INTRODUCTION

One definition of epidemiology is the study of the distribution and determinants of disease frequency in populations. With determinants we mean all etiologic, prognostic, or diagnostic factors influencing the frequency of a disease. When we talk about risk factors, we mean causal determinants. There are many reasons why one may study epidemiology of glaucoma: to determine the magnitude of glaucoma and the burden of this disease on the population, to cope in a proper way with anticipated problems, to determine priorities in medical care, and to have data to allocate (research) funds.

As ophthalmic researchers, we primarily study the epidemiology of glaucoma to obtain insight in factors that might prevent, delay, or reduce irreversible visual loss. Moreover, glaucoma epidemiology might provide us with much needed etiologic clues, generate better hypotheses, and challenge our paradigms with regard to glaucoma. This chapter will focus primarily on primary open-angle glaucoma (POAG), and whenever we mention glaucoma, it will be POAG, unless specified otherwise. We will discuss definitions of glaucoma and what problems one may encounter in defining glaucoma in a clinical or epidemiologic research setting. We will also consider differences and advantages or disadvantages in study designs, prevalences, and incidences of glaucoma and an overview of the presently known risk factors for glaucoma.
DEFINITIONS OF GLAUCOMA

Through the years, the definition of POAG has changed many times since this disease was described in 1861 by Donders’ collaborator introducing the term glaucoma simplex (1). Until that time, glaucoma was considered to be a disease primarily marked by inflammation. Changes in definitions or criteria for POAG will continue as our knowledge grows. Essentially, the name POAG masks our ignorance of its pathophysiological mechanisms. When we have unraveled all genetic and other causes of POAG, the word “primary” could disappear. POAG these days may be defined as “a disease of retinal ganglion cells, characterized by a structural change in the optic disc that is best described as excavation, and by a typical, slowly progressive loss of function that begins in the mid-peripheral field and expands both toward the center and peripherally” (2). The excavation is often called glaucomatous optic neuropathy (GON), and we will further use glaucomatous visual field loss (GVFL) to describe its corresponding function loss. Albeit this given definition of POAG as a combination of GON and GVFL seems comprehensive, in daily practice it can be hard to reach its diagnosis. It is difficult to compare scientific reports due to variations and interpretations of glaucoma definitions. Intraocular pressure (IOP) as a risk factor for POAG is used too often to define glaucoma or to screen for it. Half of the POAG cases in population-based studies have a normal IOP \( \leq 21 \text{ mmHg} \) (3). Central corneal thickness is also known to influence IOP measurement but is rarely taken into account in glaucoma publications. An analysis of glaucoma therapy studies in peer-reviewed journals between 1996 and 1999 revealed that only 28% included optic disc morphology in their definition of glaucoma, against 100% IOP and 41% visual field examination (4). One purpose of scientific papers is to present them to peers for evaluation and a still common statement that a diagnosis of POAG was made by a glaucoma specialist, without specifying the criteria employed, should be abandoned. Also we feel that the commonly used adjudication by one or two experts in case of conflicting data is a source of bias, when no a priori criteria are mentioned. The lack of consensus on criteria (5) partially explains the variation in prevalence and incidence of glaucoma that we will see later.

One of the positive side-effects of epidemiology is that it sharpens the clinician’s mind for exact and transparent POAG criteria and that it may make doctors more aware of possibly different attitudes in a clinical or research setting (see Table 1). There are many publications on IOP and glaucoma, and it is rarely mentioned that there is about 2 mmHg interobserver variation (standard deviation of the difference) in measuring the IOP with the Goldmann applanator (6). Few studies mention how they exactly performed the IOP measurement with specific equipment. For applanation tonometry, the amount of fluorescein in the tear film, the width of the mires, squeezing the eyelids, and the patient holding his breath will influence the result. There is also a discrepancy in coming to an IOP value in an eye, for example, is one measurement enough, the average of two or three measurements, the median of three, or the first identical value while repeatedly measuring (6)? We concluded that the median of three is best (6). There is also variation in handling the IOPs of the two eyes when classifying a patient.

Only recently criteria were formulated (after 50 years of Goldmann perimetry!) to define progression of GVFL (7–10). It also became clear that determining GON with semi-automated imaging is more reliable than ophthalmoscopy alone (11). A problem in