Incidence and Prevalence

The exact incidence and prevalence of open-angle glaucoma (OAG) in the elderly are unknown. Studies in the United States and Europe have reported that between 0.4 and 4.1 percent of the general population has some form of glaucoma (72,118), The broad range of study findings reflects the different study designs, populations, disease definitions, and measurement methods.

A study of the population of Framingham, Massachusetts helps to narrow this range down as it applies to OAG in the U.S. elderly. In this study, approximately 1.2 percent of the population over age 52 had OAG (58,60). This number is based on a conservative definition of OAG and is considered by the researchers to be an underestimate (60).

The risk of developing glaucoma increases dramatically with age (see table 1). OAG in people under age 40 is very rare (72), but in the Framingham, Massachusetts study, approximately 0.9 percent of people aged 65-69 and 4.4 percent of people aged 80-84 had the disease (94). Given this trend and the figures discussed above, a **reasonable estimate of the total number of people over age** 65 with OAG today is thus about 2 to 3 percent, or between approximately 600,000 and 900,000 **elderly peop1e[2].**

The National Society to Prevent Blindness estimates that about 8 percent of visual impairment and about 14 percent of blindness in the elderly is due to some kind of glaucoma (84).[3] If these figures are correct, approximately 4,600 elderly people are blind as a result of glaucoma; presumably, the majority of them have OAG, the most common form of glaucoma.

Precise data on the number of new OAG cases diagnosed each year in the Unites States do not exist. Incidence estimates derived from the Framingham study suggest that approximately 0.5 percent of 65-year-olds and 1.1 percent of 75-year-olds will develop the disease within 5 years (94). These estimates are consistent with the findings of a Swedish study, in which 2 percent of elderly people (over age 62) developed some form of glaucoma during a 9-year period (12).

OAG does not affect all subpopulations equally. Blacks, diabetics, and people with a family history of glaucoma are much more likely than others to have the disease (72). The high prevalence of advanced OAG in blacks suggests that they might be a particularly important population to screen for this disease. Preliminary results from a study of a

Table 1.--Estimated Prevalence and Five-Year Incidence of Open-Angle Glaucoma in Framingham, Massachusetts, 1973-1975

Age	Prevalence	Incidence[a]
55-59	0. 5%	0 .2%
60-64	0.7	0.3
65-69	0.9	0.5
70-74	1.7	0.7
75-79	2.0	1.1
80-84	4 .4[b]	.-
Total	1.2	

[a] Incidence estimates are approximate and based on calculations described by the authors below. They are reported in the source as five-year incidence estimates for the lowest age in each interval in this table (e. g., Podgor et al. report a incidence of 0.2% at age 55).

[b] The number of persons in this age group in the sample five-year Population was very small.

SOURCE : M.J. Podgor, M. C., Leske, and F. Ederer, "Incidence Estimates for Lens Changes, Macular Changes, Open-Angle Glaucoma, and Diabetic Retinopathy," Am. J. Epidemiology 118(2):206-212, August 1983.

1 Incidence is the number of new cases during a specified period of time; prevalence is the total number of cases during a period of time.

2 These figures are based on an estimated 1988 population of 30,263,000 people over age 65.

3 These estimates are based on reports by certain States in 1969 and 1970.

predominately black population suggest an OAG prevalence of 5.5 percent in people overage 40 in this group (112). Furthermore, OAG may be more severe in blacks; data from a 1970 blindness registry suggest that blacks are more than eight times as likely as whites to go blind from glaucoma and go blind at an earlier age (48).[4]

Other characteristics associated with OAG are less well established. Low levels of thiamine in the blood have been correlated with OAG; dark eye color and nearsightedness have been correlated with high intraocular pressure, which is itself a major risk factor for OAG (see below) (7,28,49,124). Behavioral factors may have a small influence on risk. Some studies have found correlations between OAG and sedentary lifestyles, cigarette smoking, poor diet, and alcohol use, although the findings for smoking and alcohol use are inconsistent (7,40,59,124).

There is similarly conflicting evidence regarding the relative likelihood of OAG in men and women. Most studies have found that men and women of a given age get OAG with equal frequency, but the Framing ham study found a higher prevalence of OAG in men than in women (58,76).

The potential links between hypertension (high blood pressure), cardiovascular disease, and OAG have been of particular interest to researchers because of the theory that OAG is caused by inadequate blood supply to the optic nerve. In a review of the literature, Leske lists numerous studies that found associations between sudden reduction of blood pressure (from antihypertensive drugs or from blood loss) and onset of OAG (72). However, she notes that these studies do not rule out the possibility that hypertension itself, not just treatment of the condition, may be responsible for OAG risk. Some studies have found associations between OAG and systolic blood pressure but not between OAG and diastolic blood pressure (40, 124).[5,6]

Other studies have found associations between hypertension and high intraocular pressure but not between hypertension and OAG itself (59,74). Thus, it is well established that a relationship between OAG and blood pressure exists, but the relationship does not seem to be a simple one.

Natural Course of the Disease

In a normal eye, the fluid in the anterior (front) portion of the eye is naturally maintained at a pressure that averages about 16 mm Hg.[7] This fluid, which helps maintain the shape of the eye, is formed in an area under the lens and then flows forward through the pupil into the anterior portion of the eye (between the pupil and the cornea). Excess fluid flows out through a sieve-like opening into a duct that leads back to the bloodstream, maintaining a constant balance of pressure in the eye.

In an eye with glaucoma, the normal fluid balance is disrupted, usually because the outflow of fluid is inhibited. When this happens, the pressure in the eye (the intraocular pressure, or IOP) increases. It is presumed that the increase in pressure eventually damages the optic nerve, causing blind spots, tunnel vision, and, potentially, total blindness as vision becomes progressively more impaired (34,67).

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4 One hypothesis to explain the greater prevalence and sever i ty of OAG in blacks is that this population is less likely to receive early, adequate vision care. However, various studies (reviewed by Leske and Rosenthal) suggest that less adequate care does not completely explain the greater prevalence and severity of disease in blacks than in whites (76).

5 Systolic blood pressure is the pressure at the height of the heartbeat pulse; diastolic blood pressure is the pressure at the lowest point in the pulse.

6 Exemplifying the fact that the relationship between blood pressure and OAG is complex, these two studies found opposite effects of systolic blood pressure. Goldberg et al. found a high prevalence of low systolic pressure in patients with low-tension OAG (40). In contrast, Wilson et al. found a correlation between untreated high systolic blood pressure and OAG risk (124).

7 Millimeters of mercury (mm Hg) is a standard measurement of pressure.

There are several general types of glaucoma (see table 2). In some cases, glaucoma is the secondary result of trauma or some condition (such as a malignancy) that causes a sudden, drastic rise in IOP. In other cases, the condition is present at birth (congenital glaucoma). Or, the glaucoma is the result of abnormal eye anatomy which can result in sudden blockage of the area through which fluid flows out of the eye (closed-angle glaucoma). The most common form of glaucoma, however, and the target of current glaucoma screening programs, is OAG.

Table 2.--Common Forms of Glaucoma

Primary Glaucoma
Chronic open- angle
high tension
Low tension
Closed - angle
acute
chronic (recurring attacks)
Congenital
Secondary Glaucoma
May be secondary to:
trauma
infection
tumors
intraocular hemorrhage
other causes

SOURCES : Adapted from D. Campos-Outcalt and J.M. Carmi chae 1, "New perspectives on Glaucoma Screen ing, " J. Fami ly Practice 12(3):451-457, 1981; and R. Berkow, cd., The Merck Manual, 15th edition (Rahway, NJ: Merck & co., 1987).

OAG accounts for 50 to 80 percent of all glaucoma (9,52). In contrast to some other forms of glaucoma, there are no sudden events precipitating OAG. Rather, the primary predisposing factor for this disease is a gradual increase in IOP. An IOP of 21 mm Hg is statistically two standard deviations above the mean of 16 mm Hg and is the cutoff often used by eye care professionals to categorize a person at high risk of visual loss from OAG. People with IOPs greater than this cutoff, but without any other signs of OAG, are frequently described as having ocular hypertension (OH).*

An estimated 7 to 13 percent of the general population has OH(72). The prevalence of OH is higher in the elderly; in the Framingham study, nearly one-fourth of the elderly had IOPs of 20 mm Hg or more (58) (see table 3).

OH is the single greatest risk factor predicting future OAG. The extent of risk posed by OH has been the subject of a

8 The use of the term "ocular hypertension" is inconsistent in the literature and controversial among ophthalmologists. In this paper, the term is used to mean elevated intraocular pressure without evidence of visual field defects. Some studies use the term to include patients with optic disc changes (but no visual field defects); others do not. Where the studies clearly group patients with optic disc changes separately from those without them, OTA has done so as well and includes only the latter group in the analysis of the risk posed by OH.

Table 3--- Distribution of Intraocular Pressure[1] in the Elderly, Framingham, Massachusetts, 1973-1975

Age	Number screened	Percent distribution			
		<20 mm Hg	20-24 mm Hg	25-29 mm Hg	30+ mm Hg
65-74	780	75.5	19.4	4.0	1.2
75-85	383	75.9	19.1	2.9	2.1

[1] Higher value in mm Hg of right or left eye.

SOURCE: H.A. Kahn, H.M. Leibowitz, J.P. Ganley, et al., "The Framingham Eye Study," Am. J. Epidemiology 106(1):17-32, July 1977.

number of studies, summarized in table 4.[9] In each of these studies, patients with OH were monitored without treatment. Outcomes vary considerably, as do the length of the study and the precise definitions of OH (e.g., above 20, 21, or 22 mm Hg). The geographic populations studied are also very different, including people of Japan, Sweden, England, the United States, Australia, South Africa, and Norway.

Nonetheless, there is enough consistency among studies to suggest that people with OH have the following probabilities of developing

9 None of these studies focused exclusively on the over -65 popul at ion, but because of the increased prevalence of disease in the elderly, many study subjects were in this group.

Table 4.--Development of Manifest Open-Angle Glaucoma in Individuals with Untreated Ocular Hypertension In At Least One Eye

Source	Percent of ocular hypertensives in specified IOP range developing OAG[a,b]			
	< 20 mm Hg	20-24 mm Hg	25-29 mm Hg	30 mm Hg or greater
1-Year Studies				
Kitazawa, 1981			16%	
4- to 7-Year Studies				
Armaly, 1969	< 1%	< 1%	1%	0%
Cockburn, 1982[c,e]		10%		
David et al., 1977[d]		0%	1%	33%
Linner and Stromberg, 1967[e]		2%		f
Perkins, 1973		3%		
Wilensky et al., 1974		0%	6%	
9- to 10-Year Studies				
Kitazawa et al., 1977		9%		
Linner, 1972[e]		13%		
Bengtsson, 1981		7%		
17- to 20-Year Studies				
Hovding and Aasved, 1986		30%		
Lundberg et al., 1987	5%	38%		

[a] These ranges do not correspond exactly to the ranges reported in each study. For example, the results of a study reporting the number of OAG cases developing in individuals with IOP of 21-25 mm Hg in at least one eye would be placed in the second column (labelled 20-24 mm Hg).

[b] A line is used to indicate the results of a study that apply to a broader range of IOP than the individual categories in this table. For example, Kitazawa (1981) reported only on the number of OAG cases developing in patients with IOPs of greater than 25 mm Hg. Thus, his results apply to a group that includes both the last two columns in this table (the columns covered by the line).

[c] The patients in Cockburn's study uere apparently all untreated, but the author is not explicit on this point.

[d] Patients in this study were reported to be under observation for 1 to 11 years, with an average of 41 months.

[e] These authors included criteria other than visual defects when determining whether a patient had developed OAG (e.g., changes in the optic disc or IOP > 30 mm Hg were also considered sufficient criteria).

[f] This figure includes all simple glaucoma, not just OAG.

SOURCES: See references.

manifest OAG--i.e., glaucomatous visual field defects--in one or both eyes within 5 years:

- less than 1 percent of screened people with "normal" IOPs (20 mm Hg or less),
- approximately 3 to 10 percent of all untreated people with IOPs greater than 20 mm Hg,
- approximately 6 to more than 16 percent of all people with IOPs greater than 25 mm Hg, and
- approximately 33 percent of people whose IOPs exceed a cutoff of 30 mm Hg.

These estimates may be too high. One study listed in table 4 found an unusually low prevalence of visual defects developing in people with OH, even lower than the lower bounds suggested here (4). It found no visual defects developing in any persons with IOPs of 30 mm Hg or greater, in contrast to the results in other studies.

Two recent studies have found that over the very long run, **people with OH are about 7 times more likely than people with normal IOPs to develop OAG.** Swedish researchers found that 34 percent of untreated OH patients developed OAG within 20 years of screening, compared with only 5 percent of people whose IOPs were normal at the time of screening (8 1). (People with IOPs greater than 30 mm Hg were not included in this study, so the overall likelihood of people with OH developing OAG was probably even higher than reported.) Researchers in Norway found similar results. In their study, 30 percent of untreated OH patients (including people with IOPs greater than 30 mm Hg) developed OAG over a 17 to 20 year period (55).

Some people develop OAG without ever having high IOPs.[10] These people, often designated "low-tension glaucoma" cases, appear to be unusually prone to optic nerve damage even when the measured IOP is within the range generally considered normal (30). Hollows and Graham found that about one-third of all OAG cases in their survey had IOPs below 21 mm Hg at the time of first examination, although some of these patients had higher IOPs at later followup visits (52). In Armaly's ten-year study, four people developed OAG; at the time visual field defects developed, two had average IOPs of 21 mm Hg and two had higher average IOPs (4).

At the other extreme, some people can have IOPs of greater than 30 mm Hg for many years without developing visual field defects. Armaly found no evidence of visual field defects in any of the eyes in his study that had IOPs of 30 mm Hg or greater at the initial examination; six of these eyes were followed for 9 years (4).

It appears that at least two factors are at work: one that affects the level of IOP, and one that determines how sensitive the optic nerve is to the effects of that pressure.[11] Thus, there is a clear increase in the risk of developing OAG as pressure increases (5), with an especially **high risk at very high pressures (greater than 35 mm Hg)** (95). **Nonetheless, a few people may develop the disease at quite moderate pressures, while the majority of people with mildly elevated pressures do not develop visual field defects even after many years.**

The classical clinical course of OAG progresses from high IOP to a characteristic cupped or other abnormal appearance of the optic disc (the area of the retina where the optic nerve enters), to the development of visual field defects--dim or blind spots that appear as portions of the optic nerve die out (initially detectable only by tests and, as they

10 In some cases these individuals do have above-normal IOPs at some time in the day, but their pressures are normal when measured in an office setting. However, at least a few people seem to have true low-tension OAG, in which there is no discernible cause of visual damage and the IOP never exceeds 21 mm Hg (30).

11 Other theories to explain the inconsistencies between pressure and visual impairment have been proposed; for example, that low-tension glaucoma is actually a different disease from high-tension open-angle glaucoma. Given the lack of evidence for this hypothesis, the idea that the two types are simply manifestations of different tolerances for a given IOP has considerable appeal (30).

become more extensive, causing actual visual impairment). In the absence of other potential causes, the existence of these visual field defects confirms a clinical diagnosis of OAG.

The dilemma of how to diagnose and treat people with OAG as early as possible without treating many people unnecessarily has dogged eye care professionals for many years. Although it is clear that the majority of individuals with elevated IOPs at the time of first screening do not go on to develop OAG, even after 20 years (55,81), it is equally clear that the disease is present before it is manifested in a decrease in visual capacity. Quigley and colleagues have demonstrated that up to 50 percent of optic nerve fibers are already lost by the time changes in the visual field are detectable (98).

Researchers have used such varying definitions of OAG onset as: IOP greater than 30 mm Hg; suspicious changes in the optic disc; abnormal results on tests designed to measure the fluid outflow in the eye; changes in the visual field that follow a particular pattern; and a multitude of combinations of these and other criteria. In assessing the literature on outcomes associated with **OAG,** OTA has chosen to give greatest weight to those studies that include visual field defects as a necessary criterion for a definite diagnosis of OAG. There are two reasons for doing so. First, visual field defects can be measured more objectively than can changes in the optic disc, and their existence is hard evidence of established disease. When visual field defects are measured in a study and are included as a necessary criterion for a diagnosis of OAG, it is unlikely that study subjects who are in fact healthy will be classified as diseased. Second, individuals with OAG do not suffer visual disability until after they develop visual field defects. Nonetheless, even before visual defects arise, the disease process is well underway.