increases in those with it before exposure but is infrequent in those not exposed
- The relationship between the risk factor and the problem makes biologic as well as logical sense

An outbreak investigation follows logical steps, often revisited as it unfolds:

1. Define the manager's primary complaint and confirm the existence of a problem
2. Establish or verify the pathological and etiological diagnosis, sampling a sufficient number of representative cases
3. Establish a case definition with the goal of excluding animals having sporadic, one of a kind background problems but covering most affected animals
4. Map out the pastures, lots, housing and processing areas
5. Draw out the production cycle of the affected group, including the timing of events such as vaccination and weaning and moves through processing areas and between housing areas
6. Establish problem presence and magnitude using objective data (e.g., pocket, calendar and computer records) where possible, secondary data (e.g., invoices for products and services) when not and, last of all, by comparing people's memories. The three components are:
 - Demographics of affected vs. non-affected animals (*Who?*) What are the characteristics of affected and unaffected animals in terms of source, age, production level, position in social hierarchy, stage of production cycle and exposure to potential risk factors?
 - Timing (temporal pattern - *When?*) When in calendar time and in the production cycle does the problem occur? When did the index case occur? Any processing and movement events involved?
 - Place (spatial pattern - *Where?*) Where were affected and unaffected animals located on the premise map?
7. Summarize the data by groups, defining the populations at risk, following cohorts through the risk period to calculate individual risk in each group
8. Have everyone explain their favorite hypotheses (differential diagnoses) about key determinants (risk factors), particularly those that could be modified on this premises, by drawing out **cause-and-effect model**, **concept map**, **causal loop diagram** or **Ishikawa diagram** of how the risk factors might interact to cause the observed difference in outcomes. Asking **5 Whys** may help identify cause and effect relationship components.
9. Evaluate these hypotheses (differentials), such as by calculating **odds-ratios** to assess the association strength between a **root cause** and the outcome or by looking the presence of other effects predicted by the association
10. Design interventions against root causes or prospective studies for further information
11. Record your findings and recommendations and predict when changes should be seen
12. Monitor the results for these changes

Pitfalls include innumeracy, logic errors and **cognitive biases**. **Innumeracy** includes using numerator counts to compare risk in different-sized groups (dangling numerators), including animals not at risk in risk denominators, and not including precision estimates (standard errors, confidence intervals) when comparing group summary measures. Logic errors include mistaking association for causation or violating key postulates. Because cognitive biases are hard-wired into our reasoning processes, their impact is reduced by the design of the investigation process itself. Reducing **confirmation bias** requires including the unaffected in testing and comparisons and doing complete rather than selective necropsies. More mistakes are made due to not looking than to not knowing. Reducing **recall bias** requires asking neutral questions, establishing counts from empirical evidence, confirming with secondary data, such as from invoices for products and services when evidence for counts is absent or incomplete, and confirming answers with multiple farm personnel. Reducing **anchoring bias** requires drawing out causal diagrams that explain observations, particularly discrepant ones, in the pathway between the outcome and the alleged root cause in everyone's hypotheses about what went wrong. These diagrams help uncover reasoning gaps that are being masked by the **illusion of explanatory depth (IOED)** and generate buy-in for the best solution. Without strong support for a causal path, we are likely to fall victim to **hindsight bias** and have the problem recur.



MISCELLANEOUS

Suggested Reading

[Journals]

Doho, I.R. Dealing with deficient and missing data. *Preventive Veterinary Medicine* 2015;122(1-2):221-228. doi:10.1016/j.prevetmed.2015.04.006

McKenzie, B.A. Veterinary clinical decision-making: Cognitive biases, external constraints, and strategies for improvement. *JAVMA* 2014;244(3):217-276.

Osweiler, G.D. Diagnostic guidelines for ruminant toxicosis. *Veterinary Clinics: Food Animal Practice* 2011;27(2):247-254.

Otter, A., Davies, I. Disease features and diagnostic sampling of cattle and sheep postmortem examinations. *In Practice* 2015;37(6):293-305 doi: 10.1136/inp.h2482

Smith, D.R. Field disease investigation of neonatal calf diarrhea. *Veterinary Clinics: Food Animal Practice* 2012;28(3):465-481. doi: 10.1016/j.cvfa.2012.07.010

Smith, D.R. Field epidemiology to manage BRD risk in beef cattle production systems. *Animal Health Research Reviews* 2014;15(2):180-183. doi:10.1017/S1466252314000243

Smith, D.R. Investigating outbreaks of disease or impaired productivity in feedlot cattle. *Veterinary Clinics: Food Animal Practice* 2015;31(3):391-406. doi: 10.1016/j.cvfa.2015.05.003

Swecker, W.S., Thatcher, C.D. The investigation of nutritional disorders. *Veterinary Clinics: Food Animal Practice* 1988;4(1):127-144.

Waldner, C.L., Campbell, J.R. Herd health investigations in cattle practice. In: Cockroft, P.D., ed. *Bovine Medicine*. 3rd ed. John Wiley & Sons, 2015:117-123.

[Books]

Gregg, M., ed. *Field Epidemiology*. 3rd ed. Oxford University Press, 2008.

Hulley, S.B., Cummings, S.R., Browner, W.S., Grady, D.G., Newman, T.B. *Designing Clinical Research*. 4th ed. Lippincott Williams & Wilkins, 2013.

Ruegg, P.L. Barnyard Epidemiology and Performance Assessment. *Veterinary Clinics: Food Animal Practice* 2006;22(2):1-270.

Thomson, D.U., White, B.J. Feedlot Production Medicine. *Veterinary Clinics: Food Animal Practice* 2015;31(3):323-520 doi:10.1016/j.cvfa.2015.05.003

Thrusfield, M.V. *Veterinary Epidemiology*. 3rd ed. Blackwell Publishing Co, 2007.

Wobeser, G.A. *Disease in wild animals: Investigation and management*, 2nd ed. Springer-Verlag, 2007.

[Internet Resources]

Gay, J.M. A Systematic Approach to Herd Disease Outbreak Investigation, 2010
<http://people.vetmed.wsu.edu/jmgay/courses/documents/WCABPHerdProblemSolving10Procdngs.pdf>

WHO. Foodborne Disease Outbreaks: Guidelines for investigation and control, 2008
http://www.who.int/foodsafety/publications/foodborne_disease/outbreak_guidelines.pdf

Author John M. Gay

Consulting Editor Kaitlyn Lutz