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A Concise Guide to Observational Studies in Healthcare

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WILEY Blackwell BMJIBooks

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Registered Office

John Wiley & Sons, Ltd, The Atrium, Southern Gate, Chichester, West Sussex, PO19 8SQ, UK

Editorial Offices

9600 Garsington Road, Oxford, OX4 2DQ, UK The Atrium, Southern Gate, Chichester, West Sussex, PO19 8SQ, UK 111 River Street, Hoboken, NJ 07030-5774, USA

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Library of Congress Cataloging-in-Publication Data

Hackshaw, Allan K., author.

A concise guide to observational studies in healthcare / Allan Hackshaw. p. ; cm.

Includes bibliographical references and index.

ISBN 978-0-470-65867-3 (pbk.)

I. Title.

[DNLM: 1. Observational Study as Topic-methods-Handbooks. 2.

Outcome and Process Assessment (Health Care)-Handbooks. 3.

Epidemiologic Research Design-Handbooks. W 49]

R852

610.72-dc23

2014018407

A catalogue record for this book is available from the British Library.

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Foreword

Epidemiology is at the heart of medicine. Without knowledge of the epidemiology of disease and its methods of study, it can be impossible to interpret the results of observational studies. Epidemiology has an important role to play in determining causes of disease and in the interpretation of clinical tests since this depends on knowledge of the prevalence of the diseases for which such tests are done. Observational studies are the mainstay of epidemiology. Correctly interpreted, observational studies transform the unstructured natural variation of diseases and the exposures that cause them into intelligible insights that can be used to improve health and well-being. *A Concise Guide to Observational Studies in Healthcare* demonstrates how this is done and includes many practical examples.

It is easy to complicate epidemiology with mathematical formulae and specialist jargons that are difficult to understand. What are the differences between relative risk, odds ratio and hazard ratio? What is the difference between bias and confounding? How should a meta-analysis be presented and interpreted? Why are the terms detection rate and false positive rate better than sensitivity and specificity? What is the difference between a standard deviation and a standard error? Hackshaw carefully explains all these and more with elegance. The book succeeds in pulling together the essence of how observational studies can be used and interpreted in medical practice.

Hackshaw simplifies the principles and methods of the subject, covering a wide range of topics in a book short enough to be read over a weekend and one that will undoubtedly inspire readers to delve further into the subject.

A Concise Guide to Observational Studies in Healthcare is a useful companion to Hackshaw's 2009 book on clinical trials. As with his previous book, this one is aimed at the general, medical and scientific reader, providing an introduction to the subject without requiring detailed specialist knowledge, an objective the author has accomplished with skill and rigour.

Professor Sir Nicholas Wald, FRS, FRCP Wolfson Institute of Preventive Medicine Barts and The London School of Medicine and Dentistry

Preface

Research studies are required for developing effective public health policies and clinical practice. Observational studies are perhaps the most common type of research, and they are essential for describing the characteristics of a group of people or finding ways to understand, detect, prevent or treat disease, or avert early death.

The purpose of the book is to provide researchers and health professionals with a focussed and simplified account of the main features of observational studies. It is important to first understand the key concepts. Specifics about the calculations involved in analyses should come after and are covered in other textbooks. The book is aimed at those who conduct their own studies or participate in studies coordinated by others, or to help review a published report. No prior knowledge of design, analysis or conduct is required. Examples are based on clinical features of people, biomarkers, lifestyle habits and environmental exposures, and evaluating quality of care.

This book is a companion to the book A *Concise Guide to Clinical Trials* (Hackshaw A, BMJ Books/Wiley-Blackwell). An overview of the key design and analytical features are provided in <u>Chapters 1-4</u>; then each study type is discussed using published studies (<u>Chapters 5-8</u>), showing how they were conducted and interpreted. <u>Chapter 9</u> introduces prognostic markers, a topic which is often misunderstood, while <u>Chapter 10</u> covers systematic reviews and how to deal with inconsistent results. <u>Chapter 11</u> summarises how to conduct and publish an observational study.

One of the important goals of the book is to show that study features such as the design of questionnaires and interpreting results are common to most study types, so these topics are repeated throughout the chapters. By having many examples, the reader can see how a variety of study designs and outcomes can be interpreted in a similar way, which will help to reinforce key aspects.

The content is based on over 23 years of experience teaching evidence-based medicine to undergraduates, postgraduates, and health professionals; writing over 130 published articles in books and medical journals; and designing, setting up and analysing research studies for a variety of disorders. This background has provided the experience to determine what researchers need to know and how to present the relevant ideas.

I am most grateful to Jan Mackie, whose thorough editing of the book was invaluable. Final thanks to Harald Bauer.

Professor Allan Hackshaw Deputy Director Cancer Research UK & UCL Cancer Trials Centre University College London

Chapter 1 Fundamental concepts

This chapter provides a summary background to observational studies, their main purposes, the common types of designs, and some key design features. Further details on design and analysis are illustrated using examples in later chapters, and from other textbooks [1–3].

1.1 Observational studies: purpose

Two distinct study designs are used in medical research: **observational** and **experimental**. Experimental studies, commonly called clinical trials, are specifically designed to intervene in some aspect of how the study participants live their life or how they are treated in order to evaluate a health-related outcome. A key feature of a clinical trial is that some or all participants receive an intervention that they would not normally be given. Observational studies, as the term implies, are not intentionally meant to intervene in the way individuals live or behave or how they are treated. Participants are free to choose their lifestyle habits and, with their physician, decide which interventions they receive when considering preventing or treating a disorder. Box 1.1 shows the most common purposes of observational studies.

Box 1.1 Common purposes of observational studies

- Examine the opinions of a single group of people on a health-related topic(s)
- Describe the health-related characteristics (e.g. demographics, lifestyle habits, genes, biological measurement, or imaging marker) of a single group of people
- Estimate the occurrence of a disorder at a given time, or trends over time
- Examine features of a disorder (e.g. how it affects patient's lives, how they are managed/treated, and short- or long-term consequences)
- Find associations between the health-related characteristics among a single group of people or across two or more groups
- Examine risk factors (including casual factors) for a disorder or early death
- Examine prognostic factors (i.e. those that can predict the occurrence of a disorder or death from the disorder)
- Evaluate a healthcare intervention for prevention or treatment



Find new scientific information
Plan the use of future resources
Change public health education, policy, or practice
Change clinical practice



Disease prevention, detection, or treatment

1.2 Specifying a clear research question: exposures and outcomes

The **research question(s)**, which can also be referred to as **objectives**, **purpose**, **aims**, or **hypotheses**, should be clear, easy to read, and written in non-technical language where possible. They are usually developed to address a research issue that has not been examined before, to corroborate or refute previous evidence, or to examine a topic on which prior evidence has had shortcomings or been scientifically flawed.

There is a distinction between **objectives** and **outcome measures** (or **endpoints**). An outcome measure is the specific quantitative measure used to address the objective. For example, a study objective could be 'to examine the smoking habits of adults'. Possible corresponding endpoints could be either 'the proportion of all participants who report themselves as smokers' or 'the number of cigarettes smoked per day', but they are quite different endpoints. Box 1.2 shows examples of objectives and outcome measures.

Box 1.2 Examples of objectives and outcome measures (endpoints)

Objective	Outcome measure
To examine the effectiveness of statin therapy in people with no history of heart disease	Mean serum cholesterol level
To evaluate blood pressure as a risk factor for stroke	The occurrence (incidence) of stroke
To examine the smoking and alcohol drinking habits of medical students	The number of cigarettes smoked per day and the number of alcohol units consumed in a week
To determine whether there is an association between arthritis and coffee consumption	The occurrence of arthritis
To examine the association between age and blood pressure	Age and blood pressure measured on every subject

It can be easy to specify the research question or objective for studies that involve simply describing the characteristics of a single group of people (e.g. demographics, or biological or physical measurements). For example:

• What proportion of pregnant women give birth at home?

- What is the distribution of blood pressure and serum cholesterol measurements among men and women aged over 50?
- Are patients satisfied with the quality of care received in a cancer clinic?

Clinical trials often have a single primary objective, occasionally two or three at most, each associated with an endpoint. However, there can be more flexibility on this for observational studies unless they have been designed to change a specific aspect of public health policy. Many observational studies have several objectives, some of which may only arise during the study or at the end, and they can also be exploratory.

Examining the effect of an exposure on an outcome

While some researchers seek only to describe the characteristics of a single group of people (the simplest study type), it is common to look at associations between two factors. Many research studies, both observational studies and clinical trials, are designed to:

Examine the effect of an exposure on an outcome

<u>Box 1.3</u> gives examples of these. To evaluate risk factors or causes of disease or early death, an outcome measure must be compared between two groups of people:

- 1. Exposed group
- 2. Unexposed group