

An overview of study design

This is the first in a series of three editorials commissioned by JSAP. The series will review the use of statistics for data analysis in clinical papers. Please note that in this editorial the references quoted refer to examples of the types of studies mentioned.

Introduction

GOOD study design is the foundation of all good clinical research. Flaws in study design can result in incorrect inferences because of problems such as confounding (the distortion of the effect of an exposure by another exposure) and bias (an effect that causes the results of the study to deviate systematically from the truth). Confounding can be addressed during statistical analysis providing the correct information has been recorded. However bias can rarely be corrected after data collection. Collaboration between clinicians and epidemiologists at the study design stage can help to reduce such problems and ensure that results and inferences are valid.

The first step in designing a study is to think carefully about the underlying hypothesis. It is important to formulate a clear research question in order to ensure that the type of study you choose is capable of answering it. Understanding the features of different study types will help you decide on the most appropriate study to answer your research question, while making the most of available resources. This article summarises the key features of the most common study types found in clinical research.

Terminology

● Descriptive vs analytical studies

A descriptive study does not test a hypothesis but is useful for gaining more information about a subject, from which to generate new hypotheses. If you are aiming to test an *a priori* hypothesis, based on existing knowledge or findings of an earlier descriptive study, an analytical study is required. An analytical study involves the comparison of groups with and without the exposures or outcomes of interest.

● Observational vs experimental studies

In the majority of clinical studies, individuals are observed without interference by researchers. Such observational studies provide weaker empirical evidence than experimental studies because of potential confounding and bias. Preliminary evidence of associations between exposures and outcomes can be gained and used as underlying hypotheses for experimental studies.

In experimental studies, researchers “intervene” in some way, for example by assigning individuals to different treatment groups or by deliberately changing one or more variables to examine effects. Interventions are under the control of the researcher and can therefore be randomised, thereby adding to the strength of the evidence provided by subsequent statistical analysis.

● Prospective vs retrospective studies

Prospective studies are designed before data are collected, which allows researchers to devise means of reducing confounding and bias (Stegemann and others 2007). Retrospective studies use data already collected, for example, hospital records, and are therefore an inherently weaker design as the manner in which data are collected cannot be controlled (Avner and others 2008).

Common types of study in clinical and epidemiological research

● **Case reports and case series** are descriptive, observational studies, useful for exchange of information between clinicians (Barrand and Cornillie 2008). No control group is involved and only weak evidence can be provided to support any hypothesis. Findings can be used to derive hypotheses suitable for further investigation with analytical studies.

● **Cross-sectional studies** are observational studies providing a “snapshot” of information about exposures and disease in a population at one point in time (Levy and others 2008). As data are not recorded over time, prevalence (proportion of the population affected) but not incidence (rate of occurrence of new cases over time) of disease can be measured. Studies may be descriptive or analytical, although associations between exposures and outcomes are difficult to interpret as there is no information on the timing of one in relation to the other.

● **Case-control studies** are analytical, observational, retrospective studies in which the history of individuals with (cases) and without (controls) the outcome of interest is examined to determine whether they had the exposure of interest (Little and Gettinby 2008). Case-control studies are relatively quick and inexpensive and are useful for studying rare diseases, as the starting point of the study is disease status, with exposure status examined “in hindsight”. However, prevalence and incidence of disease cannot be determined as the number of cases and controls has been set by the researcher. Case-control studies are particularly vulnerable to bias. For example, owners of diseased animals may be more likely to report certain factors than owners of healthy animals (recall bias). In order to avoid selection bias, careful choice of control animals is required to ensure that they are representative of the population at risk.

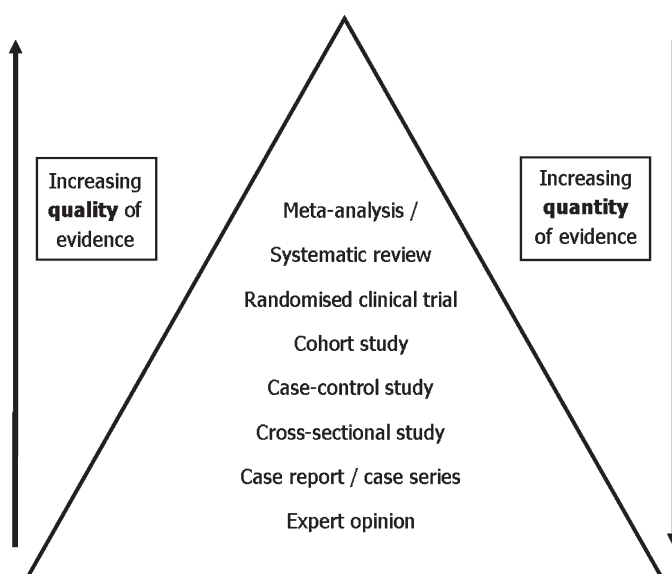
● **Cohort studies** are analytical, observational, studies in which individuals with and without certain exposures are followed over time to determine whether disease occurs. This may be done prospectively, or retrospectively using clinical records (Diesel and others 2008). Retrospective studies are quicker and less expensive but more prone to confounding and bias as data collection is not controlled by the researcher. Cohort studies are useful for studying rare exposures, as the starting point of the study is exposure status rather than disease status. Following individuals over time means that incidence rates

and temporal associations can be determined. However, they can be expensive to conduct, take longer to complete than case-control studies and are inappropriate for rare diseases or those with a long delay between exposure and disease onset. A common problem is the loss of individuals to follow-up, which may introduce bias.

- **Randomised controlled clinical trials (RCTs)** are prospective, analytical, experimental studies in which similar individuals are randomly allocated to two or more treatment groups and subsequent outcomes are compared (Stegemann and others 2007). Correctly conducted RCTs provide the strongest evidence for efficacy of treatment or prophylactic measures.

Evidence-based medicine/Combining the evidence:

The study types described above are often represented as a pyramid, ranked according to the strength of evidence they provide.



Case reports and case series are regarded as little more than expert opinion, while RCTs provide the strongest evidence.

The aim of evidence-based medicine is to found all clinical decisions on the strongest available scientific evidence. A number of systematic methods of appraising and combining research findings can be used to increase the weight of this evidence. **Critically appraised topics (CATs)** are short summaries of the available evidence pertaining to a specific clinical question, usually prepared by and shared between clinicians. **Systematic reviews**

are more extensive and rigorous summaries, often prepared by a team of experts. Data from all relevant, valid studies are extracted and combined using standard, reproducible methods, in order to address a particular hypothesis. The findings of the studies included in the review may be synthesised qualitatively or quantitatively using methods such as **meta-analysis**. Meta-analysis is an accepted statistical method of analysing combined results from a number of studies to provide a summary measure of effect, as a means of increasing statistical power.

Currently case studies and case series are the most common type of study in the veterinary clinical literature, while RCTs are the least common. In designing our research we should be aiming to increase the number of studies closer to the peak of the evidence pyramid in order to maximise the quality of evidence on which ultimately to base our clinical decisions.

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Jackie Cardwell qualified from the University of Cambridge in 1994. She spent six years in general practice before joining the Animal Health Trust, where she undertook a PhD in the epidemiology of racehorse respiratory disease. During her PhD, Jackie continued with regular small animal locum work in private practice. She has recently moved to the Royal Veterinary College, as a lecturer in epidemiology.