Clinical Ophthalmic Oncology

Basic Principles

Arun D. Singh
Bertil E. Damato
Editors

Third Edition

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Preface

Ophthalmic tumors are rare and diverse so that their diagnosis can be quite complex. Treatment usually requires special expertise and equipment and in many instances is controversial. The field is advancing rapidly, because of accelerating progress in tumor biology, pharmacology, and instrumentation. Increasingly, the care of patients with an ocular or adnexal tumor is provided by a multidisciplinary team, consisting of ocular oncologists, general oncologists, radiotherapists, pathologists, psychologists, and other specialists.

For all these reasons, we felt that there was a need for the new edition of the textbook providing a balanced view of current clinical practice. Although each section of *Clinical Ophthalmic Oncology*, *3rd Edition*, now represents a stand-alone volume, each chapter has a similar layout with boxes that highlight the key features, tables that provide comparison, and flow diagrams that outline therapeutic approaches.

The enormous task of editing a multiauthor, multivolume textbook could not have been possible without the support and guidance by the staff at Springer: Caitlin Prim, Melanie Zerah, ArulRonika Pathinathan, and Karthik Rajasekar. Michael D. Sova kept the pressure on to meet the production deadlines.

It is our sincere hope that our efforts will meet high expectation of the readers.

Cleveland, OH, USA — Arun D. Singh, MD
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Principles of Cancer Epidemiology

1

Annette C. Moll, Michiel Robert de Boer, Lex M. Bouter, and Nakul Singh

Introduction

During the last decade, evidence-based medicine (EBM) has become a dominant approach in many medical fields, including ophthalmology [1, 2]. Clinical epidemiological studies provide evidence that can aid decision-making processes. An overwhelming amount of clinical epidemiological papers are being published every year, and critical appraisal of the findings can be challenging, especially for the busy clinician who is not formally trained in the field of clinical epidemiology. Therefore, the available evidence is increasingly bundled in clinical guidelines. The aim of this chapter is to provide readers with some basic knowledge to allow them to judge the value of clinical epidemiological papers and thus of the pillars of evidence-based clinical guidelines. Examples from ocular oncology will be used to illustrate the methodological principles.

Research Question

A clinical epidemiological study should always start with a well-defined research question. Similarly, when reading a paper, one should always first identify the question(s) the authors wish to address (Fig. 1.1). Research questions can be aimed at explanation or description. Explanatory research examines causal relationships, while descriptive research is merely descriptive. In addition, research questions are also often being categorized as etiological, diagnostic, or prognostic (Table 1.1). For example, an explanatory research question related to etiology in the field of ocular oncology is as follows: are children born after in vitro fertilization at higher risk of developing retinoblastoma as compared to children born after natural conception? [3] A correct explanatory research question should contain information on the *p*atients, *i*nterventions, *c*ontrast, and *o*utcomes (*PICO*) at issue.

Outcome Measures

Traditionally, prevalence, incidence, and mortality (survival) have been the outcome measures in clinical cancer epidemiology studies. More recently,

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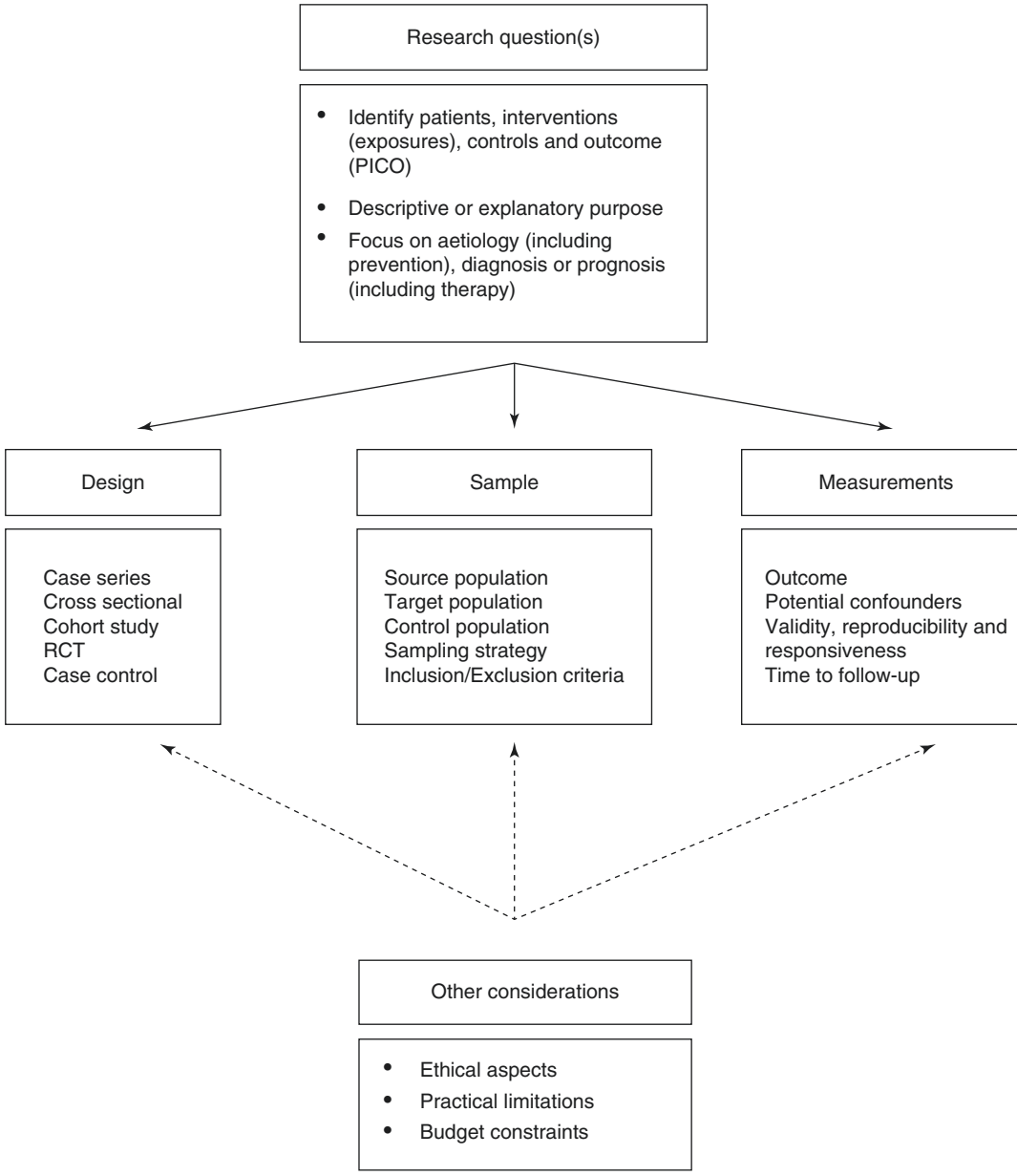

Fig. 1.1 Steps in designing a clinical epidemiological research

Table 1.1 Types of epidemiological research

Type of research	Purpose	Example
Etiology (including prevention)	To examine possible etiological factors for the occurrence of a disease	Association between ultraviolet radiation and uveal melanoma
Diagnosis	To examine the usefulness of diagnostic tests for the disease	Accuracy of magnetic resonance imaging in determining choroidal invasion of retinoblastoma
Prognosis (including interventions)	To examine possible prognostic factors for the disease	Association between external beam therapy for retinoblastoma and the incidence of second malignant neoplasms

quality of life measures have become increasingly popular. In ophthalmic oncology, visual acuity is also an important outcome measure.

Prevalence

Prevalence refers to the proportion of the study population with the condition of interest. Usually prevalence is given for a specific moment in time (point prevalence), but sometimes it is estimated for a period of time (e.g., 1 year or lifetime prevalences). For example, the lifetime prevalence of uveal melanoma in a Caucasian population with oculo(dermal) melanocytosis is estimated to be 0.26% [4].

Incidence

Whereas prevalence relates to existing cases, incidence relates to the proportion of new cases in the study population. It is important that the population under investigation is *at risk* of developing the condition. For example, persons with bilateral enucleation are no longer *at risk* of developing uveal melanoma. There are two different measures of incidence: cumulative incidence (CI) and incidence density (ID). CI is the proportion of new cases in a population at risk over a specified period of time. For example, the CI of second malignant neoplasms in hereditary retinoblastoma patients is 17% at the age of 35 years [5]. ID refers to the rate of developing the condition during follow-up, usually expressed as a proportion per person-year at risk.

Mortality

Cancer is among the leading causes of mortality. In order to understand the processes that either hasten or delay this outcome, it is necessary to rigorously define the burden of disease. Clinical epidemiologists have created several concepts of mortality, all with their own definition, interpretation, and uses. Unfortunately, many of these concepts use similar nomenclature, so it is important to always clarify the definition of mortality at hand. Broadly speaking, mortality rate refers to the incidence of death, and survival rate is its complement, i.e., survival rate = 100 – mortality rate.

Population mortality is the chance that a person in the general population will die from a specific disease over a specified time frame. It is a useful concept for measuring the burden of disease in a population. For example, the population mortality for heart disease was 197.2 per 100,000 population per year in 2015. Therefore, it is a measure more important for public health policymakers as opposed to clinicians. This measure is calculated from death certificates, where cause of death is known [6].

Overall mortality is the chance that a person with a disease will die within a time period after diagnosis. It is important to specify a time period for the mortality statistics – in the long run, mortality is 100% for any condition. Of note, this definition is indifferent to cause of death. Overall mortality is the most common measure of mortality in the literature and is often used to guide prognosis. This measure is helpful in identifying risk factors for poor prognosis, as well as measuring disparities between populations. The interpretation of this measure is complicated by biases, including lead time, length, and overdiagnosis biases.

Cause-specific mortality is the chance that a person with a disease will die within a time period after diagnosis due to the disease. This is in contrast to overall survival, which does not distinguish between causes of death. Cause-specific mortality most closely measures the "deadliness" of a disease, but similar to overall mortality, it can be affected by lead time, length, and overdiagnosis bias.

Relative mortality is a proportion that compares the overall mortality of people with a disease to that of an unaffected, but otherwise identical population. Relative mortality measures the excess mortality associated with a diagnosis compared to the general population. It is a convenient measure to calculate because it does not require cause of death to be recorded. It is also a helpful measure for understanding the deadliness of a disease that affects the elderly, where patients are at risk from dying from other causes. To calculate relative survival, overall survival of a