Study designs in dermatology

A review for the clinical dermatologist

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Learning objectives
After completing this learning activity, participants should be able to describe the most common study designs encountered in dermatology, including observational, prospectively controlled, case control, cohort, and randomized control studies and metaanalyses, and recognize the appropriate use of statistical tests and matching in study design.

Disclosures
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A working knowledge of common research study designs and their advantages and disadvantages is necessary for critical reading of the literature by clinicians. However, understanding study designs and related statistical methodologies may be perceived as being complex and difficult to execute. This review aims to provide a practical foundation for basic study designs and to help physicians identify pitfalls that commonly occur in clinical studies and their level of evidence. Topics covered include the pros and cons of observational versus prospectively controlled studies, case-control, cohort, randomized controlled studies, adaptive controlled trials and metaanalyses, and the role of matching in studies. (J Am Acad Dermatol 2015;73:721-31.)

Key words: adaptive controlled trials; bias; case-control study; cohort study; cross-sectional study; epidemiology; matching; metaanalysis; observational study; prospectively controlled study; randomized controlled study; retrospective; study design.

INTRODUCTION

Study designs and related statistical methodology are integral parts of dermatology research and publication, bridging clinical and basic science research with clinical dermatology practice. These tools are at the center of analysis, interpretation, and presentation of data and are the cornerstone of evidence-based research in science and all fields of medicine, including dermatology.

Over the past few decades, dermatology research has burgeoned from case series and small-scale clinical trials to include large-scale, randomized, controlled studies and, in some situations, sophisticated epidemiologic studies. Despite the proliferation of complex studies involving multiple statistical techniques, study design and methodology have not been given much attention in the dermatology literature.

The goal of this review is to provide the reader with a foundation for practical basic study designs and statistical and epidemiologic methodologies and to help physicians identify common pitfalls that are ubiquitous in clinical and basic science dermatology research. In particular, this review is targeted at

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providing a foundation for dermatologists and others involved in the delivery of dermatologic care. Those who regularly read the dermatology literature require a keen ability to critically read manuscripts and to recognize strengths and weaknesses in both study design and the methodologies used, which may ultimately affect the strength of the conclusions set forth in a manuscript.

Study design

Key points

- **Retrospective studies may particularly be complicated by less rigorous planning, poorer data quality, an inability to control for confounding factors, and several potential biases**
- **Cohort studies compare exposed and unexposed subjects in terms of subsequent outcome**
- **Case-control studies compare subjects with and without a particular outcome in terms of preceding exposure**
- **Randomized controlled studies are the standard of single-study designs**
- **Metaanalyses involve the statistical analysis of the combined results of multiple studies and are limited by the quality and heterogeneity of the individual studies included**

The dermatology literature is replete with various study designs, including case reports, case series, cohort studies, case-control studies, and controlled therapeutic trials (Table I; Fig 1). Factors that influence the choice of study design include availability of time to complete the study, research funding available and type of funding, and how common is the disorder being studied (ie, prevalence/incidence or the number of patients available in the practice or clinic setting and the time to generate the patients), ethical issues, and statistical design.

The findings reported in a case report are limited because they are anecdotal; in general, there is limited evidence and no role for study design or statistics.

Observational versus experimental studies

Key points

- **Experimental studies control subjects' assignment to an exposure or treatment group**
- **The Strengthening the Reporting of Observational studies in Epidemiology guidelines are generally accepted for the proper reporting of observational studies**

Studies can be divided into 2 broad categories: observational and experimental. Observational studies differ from experimental studies in that subjects' assignment to an exposure or treatment group is not controlled in the study. It is not always feasible, cost effective, or ethical to perform an experimental study. Observational studies are often more practical for assessing the effects of a therapy or intervention because they may be less expensive, easier to run, and pose fewer ethical challenges by not deliberately withholding treatment in a placebo group. Observational studies are also commonly used to study associations between various exposures, such as environmental risk factors and disease outcomes.

There are multiple types of observational studies, including cross-sectional, case-control, and cohort studies. These study designs have both common and unique pitfalls that need to be appropriately reported for readers to properly assess the validity, strengths, and weaknesses. The STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) initiative developed guidelines for the proper reporting of observational studies, including prespecified hypotheses, key elements of the study design and data analysis, essential reporting of participant numbers, and characteristics and interpretation of results.[1]

There are multiple types of experimental or interventional studies, including interventional studies without parallel groups and randomized controlled trials (RCTs). Interventional studies without parallel groups are analogous to case series and will not be reviewed. RCTs will be reviewed below.

Retrospective versus prospective studies

Key point

- **Retrospective studies involve data collection before study initiation and are affected by less rigorous planning**

Studies can be further divided into retrospective and prospective studies. These terms refer to whether the data were collected before or after the initiation of the study. Retrospective studies involve retrospective analysis of already collected data, usually from data sources ranging from small, single-site chart and electronic medical record reviews to international epidemiologic databases and comprehensive health management organization cohorts. In prospective studies, data are collected throughout the study period. Of note, the term prospective is also colloquially used to describe longitudinal studies, where patients are followed