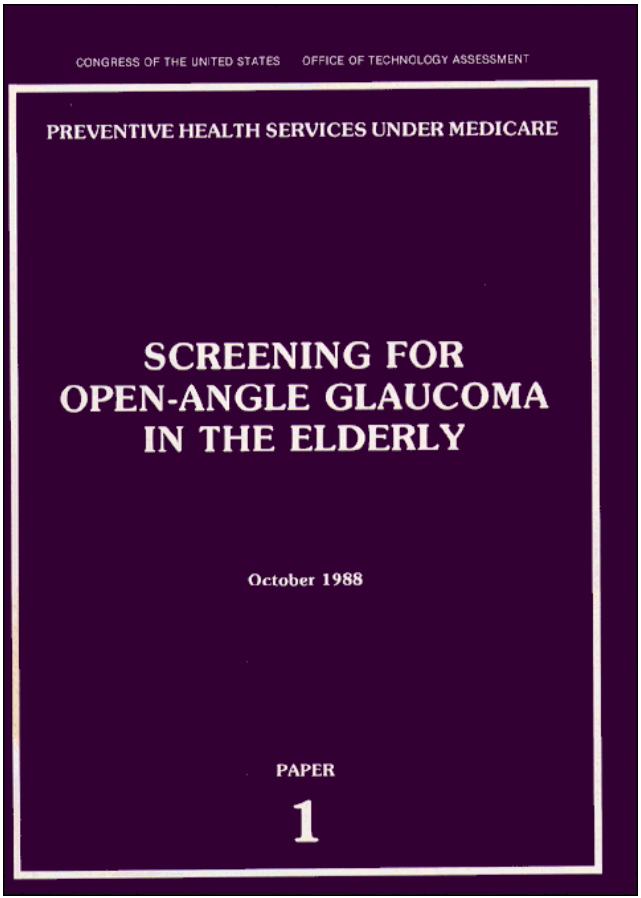
Screening for Open-Angle Glaucoma in the Elderly

October 1988

NTIS order #PB91-192872



Screening for Open-Angle Glaucoma in the Elderly

by

Elaine J. Power

Judith L. Wagner
Brigitte M. Duffy

Health Program
Office of Technology Assessment
Congress of the United States
Washington, DC 20510-8025

October 1988

A Staff Paper
in OTA's Series on
Preventive Health Services Under Medicare

Carol Guntow and Karen Davis prepared this Staff Paper for publication.

OFFICE OF TECHNOLOGY ASSESSMENT
CONGRESS OF THE UNITED STATES

The views expressed in this Staff Paper do not necessarily represent those of the Technology Assessment Board, the Technology Assessment Advisory Council, or their individual members.

CONTENTS

Chapter *Page*

1. Summary 1
Introduction 1
Summary of Findings 2
Conclusions 6
Research Needs 7

2. The Epidemiology of Open-Angle Glaucoma 9
Incidence and Prevalence 9
Natural Course of the Disease 10

3. Treatment for Open-Angle Glaucoma 15
Description 15
Treatment Outcomes 16
Treatment Effectiveness 17

4. Screening Technologies 23
Screening Considerations 23
Description of Screening Technologies 23
Screening Test Accuracy 25

5. Medicare Coverage of Screening for Open-Angle Glaucoma 31
Costs to Medicare 31
Implications of Scheduled Frequency of Screening and Screening Utilization for Medicare Costs 32
Costs and Effectiveness of Screening in Preventing Blindness 34
Problems in Implementing Medicare Coverage of OAG Screening 34

Appendix
A. Advisory Panel--Project on Preventive Health Services Under Medicare 37
B. Acknowledgments 38
C. The Costs of Screening for Open-Angle Glaucoma 39

References 53

Tables

Table *Page*

1. Estimated Prevalence and Five-Year Incidence of Open-Angle Glaucoma in Framingham, Massachusetts, 1973-1975 9
2. Common Forms of Glaucoma 11
3. Distribution of Intraocular Pressure in the Elderly, Framingham, Massachusetts, 1973-1975 11
4. Development of Manifest Open-Angle Glaucoma in Individuals With Untreated Ocular Hypertension In At Least One Eye 12
5. Three Estimates of Rate of Visual Impairment for Eyes of Patients With Treated Open-Angle Glaucoma 16

CONTENTS (cont'd)

6. Summary of Evidence Regarding the Effectiveness of Treatment for Ocular Hypertension in Preventing Open-Angle Glaucoma 19
7. Studies Relating Long-Term Outcomes of Treatment to Lower Intraocular Pressure in Patients Without Visual Field Defects 20
8. A Comparison of Estimates of Accuracy for Three Glaucoma Screening Technologies 25
9. Calculation of Estimated Cost per Confirmed Case of Open-Angle Glaucoma and Number of Cases Diagnosed 40
10. Calculation of Incidence of Open-Angle Glaucoma (OAG) in the Elderly Population 41
11. Glaucoma Screening Test Accuracy Assumptions 42
12. Cost Assumptions 45
13. Number of Open-Angle Glaucoma Cases Diagnosed Under Extreme Assumptions of Test Accuracy and Followup Rates 46
14. High and Low Bounds of Total Costs of Screening and Confirmatory Followup for Open-Angle Glaucoma in Initial Years of a Screening Program 47
15. High and Low Bounds of Cost Per Confirmed Case of Open-Angle Glaucoma in Initial Years of a Screening Program 48
16. High and Low Bounds of Total Costs of Screening and Confirmatory Followup for Open-Angle Glaucoma In Later Years of a Screening Program 49
17. High and Low Bound of Cost Per Confirmed Case of Open-Angle Glaucoma in Later Years of a Screening Program 50
18. Assumptions for Low- and High-Cost Bounds of a Model for Estimating Costs of Screening for High Intraocular Pressure 52

Boxes

Box *Page*

A. Components of Screening Test Accuracy 24
B. Estimation of Theoretical Upper Limits of Accuracy of Tonometry (21 mm Hg or Greater) for Identifying People With Open-Angle Glaucoma 43

Introduction

Open-angle glaucoma (OAG) is the second largest single cause of blindness in the elderly, afflicting an estimated 2 to 3 percent of this age group at any time. Approximately 4,600 elderly people will go blind from some form of glaucoma this year, many from OAG (84).[1] Many other elderly people have substantial visual disability short of blindness as a consequence of the disease.

There are many different forms of glaucoma, all characterized by progressive loss of vision associated with increased intraocular pressure (IOP) and subsequent deterioration of the optic nerve. OAG, the most common type of glaucoma and the only one currently targeted by mass screening programs, is the subject of this paper.

Despite considerable study, the exact cause of OAG remains elusive. It is a disease strongly associated with old age; OAG is very rare in people under age 40, but it is common among the elderly. Although the exact incidence of OAG is not known, a "best guess" based on prevalence data is that at least 2 in every 1,000 elderly people develop the disease each year.

The single most important predictor of future OAG is the existence of elevated IOP, commonly defined as pressure within the eye of 21 mm Hg or greater. Between one-tenth and one-fourth of the elderly have this characteristic. Of those in whom the elevation is modest (2 1 to 30 mm Hg), about one-third will go on to develop OAG over the next 20 years. For those with very high IOPs (greater than 30 mm Hg) the risk is much greater; it will take only about 5 years for OAG to become manifest in about one-third of this population.

In classic OAG, the next sign of disease, after elevated IOP, is abnormality of the optic disc (the area where the optic nerve enters the eye). This abnormality is a result of damage to the optic nerve. As nerve damage becomes more extensive, defects--dim or blind areas--develop in the field of vision. These visual field defects initially go unnoticed by an individual but eventually become extensive enough to cause visual impairment, including blindness.

Not all people with OAG follow this classic model, and diagnosis of early OAG is often not a simple matter. First, elevated IOP and OAG are not always related. Many people with elevated IOPs will not develop any other signs of OAG. In addition, some people develop OAG despite having apparently normal IOPs. It appears that some people have eyes that can cope well with modest elevations in IOP, while other people have eyes that are particularly susceptible to damage at seemingly normal IOP levels.

Second, an optic disc that appears somewhat abnormal is not necessarily indicative of OAG. The disc may in fact be normal for that individual, or the abnormality may be related to some other eye disorder. There are certain characteristics that are especially strongly linked to OAG--for example, a disc whose central area occupies an abnormally large proportion of the disc as a whole. But since the assessment of these features is subjective, the accuracy of an examiner in diagnosing OAG based on them depends heavily on the examiner's skill and experience.

Third, not all people in whom visual field defects are detected have OAG. Their fields of vision may be deteriorating due to some other cause.

---

1 This number is based on rates reported by the National Society to Prevent Blindness but is updated based on an estimated 1988 elderly population of 30,263,000.

Thus, when a person has all the classic signs of manifest OAG, *and* when other possible causes of these signs (e.g., another form of glaucoma) have been ruled out, the examiner can be reasonably confident of a diagnosis of OAG. A diagnosis inconsiderably more difficult when only one or two signs are present--for example, when a person has elevated IOP and apparent abnormalities of the optic disc, but no visual field defects. Such a person may be termed an *OAG suspect,* with a definitive diagnosis held in abeyance until visual field defects develop, making it clear to the examiner that the eye is truly suffering from manifest disease.

The larger group of people who have elevated IOPs but no other signs of disease are often said to have *ocular hypertension* (OH), to distinguish them from people with more specific signs of OAG. This group includes some people for whom a moderately elevated IOP is normal (or at least well-tolerated by the eye); some in whom OAG is beginning to develop; and some for whom the elevated IOP is a sign of abnormality or disease, but not of OAG.

The complexities of establishing that OAG is present are reflected in the definitions of the disease used in various studies in the literature. Some studies define a patient as having manifest OAG only if both an abnormal optic disc and visual field defects are present (13). Others, however, consider subjects to have OAG not only if they have these features but also if they have less conclusive signs--for example, subjects who have an IOP of greater than 30 mm Hg, but no other signs of disease (24). These differing definitions are a partial explanation for the varying results among studies discussed in this paper. Greater weight has been given in this analysis to studies in which visual field defects were measured and used as a criterion for a diagnosis of OAG. This was done on two grounds: first, that the development of visual field defects where none previously existed is unequivocal evidence that disease exists; and, second, that this criterion is less subjective than the assessment that an optic disc is abnormal and thus is more comparable among studies.

Summary of Findings

Screening is the detection of disease in asymptomatic people. To be an appropriate disease for screening, OAG must meet three minimum criteria:[2]

1. OAG must have a recognizable latent or early stage, during which persons with the disease can be identified before symptoms develop. If there is no such early stage, screening is useless, since patients will appear when they develop the symptoms in any case.
2. There must be an accepted and effective treatment for patients with OAG. Furthermore, the treatment must be more effective at preventing visual impairment and disability when initiated in the early (symptomatic) stage than when begun in the later, symptomatic stages of the disease.
3. There must be an appropriate, acceptable, and reasonably accurate screening test.

These three criteria are discussed below.

Early-Stage OAG

OAG does have an early stage at which the disease can be diagnosed but the patient has no outward signs. Once both optic disc changes and visual field defects have developed, a diagnosis of OAG can be made with reasonable confidence, even though the patient does not usually notice a change in visual ability until the defects have become fairly extensive.

Although they precede actual visual impairment, visual field defects do not develop until the disease is well established and has already caused injury to the eye. Consequently, there has been great interest in identifying people with OAG at earlier stages--when abnormalities of the optic disc first appear, or even when the disc still ap-

---

Z These three criteria are derived from the basic principles of screening first set out by Wilson and Junger twenty years ago (125).

pears normal but elevated IOP is present. The difficulties with these criteria for identifying people with OAG were mentioned earlier. People with OH are at higher risk for OAG than are others in the population, but they are not all destined to develop manifest OAG within their lifetimes. People with abnormalities of the optic disc are often designated OAG "suspects, " but not all of them have that particular disease. Still, if treatment is safe and sufficiently effective in preventing impairment in those who have OAG, people may wish to be treated upon the finding of signs associated with the earliest stages of the disease, even if some of those people do not, in fact, have OAG and are therefore treated unnecessarily. Thus we are led to the next question: effective is treatment?

Treatment

Treating people with OAG has been established medical practice since the nineteenth century. Standard treatment consists of medication to lower IOP. If medication alone is insufficient in achieving this, a physician may perform surgery to create an artificial opening through which fluid can flow out of the eye, lowering IOP. New drugs (with fewer side effects) and laser surgery[3] (with fewer complications) have been added to the array of therapeutic alternatives over the past decade, but the basic treatment framework remains.

Many eye care practitioners treat people they consider to be at high risk of OAG as well as those with manifest disease (i. e., visual field defects). A patient might be considered "high risk" in the opinion of that particular practitioner if the patient has a high IOP, suspicious abnormalities! of the optic disc, a family history of OAG, or any combination of these and other factors.

Just as the assessment of who is sufficiently "high risk" to be treated is considered a matter of individual judgment, treatment policies and preferences vary considerably among physicians and optometrists.[4] For example, one physician might prescribe medical treatment for a patient with an IOP of 24 mm Hg and a family history of OAG, even if no more definitive signs of OAG are present. Another might treat only patients in whom highly abnormal optic discs and/or visual field defects are detectable. Both would be within the range of currently accepted medical practice.

The difficulty of deciding who should be treated is compounded by the uncertainties of treatment effectiveness. On the one hand, treatment is inconvenient, costly, and uncomfortable; for a few patients, treatment is itself a risk to health. It has distinct drawbacks even for those with manifest OAG. On the other hand, if treatment is very effective at preventing visual impairment from OAG, *and* if it is more effective if initiated earlier in the course of the disease, it may be desirable to treat some or all people with OH, even at the expense of treating many of them unnecessarily y.

That treatment of both OH and manifest OAG is effective is an accepted tenet of the medical profession,[5] but it has not been documented in the literature to date. The relationship between IOP and OAG is well-established; it has been shown that higher IOP is associated with higher risk of OAG, and that a rapid rise in IOP to very high levels induces glaucoma (5,38,95). What is absent is sufficiently convincing evidence that the reverse is true: that lowering IOP by conventional means also lowers the risk of OAG in those with OH, and that lowering IOP slows or prevents visual impairment in those who have manifest OAG.

3 The most promising form of laser surgery, argon laser trabeculoplasty (ALT), is not quite analogous to traditional surgery to lower IOP. Rather than creating new openings to enhance fluid flow from the eye, it scars the tissue around the existing natural openings, stretching the openings and enabling better out flow.

4 Thirteen States permit optometrists to treat glaucoma patients with medications. In 11 of those States , the opt omet r i s t need not consu l t a physician before initiating treatment (122).

5 One medical researcher has recently questioned the effectiveness of OAG treatment (32).

No adequate studies comparing treated with untreated patients with manifest OAG exist, because physicians have considered it unnecessary and unethical to mount such a study. Consequently, one must turn to the results of studies of treatment for patients with OH (i.e., elevated IOP only) and infer the results to treatment for manifest OAG.

A few studies comparing treated and untreated patients with OH have been conducted; their findings are mixed, ranging from effective to no effect to harmful. All have deficiencies in design that either make it difficult for the study to find an effect (for example, small sample sizes or short study duration), render the conclusions suspect, or make the findings inapplicable to the larger population.

Two very recent clinical trials, whose final results are still unpublished, may establish the effectiveness of treatment in preventing OAG in persons with OH. Preliminary results from these studies suggest that if an effect exists, it may be substantial. It remains to be seen whether the final study results will reach statistical significance. (It is possible for even a substantial difference in outcomes between groups to be due to chance; if the results of these studies reach statistical significance, this explanation is unlikely and a true effect of treatment probably exists). Both studies are nearing completion (68,71).

If treatment of OH is shown effective in preventing or delaying the onset of manifest OAG, and if treatment of manifest OAG is therefore presumed effective in preventing or delaying visual impairment resulting from the disease, the *degree* of effectiveness may still depend heavily on the criteria used to decide when the current level of treatment is sufficient. Under the treatment practices of the past, most patients with manifest OAG still suffered gradual visual deterioration. These treatment practices included acceptance of the idea that if an elevated IOP could be lowered to the high end of normal--e. g., from 30 mm Hg to 21 mm Hg--treatment was adequate. In the past decade, as evidence has accumulated that people suffered visual deterioration despite this level of treatment, many ophthalmologists have emphasized more aggressive treatment, striving for even lower IOPs if any signs of deterioration occur. They believe that current treatment practice is thus more effective than in the past. This difference has not been documented; it is an important hypothesis to investigate, both in order to assess the potential gains and in order to determine whether more aggressive treatment leads to an increase in the severity or frequency of side-effects.

Screening Technologies

Three technologies have been used in OAG screening:

- *tonometry,* which measures IOP by calculating the resistance of the eye to a force;
- *ophthalmoscopy*, a tool enabling an examiner to scrutinize the optic disc of a patient and detect abnormalities characteristic of OAG, and
- *Perimetry, which* detects defects in the visual field through a patient's responses to dots of light introduced at various points in the field.

Each of these three technologies is designed to identify a somewhat different group of people. Tonometry is designed to detect people with elevated IOPs who are thus at risk of OAG, and it is effective at doing so. It is much less effective at identifying people who already have manifest OAG (since some people have the disease without having elevated IOP). Thus, when tonometry is used to screen for elevated IOP, it has a relatively small false positive rate (it is not zero, because some people whose IOPs were slightly high at the screening are normal upon reexamination). When tonometry is used to screen for manifest OAG, however, it has a high false positive rate, because most people with elevated TOPS do not have manifest OAG.

Both ophthalmoscopy and perimetry also may produce false positive tests for manifest OAG, because people may have apparently abnormal optic discs or visual field defects for reasons other than OAG. However, the rate of false positives under ideal conditions

is much lower for both of these tests than for tonometry.

Still, despite the potentially greater accuracy of these two technologies in detecting manifest OAG, neither is without drawbacks. Ophthalmoscopy can detect the first visible signs of deterioration due to OAG--i.e., degeneration of the optic nerve. But since evaluations of the optic disc are subjective, it has a high inherent variation that depends on the experience of the examiner. Perimetry is designed to detect defects in the visual field, the most definitive outward sign of manifest OAG. Its most significant inherent limitation is that it cannot identify patients with OAG before visual field defects occur (although it can identify them before visual *impairment* occurs).

In practice, the relative accuracies of these three technologies, alone or in combination, in correctly identifying people with manifest OAG are very poorly documented. Only one study was found that compared the effectiveness of all three technologies in detecting manifest OAG in the same population. The study has not been published (although an abstract of results is available), and because the setting of the study was mass screening performed in community facilities (e.g., churches), its findings may not be applicable to screening performed in the offices of physicians and other eye care practitioners. A few other studies exist of the accuracy of specific technologies alone, but the study designs and the results vary widely. Consequently, it is possible to make some reasonable guesses about the relative accuracy of the three technologies and the factors that affect their accuracy, but major questions remain about average effectiveness in practice.

Implications for Medicare

The prevalence of OAG is sufficiently high to warrant considering the disease a substantial health problem. In an ongoing screening program, however, it is not the total number of existing cases but the number of new cases that the program will detect. Because new cases of manifest OAG are relatively rare, even among the elderly --a few cases per 1,000 elderly per year- -any screening program will incur considerable costs to detect those cases.

To gain a sense of the magnitude of potential costs that might be incurred by Medicare if an OAG screening benefit were offered, the average costs of identifying and confirming a case of manifest OAG in an every-other-year screening program were estimated. Under the assumptions of the model, and assuming that Medicare paid 80 percent of all allowed charges associated with the screening and follow up/confirmatory visits, it is estimated that Medicare costs for an OAG screening program would range from approximately $160 million to $800 million per year. These costs do not include the costs of treating the glaucoma cases detected by the program. The costs of a screening program to identify those with elevated IOP (most of whom would have only OH, but some of whom would also be found to have manifest OAG) would be similar. Again, however, the costs cited here do not include either the costs of treating OH patients or the costs of long-term followup of untreated OH patients.

The potential number of OAG cases diagnosed as a result of a screening program for manifest OAG is highly uncertain. Such a program might detect anywhere from 10,000 to 90,000 cases of manifest OAG per year in an ongoing program, depending on factors such as the accuracy of the screening tests and the true incidence of OAG in the elderly. (In the initial years of such a program, when a backlog of undiagnosed OAG cases exist, anywhere from 50,000 to 340,000 cases might be detected.) If the goal of the program was to identify all individuals with high IOP, the program would ultimately detect between 30,000 and 350,000 cases per year (with between 300,000 and 3 million per year detected in initial years).

The accuracy of the screening tests has a particularly important impact on costs. The costs of a screening program depend heavily on the number of people with positive tests who are referred for a followup visit, and whether a substantial proportion of those are false positives. If many people test positive, and thus many undergo a comprehensive fol-

lowup visit, total costs will be high. If most of these are true positives, however, the cost per case found will be relatively low; if most of them are false positives, the cost per case found will be high.

These screening costs should be compared to the costs of treatment and the economic and net health benefits resulting from treatment. OTA has not attempted such a comparison because of the major uncertainties associated with treatment effectiveness. The higher the screening costs, the greater the benefits of treatment must be to justify screening. Potential benefits include improved visual function, improved quality of life, lessened dependency on others, and lower expenditures for public programs that provide financial and personal assistance to the disabled.

Apart from the potential benefits of screening itself, the potential benefits of *Medicare coverage* for OAG screening depend heavily on how many people would be encouraged to undergo screening if the service were covered. Over 50 percent of the elderly already undergo frequent OAG screening; for these people, Medicare coverage will bring some relief from out-of-pocket costs but no additional benefits in preventing visual impairment. (A small benefit is possible if, as a result of Medicare coverage, these people were screened in settings where test accuracy was higher than wherever they receive the service at present.)

Elderly people who would not have undergone screening without Medicare coverage, on the other hand, could potentially improve their health. OTA assumed that total utilization of a Medicare biannual screening program would be 75 percent-- i.e., one-third of those screened would not have undergone screening without Medicare coverage. If this assumption is correct, then between 3,000 and 30,000 people per year would have manifest OAG diagnosed earlier (i. e., before they would otherwise be screened or developed symptoms), and between 10,000 and 100,000 people per year might have high IOP identified (if tonometry were the screening test used), if Medicare covered screening for OAG.

This analysis examined only the costs and yield of glaucoma screening as a single service. It did not examine the benefits of detecting disorders other than OAG as a result of the glaucoma screening visit. Nor did it examine the effectiveness and cost of a comprehensive eye visit in its entirely.

Conclusions

An OAG screening program for the elderly, whether aimed at detecting only those with manifest disease or also those at risk due to high IOPs, is likely to be fairly expensive.[6] The potential benefits of such a program are substantial, but whether those benefits can actually be realized is still highly uncertain. It depends heavily on two unknown factors: first, on the true accuracy of the various screening tests in the settings in which they would be used; and, second, on the effectiveness of treatment in preventing, halting, or delaying the progression of visual impairment due to OAG.

Most critical to the question of whether screening for OAG is useful is whether treatment of people with OH (if screening for high IOP) or OAG (if screening only for manifest disease) alters the course of the disease. The evidence in the literature to date leads neither to the conclusion that treatment is effective nor that it is ineffective; by and large, the few relevant studies are too small to detect an effect even if one exists. A consensus panel of eye care professionals would undoubtedly conclude that treatment is effective, although such a panel would likely also acknowledge that support for this belief has been inadequately documented. The opinions and personal experiences of eye care experts are compelling, but they are also subjective.

In light of the preliminary results reported from unpublished research, it is likely that treatment does reduce the incidence of OAG among those at high risk

6 As a rough measure of comparison, the annual total cost of screening for OAG would be approximate 1 y one- tenth to one- third of the $3 bi 11 ion annual cost of the Medicare End-Stage Rena 1 Disease program (116).

and, probably, delays visual impairment among those in whom OAG is already man if est. If this expectation is borne out, screening would be effective in reducing visual impairment due to OAG. That said, certain reservations regarding glaucoma screening deserve reiteration:

- The amount of impairment that might be prevented through a screening program is unknown. The degree of effectiveness of such a program depends on the unknown degree of effectiveness of treatment in preventing or delaying the development of OAG (in those with OH) or the development of visual impairment due to OAG (in those with manifest disease). It also depends on the accuracy of the various potential screening tests in the settings in which they might be performed, which is unknown except within a very broad range.
- Consequently, both the benefits of screening -- i.e., visual impairment prevented -- and the costs of screening and resultant treatment are highly uncertain. OTA's estimates, which include only costs to Medicare for the screening episode and confirmatory visit, cover a five-fold range (from about $160 million to $800 million). Treatment costs for those who are detected with the disease prior to onset of symptoms would add to the total cost of screening.
- The field of OAG screening and treatment is one that deserves more self-examination and critique than it has received. The potential research agenda for this field is large, and some important areas are outlined below.

Research Needs

Sustained investment in clinical research on OAG treatment is crucial to evaluating the effectiveness of current treatment technologies and protocols and to developing better ones. For example, a clinical trial currently sponsored by the National Eye Institute comparing standard medical treatment with a new treatment-- early argon laser trabeculoplasty (ALT)--may give some insight into treatment effectiveness. Although "no treatment" is not an option in this trial, the trial does include rigorous documentation of the outcomes of two different types of treatments. Since ALT is a relatively new technology but appears to be widely used, documenting its effects is critically important.

The theory that outcomes will be improved if treatment is more aggressive also deserves in-depth examination. Current expert opinion supports the idea of increasing the intensity of treatment whenever visual deterioration is suspected, regardless of the absolute level of IOP. This more aggressive treatment practice has merit considering the history of deterioration of many treated patients in the past. Its incremental effectiveness over more conservative drug therapy should be studied to determine whether very low IOPs can be sustained for long periods of time, and whether such a consequence reduces vision loss. An examination of this practice could also illuminate any increase in side-effects that might result from it. If the effectiveness of this practice is demonstrated, the information should be disseminated so that treatment practices of eye care practitioners can be changed.

The natural history of OAG is still perplexing. It is still unknown which people with OH will develop OAG and how to identify people without OH who nevertheless will develop the disease. Researchers have tackled these questions with some energy over the past decades, but they are still far from the answers.

Useful information could be obtained on one important aspect of the natural history of OAG without a major investment of resources. The natural course of untreated OAG is unclear and subject to a great deal of individual interpretation. Documented case studies of patients who were untreated for personal reasons would help establish a baseline against which treatment outcomes could be assessed.

The tradeoff between immediate inconvenience and discomfort and long-term prevention of impairment is one faced by every eye care practitioner and every patient

with elevated IOPs contemplating the initiation of treatment to decrease the risk of developing OAG. A more precise estimate of the magnitude of the costs and benefits of that tradeoff- -for example, a quantified compilation of the frequency and intensity with which different side-effects of the various medications occur--can be greatly aided by research. Such an information base would help physicians predict which patients are most likely to be aided by treatment. But the essential dilemma of how to balance the benefits and drawbacks of treatment for a particular individual is likely to remain for a very long time.

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).

---

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%		
Perkins, 1973		3%		f
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.

Description

Patients may be treated for potential or confirmed open-angle glaucoma (OAG) at any of four stages:

1) after the intraocular pressure (IOP) has reached a level suspected to be intolerable to that individual's optic nerve, but before any other characteristics of glaucoma appear;
2) after changes in the optic disc have appeared, but before any visual field defects have occurred;
3) after defects are apparent to the physician but before the patient is visually impaired in any way; or
4) after some visual impairment occurs, to prevent further impairment.

Treatment cannot reverse impairment; it is prescribed on the assumption that it can prevent visual deterioration by lowering the pressure in the eye and preventing further damage to the optic nerve. Eye care professionals believe that the earlier treatment is begun, the greater the likelihood that visual impairment can be prevented. This belief has been bolstered by evidence that a substantial proportion of the optic nerve dies before a patient becomes visually impaired (98).

Treatment for OAG follows a well-established pattern (34,67). Initial treatment nearly always consists of topical application of one of three drugs: epinephrine, pilocarpine, or timolol. Although these drugs act in different ways, the goal of each is to lower the IOP (either by decreasing formation of fluid or by enhancing outflow), thus presumably preventing further damage to the optic nerve. If one of these drugs is inadequate in lowering pressure, they may be combined, given at higher dosage, and/or substituted with similar, alternative drugs. If pressure still remains high, a stronger, systemic drug with more side effects (e. g., acetazolamide) may be added. Finally, if even maximum tolerable medication is inadequate, an ophthalmologist will perform laser or filtering surgery to enhance outflow of the ocular fluid.

The medications used to lower IOP must be taken for life, and all have numerous common side effects (e. g., blurred vision, headache, nausea, and increased blood pressure and heartbeat (33)). Some medications also increase the risk of cataract formation (8,101). These side effects and sequelae, plus the cost of the medications and the inconvenience of applying them up to 4 times per day, have resulted in noncompliance rates of up to 58 percent in various studies (6,61). Timolol, one of the only two new medications to be approved for glaucoma treatment in recent years,[1] has become a popular first medication because it is better tolerated by patients than epinephrine or pilocarpine. (Unfortunately, an initial lack of understanding of timolol's full effects led to several deaths in glaucoma patients with respiratory and cardiovascular diseases exacerbated by the drug (86)). Other topically-applied drugs that are chemically similar to timolol are under investigation in the hope that they may be more effective or have more limited systemic effects (2, 15,17,22,121).

Despite the disadvantages of glaucoma medications, they are still usually considered preferable to surgery. Traditional filtering surgery--the creation of an artificial opening through which fluid can flow out of the eye--is reported to be successful in lowering IOP in 60 to 90 percent of patients, depending on patient characteristics (57). However, filtering surgery also carries the risks of permanent damage to the eye from infection, excessive drainage (causing soft, shrunken eyes), and hemorrhage (57). OAG patients who have undergone filtering surgery are much more likely than other OAG patients to

1 The second relatively new medication for glaucoma is dipivalyl epinephrine, a form of epinephrine that becomes active only after interaction with the eye and thus causes fewer side effects (119).

develop cataracts (110).[2] Furthermore, eventual return to medication and/or additional future surgery may be necessary in some patients for continued control of IOP (37).

In recent years, argon laser trabeculoplasty (ALT) has become a frequent intermediate step for patients whose IOP is uncontrolled by medication (57). ALT consists of making tiny laser burns within the trabecular network. It is unclear why this laser scarring facilitates fluid outflow, but ALT has been shown to decrease IOP (1 14,1 17). Among the benefits of ALT are an avoidance of some of the risks of filtering surgery (e. g., infection), but unlike surgery, most patients must continue taking medication even after undergoing the procedure (37). The long-term effects of ALT scarring are unknown. The National Eye Institute is currently conducting two clinical trials of the procedure: one of ALT (instead of medication) as primary treatment in patients with early evidence of OAG, and one comparing ALT with filtering surgery in patients with advanced OAG (120).

Treatment Outcomes

A number of studies have reported the proportion of OAG patients whose visual field deteriorated while under treatment (2,25,43,45,46,69,82,83,87,97,109). The reported outcomes vary considerably, with anywhere from 11 to 82 percent of patients in these studies suffering further deterioration while under long-term treatment. Patients with advanced OAG suffer deterioration **more rapidly than patients with only minor visual field defects (69),** perhaps because the loss of additional optic nerve fibers in people with advanced disease leads to proportionately greater impairment (98). In general in these studies, longer followup results in more patients deteriorating.[3] It appears that about one-fourth of all patients with existing defects suffer deterioration within 4 years (87, 109). However, another one-fourth of patients suffer no deterioration even after many years (83).

Surprisingly little information exists on the rate at which people with OAG, treated or untreated, actually become visually impaired. Table 5 summarizes the results of three studies that reported on rates of visual deterioration in treated OAG patients. Of these reports, the one that can be interpreted most directly found that 75 percent of patients with manifest OAG went blind in the affected eye within 20 years, even when treatment was begun soon after the detection of visual field defects (43). (Of patients who

2 Cataract development is especially common in those glaucoma surgery patients in whom surgery-related complications arise (110).

3 Followup in these studies ranged from 1.4 to 42 years.

Table 5.--Three Estimates of Rate of Visual Impairment for Eyes of Patients with Treated Open-Angle Glaucoma

Source	Time period	Initial condition of eyes	Percent of eyes that deteriorated	Condition at end of measured time period
Kronfeld and McGarry, 1948	5 years	"early" OAG	16%	"advanced" OAG
	5 years	"moderate" OAG	50%	"advanced" OAG
	5 years	"moderate" OAG	20%	blindness
Hart and Becker, 1982	10 years	82% of all eyes with OAG suffered Insignificant visual loss" (not necessarily synonymous with further impairment)		
Grant and Burke, 1982	5 years	"early" OAG	25%	blindness
	10 years	"early" OAG	38%	blindness
	20 years	"early" OAG	75%	blindness

SOURCES : See references.

began treatment after changes in the optic disc but before the onset of visual field defects, 50 percent went blind in the affected eye within 20 years.)[4] The incidence of blindness was fairly constant across time in this study.

By their very nature, even recent reports of very-long-term outcomes of treated patients with OAG reflect the treatment patterns of many years ago. Some ophthalmologists believe that outcomes are better now than under treatment practices of the past. In the past, they argue, ophthalmologists were content to maintain treatment without change when a patient's IOP had been lowered to a certain level, even if the patient's visual field continued to deteriorate at that level (105). Now, they maintain, patients are treated more aggressively if their visual condition is not stable under the current treatment regimen, and patients deteriorate less rapidly. Continuing documentation of long-term outcomes could both support this contention, assuming it is true, and improve the dissemination of knowledge regarding the most appropriate treatment practices.

Treatment Effectiveness

A necessary condition for OAG screening to be effective is that treatment is effective. One might choose to screen for an OAG risk factor (i.e., high IOP), for probable early OAG (i.e., suspected optic nerve damage), for fully developed OAG as manifested through visual field defects, or not to screen for OAG or its risk factors at all. Which screening policies should be considered depends heavily on whether and at what stage treatment is effective in preventing visual deterioration.

The assumption that early treatment can prevent visual field defects pervades the literature. Studies of patients with ocular hypertension (OH) have tended to reinforce the assumption by emphasizing how few patients who were treated early suffered visual deterioration. (In fact, only a small proportion of such patients would be expected to suffer measurable deterioration even without treatment.) The belief in the importance of early detection and treatment has continued almost unabated despite the fact that a few eminent researchers pointed out the inconsistencies between documented evidence and clinical practice as early as the 1960s (23). Their conclusion, that the efficacy of treatment for OH and OAG was undocumented, has been reiterated by others in recent years (3 1). The Canadian Periodic Health Examination Task Force likewise concluded that the evidence for effectiveness of treatment for OAG consisted of the opinions of respected authorities (2 1,39).

What exactly is the evidence regarding 1) the effectiveness of treating OH to prevent OAG, and 2) the effectiveness of treating manifest OAG to prevent or delay functional visual impairment? Not surprisingly, there is no direct evidence regarding the effectiveness of treating manifest OAG. There have been no studies of comparable groups of treated and untreated patients with visual field defects, because the standard of care is to treat all such patients. However, it is possible to review the evidence for the effectiveness of treating OH and assume that if treatment of OH is effective in preventing or delaying the development of visual field defects, then treatment of manifest OAG is likewise effective. It is also possible to examine other indirect evidence of the effectiveness of OAG treatment.

Evidence of the effectiveness of treating OH to prevent OAG

To be considered direct evidence of the effectiveness of treatment of OH for preventing OAG, a study must, at a minimum, meet three criteria:

4 The lower incidence of bl indness in those treated before onset of vi sual field defects could ref lect one or both of two poss i bi l i t i es: 1) that i t nat - ura l ly takes a longer time for those with only optic disc changes to reach blindness, since they are identified at an earlier stage in the disease than are those with visual field defects; or 2) that treatment of those with abnormal optic discs was more effective because it was initiated earlier in the stage of the disease.

1. Long-term followup of the study population (at least 1 year, and preferably much longer if differences are to be detectable),
2. Monitoring of visual field changes in the study population, and
3. Existence of well-defined treated and untreated groups of patients (or eyes of patients). Ideally, these patients (or eyes) should be randomized prospectively into the two groups, although studies in which patients are matched for salient characteristics also provide useful evidence. *The study must control in some way for differences in the level of IOP among treated and untreated patients* or must be reported in such a way that the evaluator can control retrospectively for this factor, because people with high IOPs are more likely to get OAG than those with low IOPs irrespective of treatment.[5]

Although study size per se is not one of the criteria, the number of subjects studied is crucial to the ability to detect differences and attribute them to treatment. For example, if the incidence of OAG among all people with OH were *2* percent per year, and treatment reduced this by 50 percent --i.e., to an incidence of 1 percent per year--a 1 -year study would require hundreds of subjects to show this result with a probability of less than 5 percent that the result is due to chance (even assuming full compliance of all subjects).

Despite the large published literature relating to OAG, OTA could identify only seven studies of OH treatment (two published only in abstract form) that meet these three basic criteria. The results of these studies are summarized in table 6. The studies are of two types: those that compared treated with untreated patients, and those in which one eye of each patient was treated, while the other eye was left untreated.

Of the three studies that compared treated with untreated patients, the one finding the most positive effect of treatment is also the most recent. Preliminary results of this study (still ongoing), which employs a prospective, randomized design, suggest that a statistically significant positive effect of treatment may be found (70). A less recent study, in which matched patients were prospectively assigned to treatment or placebo, found a positive but not statistically significant effect (only 12 placebo and 15 treated patients completed the study) (64). Finally, the oldest study, which neither randomized nor matched patients, found that treated patients were actually more likely to develop OAG (27). When patients in this last study are grouped by IOP, it appears that treated patients with the lowest IOPs (21-25 mm Hg) were significantly more likely to develop OAG than untreated patients; the differences in development of OAG between treated and untreated patients with initial IOPs of 26-30 mm Hg and over 31 mm Hg are not significant.

Studies that use eyes rather than patients as the unit to be treated pose some problems in interpretation, because treatment of one eye could affect the outcome of the untreated eye. Of the four studies that compared treated with untreated eyes, three found a significant positive effect of treatment (see table 6). The fourth study found a negative effect, but the difference between the treated and untreated groups was not statistically significant (77). In the study showing the greatest positive effect, the patients selected for the study were thought to be the subgroup most likely to benefit from the particular treatment (because the patients had previously demonstrated an IOP response to the medication chosen for the study) (102). In this same study, however, the untreated eyes did particularly poorly (i.e., a higher propor-

---

5 As a case in point, two commonly cited reports of a Danish epidemiological glaucoma study (87, 104) reported the number of OH patients who went on to develop visual field defects. In both reports, treated patients were more likely than untreated patients to develop visual field defects. The average IOP levels in the two groups (treated and untreated) were not stated in either report. The authors simply reported on the outcome of patients under standard medical care, and it is extremely likely that certain patients were treated because their higher IOPs or other factors placed them at an especially high risk of disease. Thus, these studies cannot be used to evaluate the effectiveness of treatment.

Table 6.--Summary of Evidence Regarding the Effectiveness of Treatment for Ocular Hypertension in Preventing Open-Angle Glaucoma

Source	Study size (no. of patients/eyes) Beginning	End	Study design	Treatment	Length of study	Number percent developing OAG	Effect of treatment	Statistically significant?
Patient-level studies								
Krug et al 1987	54 untreated 53 treated	(ongoing) (ongoing)	randomized	timolol	7 yrs.	13 (24%) untreated 6 (11.3%) ever-treated (as of 1987)	+	(study incomplete)
Kitazawa et al., 1981	26 placebo 26 treated	12 placebo 15 treated	matched prospectively	timolol	1 yr.	2 (7.6%) placebo 1 (3.8%) treated	+	no
David et al., 1977 (IOP 22-25)	(not applicable)	48 untreated 27 treated	retrospective, unmatched	pilocarpine, adrenoline, acetazolamide	1-11 yrs. (average 41 mo.)	0 (0%) untreated 2 (7.4%) treated	-	yes
IOP 26-30	(not applicable)	16 untreated 8 treated	(same as above)	(same as above)	(same as above)	2 (2.5%) untreated 1 (1.1%) treated	+	no
31+	(not applicable	3 untreated 14 treated	(same as above)	(same as above)	(same as above)	1 (33.3%) untreated 6 (48.2%) treated	-	no
Eye-level studies								
Hoff et al 1988	64 patients (128 eyes)	35 patients (as of 1988)	eyes randomized, double-masked	timolol	5 yrs	8 (22.8%) placebo 5 (14.2%) treated	+	(study incomplete)
Levene, 1975	72 patients (144 eyes)	59 patients	eyes randomized	pilocarpine, echothiophate iodide	ave. 55 mo. (min. 6 mo.	2 (3.3%) untreated 4 (6.6%) treated	-	no
Becker and Morton, 1966	50 patients (100 eyes)	(10 patients full 4-5 yrs)	eyes randomized	epinephrine	6 mo.-5 yrs.	7 (14% untreated 2 (4%) treated	+	not reported
Shin et al, 1976	19 patients (38 eyes)	19 patients	eyes randomized; patients were selected for expected response to medication	epinephrine	1-5 yrs.	6 (31.5%) untreated 0 (0%) treated	+	yes

SOURCES: See references.

tion developed OAG than did the eyes of untreated OH patients in the studies discussed earlier).

In addition to the above studies, several investigators have reported the outcomes of treating patients who had either OH or changes in the optic disc (but no visual field defects). These studies had no clear control groups. Relevant results of the studies are summarized in table 7; they are useful primarily as contextual information for assessing the outcomes of treatments in the comparative studies.

Indirect evidence of the efficacy of treatment for manifest OAG

A number of other studies and observations provide indirect evidence of the efficacy of treatment for manifest OAG in delaying or preventing further visual field defects. For example:

- Studies in animals in which IOP was artificially raised have been able to induce glaucomatous changes in the eye (38), implying that the level of IOP is causally related to damage to the eye.
- Several studies have found improvement in the appearance of the optic disc after treatment (44,62,91).
- Some researchers have observed, in retrospect, that patients whose IOPs were maintained at relatively low levels while under treatment (e.g., under 20 mm Hg) suffered less loss of vision over time than patients whose IOPs remained relatively high despite treatment (66). It may be that a drastic lowering of IOP is necessary in some patients before treatment is effective (62); it is possible that some studies have not detected an effect of lower IOP because the treatment was inadequate.

Table 7--- Studies Relating Long-term Outcomes of Treatment to Lower Intraocular Pressure in Patients Without Visual Field Defects

Source	Treatment duration	Percent of treated patients developing OAG	Selected characteristics and limitations
Schappert-Kimmijser, 1971	5 years	16%	OH patients only
Airaksenen et al., 1982	2 years	0	OH patients only; timolol treatment
Nielsen, 1982	4 years	0	OH patients only; timolol treatment
Graham, 1968	2 years	--	study of OH patients comparing treatment to placebo, halted after 2 years when no differences in IOP were found. Fields were not measured when study was halted.
Hildreth and Becker, 1956	0.5-1.5 years	5%	differences in IOPs and followup times between treated and untreated patients unstated
Sorensen et al., 1978	15 years	42%	patients were ocular hypertensives considered to be at especially high risk
Markowitz and Morin, 1983	4 years	16%	not all patients may have been free of visual field defects at beginning of study
Neilsen, 1982	4 years	12.1%	patients were "glaucoma suspects" without field defects
Cockburn, 1983	1.4-19.8 years	10.5%	patients were "glaucoma suspects" without field defects
Grant and Burke, 1982	20 years	52%	patients had changes in the optic disc but no visual field defects at the time treatment was begun

SOURCES: See references.

Most convincing to ophthalmologists, however, is their own experience with glaucoma patients, in whom visual deterioration is proceeding rapidly until the patients are successfully treated (36, 106). Although dramatic treatment effects are most common with closed-angle glaucoma patients, ophthalmologists' experience with these patients leads them to believe that lowering IOP is very beneficial in OAG patients as well.

Compliance as a factor in the effectiveness of treatment

One possible explanation for the lack of documentation of treatment effectiveness is inadequate patient compliance with the long-term treatment regimens prescribed in the studies. In one early study, for example, only 20 percent of patients on treatment at the beginning the study remained on treatment for the full 4 to 5 years; the remainder dropped out of treatment, primarily due to side effects (10). Researchers have noted that patients with established OAG are more compliant (i.e., keep appointments and take medications as scheduled) than patients with OH but no visual field defects (18, 107). Patient noncompliance with treatment regimens means that treatment effectiveness (in actual practice) may differ substantially from treatment efficacy (in research or ideal situations).

Conclusions

Considering both the inadequacies and contradictions in the literature and the experience and opinions of practicing eye care professionals, the following conclusions regarding treatment effectiveness seem warranted:

1. Most people with modestly elevated IOP but no visual field defects upon initial screening will not develop OAG in the near future, even if left untreated (see chapter 2).

2. Justification for the current mode of treatment for OH and OAG is based on theory, personal experience, and the postulates shared among physicians rather than on direct evidence documented in the literature.

3. The evidence regarding the efficacy of medical treatment to prevent OAG by lowering IOP is sparse, conflicting, and largely of poor quality. Two very recent studies, yet to be published, are likely to provide more convincing evidence than currently exists in the literature. It is likely, based on preliminary results, that both will show treatment of OH patients to be efficacious in preventing or delaying the onset of manifest OAG.

4. If treatment of OH is shown to be efficacious, further research will still be needed to clarify which groups of OH patients are most likely to benefit from treatment, which are likely to suffer as much harm as good if treated, and what the most effective treatment regimen is.

5. Patient compliance with medical treatment is highly variable and can be very poor, leading to potentially poor real-world effectiveness of treatment even if treatment is shown to be efficacious.

6. If treatment of OH is shown to be effective in preventing visual field defects associated with OAG, then treating manifest OAG is probably effective in preventing or delaying visual impairment. The extent of effectiveness is unknown and cannot be inferred directly from the effectiveness of OH treatment, since the degree of effectiveness may depend on when treatment is begun.

7. Even with more aggressive medical treatment than in the past, and even with early treatment of patients, it is unlikely that treatment will prevent eventual visual impairment in all patients. However, to the extent that treatment delays blindness, it is valuable in enabling many elderly people to live out their lives with sight.

8. The knowledge base for treatment of manifest OAG would be improved with research on comparative long-term effectiveness of different treatment modalities, establishing the most effec-

tive overall strategy (including criteria for when current treatment of a patient is insufficient), and delineating more clearly the best treatment at different stages of the disease and in different types of patients. Documenting the course of the disease when patients with OAG are not treated (e. g., when the patient's religious beliefs prohibit treatment) would also be extremely useful in describing the natural course of untreated OAG.

Screening Considerations

Screening for open-angle glaucoma (OAG) has two potential objectives:

- to identify people with manifest OAG so that affected individuals can be treated before becoming visually impaired, and
- to identify people with ocular hypertension (OH), the major risk factor for OAG, so that these individuals can be treated and thus reduce their risk of developing OAG.

Although current screening programs frequently combine these two objectives, they are important to distinguish for three reasons. First, the accuracy of a screening test at correctly identifying people depends on which of these characteristics is the purpose of the screen. (See box A for a description of the basic components of screening test accuracy). A test that is very good at identifying people with OH may be very poor at identifying people with manifest OAG, and vice versa. Second, OH is much more prevalent in the population than OAG, and the yield of an OH test (i.e., the proportion of all positives who are true positives) is thus likely to be much higher. And third, the potential costs and medical benefits of screening depend on which groups of people are identified. This last consideration is discussed further in chapter 5.

Description of Screening Technologies

OTA reviewed three different screening technologies that have been used, alone or in combination, in large-scale screening for OH and OAG. These are:

- *tonometry*, which measures intraocular pressure (IOP);
- *ophthalmoscopy*, which enables the examiner to see abnormalities in the optic disc; and
- *perimetry*, which measures the extent of visual field loss.

Tonometry is the most familiar of the three screening methods. It may be performed by physicians, optometrists, or (less commonly) by opticians.[1] Tonometers work by measuring the resistance of the eye to a force, which may be applied by direct contact with the eye or by shooting a puff of air (non-contact tonometry). Tonometry is the method most often used in large screening programs (78,93) and is often part of routine visits to eye care professionals.

Ophthalmoscopy requires the analysis of the appearance of the surface of the optic nerve by a physician or optometrist using an ophthalmoscope (a tool that enables the examiner to look through the pupil at the retina). This procedure can identify characteristics of the optic disc indicative of OAG. It can be performed by trained non-ophthalmologic physicians (e.g., family practitioners).[2] It has been used in community screening efforts in the United States, but it is usually used in conjunction with tonometry (78). Its use in this role has been promoted in at least one textbook on glaucoma (67).

In contrast to tonometry and ophthalmoscopy, *perimetry* identifies actual visual loss. In perimetry, dots of light of varying brightness are introduced at a pattern of points in the visual field. The patients' responses to these stimuli are recorded by the perimetrist (in manual perimetry) or by a computer (in automated perimetry). A lack of response (i.e., the patients' inability to see the light) indicates a blind spot in the visual field. (When the visual field defect is less severe, the patient may see the light but only if it is very bright.)

Perimetry can be time-consuming and expensive and has only rarely been used as a screening tool (63). It is most commonly

1 Opticians can perform only non-contact tonometry.

2 However, not all family practice residencies require some ophthalmologic training, and only two-thirds include routine glaucoma screening as a part of the care residents must provide (113).

Box A--- Components of Screening Test Accuracy

Two basic attributes are used to compare the accuracy of a screening test in identifying patients for followup: the sensitivity of the test (expressed as the proportion of people with the condition--i.e., OH or OAG--who actually test positive) and the specificity of the test (expressed as the proportion without the condition who actually test negative). Sensitivity and specificity do not depend on the prevalence of OH or OAG in the population.

Sensitivity and specificity often vary inversely. A test that is very sensitive (i.e., identifies most of the people with the disease) often also falsely identifies many people who actually do not have the disease, giving it a low specificity. However, this is not always the case. Some tests are both more sensitive and more specific than others. And, an inexperienced examiner may cause a test performed by that examiner to be both less sensitive and less specific than the same test performed by a more experienced examiner. Sensitivity is generally considered more important in OAG screening than specificity, since false positives (people falsely identified as having glaucoma) can be eliminated in the diagnostic workup, but false negatives (people falsely identified as not having glaucoma) are not referred and thus are not diagnosed. However, if specificity is very low, a program can incur substantial followup costs, lead to unnecessary treatment, and cause much distress for people who are disease-free.

Two other attributes used to compare screening tests are the positive and negative predictive values of a test, the ability of the test to correctly predict disease or health. The predictive value of a positive test is the proportion of all test-positives who actually have the disease, while the negative predictive value is the proportion of all test-negatives who do not. Thus, a positive predictive value of 5 percent means that of 100 persons who test positive, 5 have the disease.

Unlike sensitivity and specificity, predictive values do depend on the prevalence of the condition. "Given a fixed level of sensitivity and specificity, predictive values increase as the prevalence increases...[S]creening will lead to a large number of overreferrals if carried out in a population where the disease is rare; conversely, false-positives are greatly reduced when screening is done in population where the disease is common" (71). When a condition is very rare, even a very sensitive and specific test may have a modest positive predictive value.

Since true positives are a higher proportion of total positives when a condition is common in the population, the cost per case detected is lower than would be the case if a large number of false positives incurred followup costs. Thus, high prevalence is one factor leading to low cost per case detected through a screening program. (Other factors can also lead to low costs per case detected by compensating somewhat for large numbers of false positives referred for followup--for example, low followup visit costs.)

used, in conjunction with ophthalmoscopy, as a diagnostic procedure (e. g., to confirm that a person testing positive on tonometry, due to high IOP, actually has OAG). Visual field defects detected by perimetry are used as the "gold standard" definition of OAG when evaluating the accuracy of tonometry and ophthalmoscopy in identifying people with OAG.

Screening Test Accuracy[3,4]

Although glaucoma screening has been common for many years, there have been few rigorous studies of the accuracy of screening tests in correctly identifying either OH or manifest OAG. Table 8 summarizes relevant estimates of the accuracy of tonometry, ophthalmoscopy, and perimetry as screening tools for detecting OH (by tonometry) and manifest OAG (for all three technologies). Most notable in this table is the scarcity of estimates available and the enormous variation among the estimates that do exist. Particularly lacking are methodical studies of variation in accuracy among different types of examiners. The estimates that do exist, and the characteristics of the respective technologies that may affect accuracy, are described in greater detail below.

3 "Accuracy" is used here in its more general sense, the ability to identify something correctly, rather than in its strict statistical meaning.

4 These accuracies generally apply to the over-40 population. The diagnostic accuracy of the various screening technologies has not been reported in the literature for the elderly alone (over age 65).

Table 8--- A Comparison of Estimates of Accuracy for Three Glaucoma Screening Technologies

Technology	Sensitivity	Specificity	Setting/context	Source
Tonometry >21 mm Hg				
accuracy compared to elevated pressure on Goldmann tonometry	71%	97%	study of Schiotz tonometry	Bengtsson, 1972
accuracy compared to "glaucoma", defined in various ways	75%	81%	study in hospital clinic	Packer et al., 1965
accuracy compared to confirmed visual field defects	50%	..	population survey	Leske et al., 1982
	72%	30%	mass screening study	Ford et al., 1982
Ophthalmoscopy				
accuracy in live eyes compared to confirmed visual field defects	72%	64%	mass screening study	Ford et at., 1982
	76%	..	population survey	Leske et al., 1982
	44- 53%[a]	69- 77%[b]	study of examiner accuracy	Wood and Bosquanet, 1987
	84%	97%	study of ophthalmoscopy accuracy using expert examiners	Hoskins and Gelber, 1975
	100%	..	population survey with expert examiner	Graham, 1969
Perimetry				
accuracy compared to confirmed visual field defects	96%	89%	manual perimetry in population survey	Rock et al., 1972
	93%	88%	study of automated perimetry	Sommer et al., 1987
	92%	46%	automated perimetry in mass screening study	Ford et al., 1982

[a] 44% for consultants, 53% for junior doctors.
[b] 69% for junior doctors, 77% for consultants.

SOURCES: See references

Tonometry

Tonometry may be used for either of the two different screening purposes: to identify people with OH who, due to their high IOPs, are at high risk of developing **OAG;** and to identify people with manifest OAG. It is fairly successful at identifying people with OH, since IOP is the characteristic it is designed to measure. It is much less accurate in identifying people with manifest OAG, since only a small proportion of people with elevated IOP also have manifest OAG (and, conversely, a substantial minority of people with OAG do not have elevated TOPS at the screening visit).

Screening for OH. Since high IOP--the definitive characteristic of OH--is the quality measured by a tonometer, tonometry might be expected to be quite accurate in identifying people with OH. Although the potential accuracy is high, in practice a number of factors can have a substantial impact on the number of individuals in whom OH is correctly identified.

These factors fall into two categories: those associated with the technology, and those associated with the nature of IOP itself. Technology-associated factors that affect the accuracy of tonometry include the type of tonometer and the person performing the test. Of the three main types of tonometers (Schiotz, applanation, and non-contact), applanation tonometry is generally considered the most accurate (128), although all have been used for screening (56,78,93). As might be expected, tonometry is more accurate when performed by someone who does it frequently, yielding fewer false positive readings (108).

Even when applanation tonometry is performed by skilled examiners, however, factors associated with the intrinsic nature of IOP affect tonometric accuracy in identifying OH. For example, there is substantial daily variation in IOP, and two tonometry measurements of the same person during different times of the day can lead to quite different conclusions (4).

The net result of these factors, combined with random errors, is an accuracy far below the ideal. A 1968 review of studies of the prevalence of OH found five studies that reported both the number of people with OH found at the screening visit and the number in whom OH was confirmed at a followup v is it. In these studies, the proportion of people with unconfirmed OH--i. e., false positives --ranged from 27 to 86 percent of the people referred. Sensitivity and specificity could not be calculated, since people testing negative were not retested (96).

A Swedish study attempted to estimate false negatives as well as false positives. In this study, readings on a Schiotz tonometer were compared with readings with an applanation tonometer (considered the "gold standard" for the purposes of this study). The investigators found that the Schiotz readings had a 71 percent sensitivity and 98 percent specificity for identifying high IOP (11).

The accuracy of modern applanation tonometry in screening for OH remains unclear. Although it is considered more accurate than Schiotz tonometry, it still produces false positives and negatives due to factors such as interexaminer variation and the variation of IOP with the time of day. Thorburn found that when two examiners performed separate applanation tonometry tests, the readings differed by 2 mm Hg or more in 40 percent of the paired measurements(lll). The variation did not depend on the level of IOP. Armaly found that approximately 30 percent fewer eyes had IOPs of 20 mm Hg or greater in the afternoon than in the morning (4).

Screening for manifest glaucoma. Although most people with OAG have elevated IOP, tonometry alone cannot distinguish between people suffering optic nerve damage and those with equivalent IOPs who are not. Thus, it has a naturally high false positive rate for manifest OAG (and a low specificity). This rate can only be reduced by raising the IOP designated as the cutoff criterion for referral (which, in turn, raises the false negative rate and decreases sensitivity).

In an early study of the accuracy of tonometry, Packer et al. found that tonometry was 75 percent sensitive and 81 percent specific at identifying persons with glaucoma at a cutoff level of 22 mm Hg (90). These results are not directly applicable to identifying manifest OAG, since the definition of "glaucoma" used by the investigators in this study was quite broad and included many characteristics not necessarily indicative of OAG (e.g., people with narrow angles, abnormal disks, or certain results on other tests were considered to have glaucoma for the purposes of the study (89)). However, the study does provide a good example of the effect on test accuracy of changing the cutoff level for referral. The investigators found that raising the screening cutoff level from 22 mm Hg to 26 mm Hg decreased sensitivity from 75 to 59 percent, while specificity increased from 81 to 95 percent (90).[5]

Two more recent studies of the accuracy of tonometry used glaucomatous visual field defects to define OAG. In a community screening study in New Orleans, tonometry demonstrated a 72 percent sensitivity for OAG by this definition, but only a 30 percent specificity (cutoff level 22 mm Hg) (35).[6] Leske et al., in a study of the Framingham population found that tonometry (cutoff level 22 mm Hg) had a 50 percent sensitivity for detecting OAG in glaucoma suspects (i.e., the group of people testing positive on one or more OAG screening tests), implying a somewhat lower sensitivity for the entire screened population (75). Specificity could not be estimated, since people who tested negative were not rescreened.[7]

Ophthalmoscopy

Ophthalmoscopy can identify people in whom OAG has already caused visible nerve damage. It can identify people who have developed OAG earlier than can perimetry, since considerable nerve damage occurs before defects in the visual field become apparent (98). Its primary disadvantage is that analysis of the optic disc is highly subjective, and abnormalities can be very difficult to interpret. Consequently, it is difficult to be confident that a person reported to have an abnormal optic disc actually has OAG until visual field defects have also become apparent.

The sensitivity and specificity of ophthalmoscopy in identifying people with manifest OAG (i.e., visual field defects) depend on such factors as:

- whether the pupils are dilated for the procedure (less common in community screening settings, more common in office settings);
- the criteria used to define a positive test (e.g., a cup:disc ratio of .6, or an examiner's overall impression that the disc is "abnormal"); and
- the skill and experience of the examiner.

Ford et al. found the sensitivity of ophthalmoscopy for identifying manifest OAG to be 72 percent and specificity to be 64 percent in community mass screening (35). Leske et al. examined several specific test criteria and found that vertical optic cup:disc ratios gave the best results for the Framingham population; this criterion had a sensitivity of 76 percent (75).

---

5 The community screening programs organized by the National Society Prevent to Blindness usually use a cutoff of 24 mm Hg to keep the number of referrals manageable (95).

6 The results from the study by Ford and colleagues have been published only in abstract form. According to one of the investigators, all subjects screened subsequently underwent a comprehensive ophthalmic examination in order to determine the true disease status of the sujects and calculate the sensitivity and specificity of the screening procedures (130). A similar, larger study is now ongoing. It will be of interest to see if the results of the larger study confirm those of the original one, since the study cited above found surprisingly high sensitivity but surprisingly low specificity.

7 The positive predictive value of IOP in this study was 5 percent (i.e., of the people with IOP of 22 mm Hg or greater, 5 percent had visual field defects) (75). A large proportion of the people in this study were elderly.

Examiner skill is crucial to the accuracy of ophthalmoscopy in identifying manifest OAG. In studies in which glaucoma specialists performed ophthalmoscopy, or studied photographs of the optic nerve, accuracy is generally much higher than that reported in the two screening studies above. American investigators have reported a sensitivity of 84 percent and a specificity of 97 percent for ophthalmoscopy performed by glaucoma specialists (54). Studies in which photographs of optic discs were examined by specialists have found sensitivities of 71 to 88 percent and specificities of 75 to 97 percent (29,50,53,54). An English population survey to determine glaucoma prevalence found that all cases of manifest OAG identified in the survey were detectable by ophthalmoscopy (performed by a glaucoma specialist) (42).

One exception to the reports of high accuracy when ophthalmoscopy is performed by specialists is a recent English study of examiner skill. In this study, ophthalmoscopy performed by consultants was more specific for OAG--but less sensitive--than the same procedure performed by junior physicians (126).

Perimetry

Perimetry can identify people in whom actual visual field defects have occurred, but who are not yet visually impaired. It is for people with visual field defects that a diagnosis of OAG can be made with the most confidence. In part for this reason, this paper has considered OAG to be manifestly present only if visual field defects are among the signs of disease. However, it should be noted that the disease is established, and optic nerve damage is underway, before visual field defects occur. Thus perimetry will naturally be more accurate than ophthalmoscopy at detecting manifest OAG, but it detects the disease at a later stage.

The accuracy of perimetry for screening is determined by comparing screening results with multiple comprehensive perimetric examinations. Accuracy depends heavily on how much of the visual field is screened and the manner in which it is done. The accuracy of manual perimetry is more variable than that of automated perimetry, since it depends more on the skill and consistency of the person performing the test.

A method of large-scale screening by manual perimetry was developed by Armaly (4) and subsequently modified by Drance and colleagues (99). The modified test is reported to have a sensitivity for manifest OAG of 96 percent, a specificity of 89 percent, and a positive predictive value of 83 percent (99). These numbers are probably maximums; in general practice, the accuracy of manual perimetry could be much lower depending on how the examiner carried out the procedure.

Automated perimetry has some advantages over manual perimetry for mass screening (63), although it is not necessarily more accurate. It has been reported to have a sensitivity varying from 80 to 96 percent, depending on how extensive a test is performed; the main problem is a potentially high false positive rate (as high as 33 percent) if test conditions are not properly established (63).[8] The type of perimeter also affects accuracy.

Three studies demonstrate the variation in accuracy that may be found when automated perimetry is used to detect OAG. Under careful research conditions, Sommer et al. found automated perimetry to have a sensitivity and specificity of 93 and 88 percent, respectively (103). Ford et al., on the other hand, found that automated perimetry in a community screening program had a 92 percent sensitivity but only a 46 percent specificity (35). According to one of the authors in this latter study, the difficulty of many subjects in understanding how to respond correctly when undergoing perimetry for the first time led to a high false-positive rate in the community setting (130). Bengtsson and Krakau found that 3 percent of eyes in a careful mass screening program in Sweden tested positive on automated perimetry, but only half the positive eyes ac-

8 For example, false positives can be reduced by automatically retesting any point in the visual field not reported as seen by the patient on the first try.

tually had visual field defects that were glaucomatous or meriting medical attention (14). The authors did not retest people who initially tested normal and therefore could not report completely on the sensitivity and specificity of the test.

Costs to Medicare

At present, neither screening for all people with high intraocular pressure (IOP) nor for those with only manifest open-angle glaucoma (OAG) is covered by Medicare, although tonometry, ophthalmoscopy, and perimetry are all covered procedures when provided as diagnostic services or in the course of management of established disease.[1] If Medicare were to initiate a policy of covering screening for manifest OAG or for high IOP, what would be the implications for program costs and patient benefits?

As the previous chapters demonstrate, there is great variability and uncertainty surrounding the accuracy of screening tests and the effectiveness of treatment for either ocular hypertension (OH--high IOP without other signs of disease) or manifest OAG. This uncertainty makes a precise estimate of the costs and effectiveness of glaucoma screening infeasible. Nevertheless, OTA constructed a simple model of a hypothetical biannual glaucoma screening program in order to estimate the likely magnitude of the annual costs of such a program. The model incorporates a wide range of reasonable assumptions based on the available evidence. It is applied here, first, to screening for manifest OAG using the various technologies available; and second, to screening for high IOP with tonometry.

The model, presented in appendix C along with detailed assumptions and results, calculates both total program costs and the costs of detecting a case of OAG (or high IOP). Total costs include both the costs of the screening episode and the costs of a followup visit for all individuals testing positive, to confirm or deny the test result. To calculate the average cost per case of OAG (or high IOP) detected, all screening and followup costs are loaded on true cases--i.e., on those with confirmed positive tests.

The costs of an ongoing screening program--and the number of cases detected as its result--depend fundamentally on whether the program is newly implemented or has been ongoing for some time. In initial years, the number of cases that can be identified through the program will approach the prevalence of the condition. The prevalence of high IOP in the elderly is quite high, and OAG itself is not uncommon, occuring in about 2 to 3 percent of the elderly. Consequently, costs per confirmed case of high IOP or OAG will be relatively low in initial years of a screening program (since costs per case are total costs divided by total number of cases found).

On the other hand, new cases of OAG are comparatively rare--on the order of 2 per 1,000 elderly per year. Thus, an ongoing program to detect OAG can identify only a very small number of cases. It has a correspondingly high cost per true positive case identified through the program. Note that, with true new cases of manifest OAG being comparatively rare, a high proportion of people referred for followup will in fact be false positive cases, even if the screening tests are quite accurate.

As discussed in the appendix, the uncertainties surrounding several crucial assumptions of the model preclude a precise estimate of costs. These assumptions include:

- the accuracies of the different *screening* procedures as performed by different examiners in different settings,
- the incidence and prevalence of OAG in the elderly,
- the costs attributable to screening,

1 The current procedure codes for perimetry, on which payment is based, are intended to represent diagnostic, rather than screening, procedures. It is possible that costs and charges would be lower for screening perimetry, resulting in lower total cost estimates than those here. Similarly, there is no code for ophthalmoscopy that appears to be appropriately applied to screening for glaucoma; OTA's assumption that the costs of ophthalmoscopy would be the same as for tonometry may well be incorrect. The code for tonometry is not intended for screening, but in this case the procedure itself is the same regardless of the purpose.

- the extent to which people utilize the program, and
- the proportion of people testing positive who will show up at the confirmatory physician visit.

Because the uncertainties associated with these factors are so great, OTA has estimated and presented here only the likely upper and lower bounds of the costs and number of cases likely to be found through a screening program. These bounds encompass a very wide range. Nonetheless, the range is a useful indicator of the order of magnitude of costs likely to be incurred and number of cases cases likely to be identified through a screening program for the elderly.

In the initial years of an every-other-year program to screen for manifest OAG in the elderly, it would cost between $1,000 and $16,000, on average, to detect and confirm a case of glaucoma. Between 50,000 and 340,000 cases of OAG would be detected annually in the first two years, depending on the exact prevalence of OAG, the accuracy of screening tests, and the skill of the examiners using them.[2] In the later years of such a screening program, it would cost between $3,000 and $81,000 per confirmed case of OAG to detect between 10,000 and 90,000 cases per year. Annual total screening program costs would be between roughly $200 million and $1 billion in both initial and subsequent years (see app. C).

In a similar program screening for high IOP, costs would be between $100 and $1,700 per confirmed case of high IOP in initial years, and between $300 and $14,600 in later years. Total annual costs of such a program would likely be between $100 million and **$300** million initially and between $250 million and $500 million in subsequent years. This screening program would detect between 300,000 and 3 million people with high IOP per year in initial years and between 30,000 and 350,000 per year in later years. The cases of confirmed high IOP would consist primarily of people with OH--high IOP but no other signs of OAG--but would include a minority of individuals who had manifest OAG.

Medicare pays 80 percent of allowed charges after the beneficiary has met the deductible. Assuming that Medicare pays 80 percent of the total program costs delineated above leads to the conclusion that total Medicare costs of an ongoing program to detect OAG in **the elderly would likely be between approximately $160 million and** $800 million **per year. Total Medicare costs of a similar program to screen for high IOP would be between $80 million and $400 million per year.** These costs do not include the costs of treating detected cases of OAG or high IOP. Nor do they include the costs or the benefits of detecting conditions other than OAG (or high IOP) as a result of the screening visit.

The full benefits of a screening program depend fundamentally on the effectiveness of treatment. Potentially, these benefits include additional years of vision, lessened dependence on assistance in everyday tasks, and reduced expenditures for programs providing social services and support for people with disabilities. Because of the uncertainties about treatment effectiveness, the extent to which these potential benefits can be realized is unknown at present.

Implications of Scheduled Frequency of Screening and Screening Utilization for Medicare Costs

The scheduled frequency with which screening occurs and the utilization rate of glaucoma screening among the elderly have little impact on the average cost of identifying a case of OAG through the screening program. They do, however, have enormous implications for the total number of cases detected and for total program costs if the

2 These cases would not all be previously unknown. Since OTA's calculation is based on prevalence, it includes the implicit assumption that all people in the population would be screened, regardless of whether they were already known to have OAG. (In fact, a substantial number of people who voluntarily appear at community screening clinics actually have been told previously that they have OAG (56).) After the first 2 years the model assumes that previously diagnosed cases will not appear for screening, and the calculations are based on incidence.

Medicare program were to cover the service. In the model presented in appendix C, OTA assumed that 75 percent of the population would participate regularly in a program in which people were screened every 2 years. A less frequent screening schedule would result in lower total program screening costs per year, since fewer people would be screened and diagnosed each year. These lower total costs would come at the expense of fewer diagnosed cases and cases that would be more severe when diagnosed.

Screening utilization would affect case detection and Medicare costs in three important ways:

Current utilization. Approximately 50 percent of elderly people report that they have been screened for OAG within 2 years (118). For this group, Medicare coverage simply means a shift in the cost of screening from the individual patient (or provider, or non-profit organization) to the Medicare program. No new health benefits accrue, since OAG (and OH) cases in this group would have been diagnosed regardless of Medicare coverage.

In some cases, Medicare coverage would replace screening currently provided free of charge to the patient. The National Society to Prevent Blindness, a nonprofit organization that often coordinates with local hospitals or service organizations to provide glaucoma screening, screened 46,889 people age 65 and over in 1985 (0.16 percent of the population in that age group) (85). The American Academy of Ophthalmology operates the National Eye Care Project, which refers needy elderly people to ophthalmologists who volunteer their services. Since 1986, this project has referred over 137,500 people, of which at least 77,500 have seen an ophthalmologist and had an eye examination as a result (129). About 5 percent of patients seen were diagnosed with glaucoma (19).

New **utilization.** Presumably, Medicare coverage would encourage people to be examined who otherwise would never have been screened for OAG. The cost model OTA has used assumes 75 percent utilization, or a 50 percent increase over the current utilization rate of 50 percent.[3] This new group would obtain new health benefits that would not have accrued in the absence of Medicare coverage. For example, under a scenario in which screening by perimetry in an office setting would detect 50,000 cases of OAG per year (about the middle of the range estimated in the model), the utilization rate of 75 percent would mean that one-third of these cases- -nearly 17,000 of them--would not have been detected as rapidly without Medicare coverage because these people would not have been screened. The remaining 33,000 cases would have been diagnosed without Medicare coverage, but Medicare now pays their screening costs.

If screening were less frequent, the new additional utilization due to Medicare coverage would quite likely be less as well. For example, while only about 50 percent of the elderly population currently receive glaucoma screening every 2 years, a total of 75 percent receive screening at least every 3 years (1 18). Thus, if Medicare covered screening every 3 years, the additional utilization might be perhaps 10 percent over current levels (for a total of 80 to 85 percent utilization), and could be no more than 33 percent higher than at present.

Current diagnostic visits. Under the present Medicare system, a screening visit (in which the patient is asymptomatic) would not normally be reimbursed. Despite this policy, however, some current utilization is probably already supported by Medicare. For example, patients may be screened for OAG during a visit that was reimbursable for other reasons (e.g., evaluation of a cataract). Since a substantial number of elderly people have eye conditions other than OAG, and visits to the physician due to these conditions are often reimbursable, it is possible that a substantial amount of glaucoma screening is already being done during Medicare-reimbursed visits.

---

3 This represents a simplistic assumption that the 50 percent of the elderly reporting that they have been screened within 2 years are in fact routinely screened every other year.

In summary, the benefits of Medicare coverage for OAG screening depend heavily on how many people would be induced to undergo screening if the service were covered. For the over 50 percent of the elderly assumed to be already undergoing frequent screening, coverage will bring some relief from out-of-pocket costs but no additional benefits in preventing impairment. Elderly people induced to undergo screening due to Medicare coverage represent the greatest potential social benefit to the service. Under the assumptions of our model, this means that somewhere between 3,000 and 30,000 people would have manifest OAG diagnosed earlier if Medicare covered OAG screening than under the current financing scheme.

Costs and Effectiveness of Screening in Preventing Blindness

The above discussions of screening for OAG and high IOP include only the costs of detecting and confirming a case, not the expense of treating the cases found. OAG treatment can be expensive. Rough estimates by two researchers in 1980 suggested that each person with a diagnosis of OAG incurred annual charges of between $180 and $460 for medications and followup, depending on the number and type of drugs prescribed (41,4127). (Individuals with OH who are treated to lower their IOP would incur similar chargers.) OAG patients requiring filtering surgery were estimated to incur charges of $2,400 to $3,000 in the year they received surgery.[5]

Because of the uncertainties regarding the effectiveness of treatment for OH and OAG, OTA did not extend the cost-effectiveness analysis to the full effectiveness of screening in preventing visual disability. The authors of one study in the literature, however, did attempt such an analysis (41). The baseline assumptions in that analysis were generally optimistic, including high sensitivity and specificity for screening tests, low per-person costs of screening, and generous assumptions regarding the effectiveness of treatment.[6] However, when less generous assumptions were made--for example, when less favorable treatment outcomes were assumed- - costs per year of vision saved were up to 40 times greater than the lowest cost under baseline assumptions. Thus, just as this OTA analysis reports a wide range of potential program costs per OH and OAG case detected, that analysis demonstrated the extreme sensitivity of cost-per-year-of-vision-saved to assumptions regarding the effectiveness of treatment.

Problems in Implementing Medicare Coverage of OAG Screening

Covering OAG (or OH) screening as a Medicare benefit would present two problems concerning payment policies:

1. Paying for screening in community settings. If Medicare were to cover glaucoma screening, an immediate policy decision would have to be made regarding who would be paid to provide it. At present, a considerable amount of screening is provided inexpensively by non-profit organizations in community settings (e.g., at churches, schools, or hospitals). However, mass screening in community settings is a controversial issue among eye care professionals. Such efforts make glaucoma screening available to a broad spectrum of people who might otherwise not receive the service. On the other hand, a negative glaucoma test in a community screening clinic may sometimes encourage an individual not to seek any further eye care of any kind. Policy makers would have to decide if glaucoma screening were to be covered

4 Although this paper was published in 1983, the treatment cost estimates i t contained uere 1980 estimates from an ear l i er, unpubl i shed paper.

5 Unti 1 1991, Medicare will not cover any part of the costs of outpatient drugs to treat OH or OAG. Med i care does pay a proport ion of hospi ta 1, physician, and anc i 1 lary charges charges associated wi th surgery for OAG.

6 The authors assumed, first, that persons with field loss at the screening would become blind in 7.5 years without treatment (it was assumed that only a small number of 'treatment failures" would go blind if treated); and, second, that people with elevated IOP but no visual defects at screening would go blind an average of 12.5 years after screening if untreated (41).

only in community settings, only in traditional health care settings (e. g., physicians' and optometrists' offices), or in both.

There is at present no mechanism by which Medicare pays for medical services offered in community facilities such as churches or senior citizens' centers. If Medicare covered OAG screening done in these settings, the Health Care Financing Administration (HCFA) would have to develop reimbursement policies for them. For example, HCFA might pay community screening program sponsors -- hospitals, nonprofit vision societies, etc. --- a set rate per patient for all Medicare beneficiaries screened. Although feasible, this policy would take some time to establish. Processes for developing payment rates, designating eligible clinic sponsors, and regulating dangers and problems in community facilities would have to be developed.

2. **Paying for components of office visits.** The two most widely used OAG screening technologies, tonometry and ophthalmoscopy, when used as part of a routine physician office visit, are not billed separately (3), If Medicare covered OAG screening but not screening for other vision conditions, either:

1) examiners must be able to bill separately for these procedures,
2) Medicare would have to establish a policy of paying for part of a visit charge, or
3) Medicare would pay for a visit designated to include only glaucoma screening (for example, a "limited visit," as used in the cost model).

Ultimately, a Medicare decision to cover glaucoma screening would probably require the development of new codes to designate tonometry, ophthalmoscopy, or perimetry used for that purpose.

Appendix A: ADVISORY PANEL--PROJECT ON PREVENTIVE HEALTH SERVICES UNDER MEDICARE

Gordon De Friese, *Panel Chair*
Health Services Research Center
University of North Carolina, Chapel Hill, NC

Marianne C. Fahs
Department of Health Economics
Mt. Sinai Medical Center
New York, NY

John Frank
Department of Preventive Medicine & Biostatistics
University of Toronto
Ontario, Canada

Gary D. Friedman
Epidemiology and Biostatistics Division
Permanence Medical Group, Inc.
Oakland, CA

Lawrence Gottlieb
Clinical Guidelines Program
Harvard Community Health Plan
Brookline Village, MA

Mary Knapp
John Whitman and Associates
Philadelphia, PA

Risa Lavizzo-Mourey
Geriatrics Program
University of Pennsylvania
Philadelphia, PA

M. Cristina Leske
Department of Preventive Medicine
SUNY at Stony Brook
Stony Brook, NY

Donald Logsdon
INSURE Project
New York, NY

Mildred B. McCauley
American Association of Retired Persons
Washington, DC

Peter McMenamin
Chevy Chase, MD

Meredith Minkler
Center on Aging
University of California, Berkeley
Berkeley, CA

Marilyn Moon
Public Policy Institute
American Association of Retired Persons
Washington, DC

George Morley
Department of Obstetrics/Gynecology
University of Michigan Medical Center
Ann Arbor, MI

Gilbert Omenn
School of Public Health & Community Medicine
University of Washington
Seattle, WA

George Pickett
Department of Public Health Policy
School of Public Health
University of Michigan
Ann Arbor, MI

Donald Shepard
Department of Health Policy and Management
Harvard School of Public Health
Boston, MA

Barry Stults
Division of General Internal Medicine
University of Utah Medical Center
Salt Lake City, UT

Advisory Panel members provide valuable guidance during the preparation of OTA reports. However, the presence of an individual on the Advisory Panel does not mean that individual agrees with or endorses the conclusions of this particular paper.

Appendix B: ACKNOWLEDGMENTS

The OTA staff would like to express their appreciation of the following people for their advice and assistance. This acknowledgement should not be construed in any way to imply that the individuals agree with or endorse the conclusions of this paper.

Frank S. Ashburn, Jr.
Eye Associates of Washington, D. C., P.C.
Washington, DC

Morris F. Cohen
Kaiser-Permanante Medical Care Program
Oakland, CA

Peter Dudley
National Institutes of Health
Bethesda, MD

David M. Eddy
Duke University
Durham, NC

Alan Garber
National Bureau of Economic Research, Inc.
Stanford, CA

Douglas Gaasterland
Georgetown University Medical Center
Washington, DC

Susan Gleeson
Blue Cross and Blue Shield
Chicago, IL

H. Dunbar Hoskins, Jr.
The Foundation for Glaucoma Research
San Francisco, CA

Allan D. Jensen
Baltimore, MD

Terry Kay
Health Care Financing Administration
Baltimore, MD

Allan E. Kolker
Washington University School of Medicine
St. Louis, MI

Glory Tenney Kosmatka
National Society to Prevent Blindness
Schaumburg, IL

Joseph H. Krug, Jr.
Massachusetts Eye & Ear Infirmary
Boston MA

Benjamin Littenberg
Veterans Administration Medical Center
Palo Alto, CA

Stephanie Mensh
American Academy of Ophthalmology
Washington, DC

Samuel Merrill, Jr.
Congressional Research Service
Washington, DC

Karl Michelitsch
Georgetown University Medical Center
Washington, DC

Angela Mickalide
U.S. Preventive Services Task Force
Washington, DC

Steven Moore
Office of the Surgeon General
Rockville, MD

Marvin Podgor
National Institutes of Health
Bethesda, MD

M. Bruce Shields
Duke University Medical Center
Durham, NC

George L. Spaeth
Wills Eye Hospital
Philadelphia, PA

Steven H. Woolf
U.S. Preventive Services Task Force
Washington, DC

John Whitener
American Optometric Association
Alexandria, VA

Thorn J. Zimmerman
University of Louisville
Louisville, KY

Appendix C: THE COSTS OF SCREENING FOR OPEN-ANGLE GLAUCOMA

To fully analyze the costs and effectiveness of alternative screening methods in preventing visual disability, one must know:

- the costs of screening, diagnostic workup, and treatment,
- the effectiveness of the screening technologies in identifying established or potential cases of open-angle glaucoma (OAG), and
- the effectiveness of treatment in preventing disability in the identified cases.

None of these factors is adequately known. Some tenuous but reasonable assumptions regarding cost can be made about the cost of screening and diagnostic workup. There is a basis for estimating the effectiveness of the three screening technologies in identifying OAG (or its precursor, high intraocular pressure (IOP)), although there is great uncertainty about the estimates, especially as they apply to different settings and different examiners. Most uncertain of all is the effectiveness of treatment. Treatment is probably effective, but how effective it might be is not yet established.

Because of the tremendous uncertainties in the basic assumptions necessary to a full cost-effectiveness analysis, particularly the uncertainties regarding treatment effectiveness, the analysis forming the bulk of this appendix is limited to the comparative costs of identifying and verifying a case of manifest OAG. Following the analysis of the cost of screening for manifest OAG is a parallel analysis of the cost of screening for high IOP with tonometry.

The purpose of these analyses is to estimate the rough magnitude of the total national health care costs of screening for OAG in the over-65 population, and the number of cases of OAG or high IOP that might be detected through such a program. The analyses are structured so that these cost estimates, in turn, can be used as a basis for estimating the likely magnitude of Medicare program costs in the event of a decision to cover OAG screening for the Medicare population. OTA has reasonable confidence that the true costs of a screening program to identify OAG cases (or cases of high IOP) lie between the upper and lower bounds specified here, but there is at present no factual basis for assessing where in that range the true costs lie.

The

Table 9 describes the steps of the simple model used to estimate the number of OAG cases detected in a screening program and the average costs of detecting an OAG case. In this model, the screening program includes both the screening episode itself and the workup of all people testing positive. Three basic assumptions of the model do not vary. These are:

- the size of the overall elderly population (31 ,697,000),
- the frequency of screening (every 2 years), and
- the proportion of the population participating in the program (75 percent).

Changes in these assumptions have little effect on the average cost per OAG case detected, although they do affect the total number of cases found and the total cost of a screening program.[1] The program implications of these assumptions are described in chapter 5.

---

1 Screening less frequently would have three major effects. First, total program costs would be less because fewer people would be screened each year. Second, the average severity of OAG cases detected through the screening program would be greater, because the length of time between screening visits is greater. Third, it would become more likely that cases of manifest OAG would be diagnosed due to the onset of symptoms (e. g., decreased vision), rather than being detected when a symptomatic through the screening program. This last factor does affect the average cost per case detected in the screening program, since these cases are not diagnosed as a result of the program. However, the magnitude of the effect is likely to be small unless screening is very infrequent.

Table 9--- Calculation of Estimated Cost per Confirmed Case of Open-Angle Glaucoma and Number of Cases Diagnosed

Step	Calculation	Description
1.	(population) x (utilization rate) x (screening frequency rate)	Number of people screened
2.	(prevalence or incidence) x (sensitivity of screening test)	Rate of true positive cases
3.	[1 - (prevalence or incidence)] x [1 - (specificity)]	Rate of false positive cases
4.	(STEP 2) + (STEP 3)	Proportion of all screenees testing positive and referred for followup
5.	(STEP 4) x (cost per followup visit)	Followup cost rate (followup cost averaged across all screened persons)
6.	(sTEP 5) + (cost per screening episode)	Screening cost plus followup cost rate per screened person
7.	(STEP 1) x (STEP 6)	Total cost
8.	(STEP 1) x (STEP 2)	Total number of true positive cases
9.	(STEP 7) / (STEP 8)	Cost per true confirmed positive case

SOURCE: Office of Technology Assessment, 1988.

Other variables in the model are described below.

Prevalence and Incidence

In the beginning of a screening program, relatively few cases of OAG are known; most await detection by the program. Thus, the estimated costs in the first 2 years of an every-other year program are based on the *prevalence* of OAG. OTA estimated costs based on both 2 percent and 3 percent prevalence of disease in the elderly.

In the subsequent years of a screening program, only new cases and a small, constant number of false negatives from previous screenings exist to be detected by the program. The *incidence is* thus the basis for cost estimates of an ongoing program.

A summary of OTA's calculation of the incidence of OAG in the elderly is presented in table 10. In this calculation, OTA first derived annual age-specific incidence estimates from the five-year incidence rates for ages 65-79 estimated by Podgor et al. (see ch. **2,** table 1) (94). (For example, where these researchers estimated the five-year incidence of OAG at 5 cases per thousand population for the age 65-69 cohort, OTA assumed an annual incidence of 1 cases per thousand). No OAG incidence estimates for people overage 79 exist. OTA assumed that the incidence continues to rise at an increasing rate with age and arbitrarily chose annual incidence rates of 3.4 and 5 per thousand for ages 80-84 and 85 and over, respectively. (These rates are consistent with the trend in the younger age groups.) From these age-specific incidence rates, OTA then calculated the overall incidence rate for the elderly. This rate was 2 cases per thousand per year (4 cases per thousand per screening period for the model case of every-other-year screening).

This incidence rate is likely to underestimate the true number of cases available to be detected by an ongoing screening program, for two reasons. First, the overall incidence of OAG in the elderly is likely to increase over time as the proportion of the elderly in the oldest cohorts increases. Sec-

end, the OTA model does not adequately account for the OAG cases that eluded detection in previous screening years (i. e., were false negatives) but might be detected in the current year. Thus, OTA also estimated screening costs under the assumption that, for every thousand population, 4 OAG cases per year (8 cases per screening period) exist to be detected by the screening program.

Screening Accuracy

An examiner screening for OAG would most likely use one of five possible combinations of screening technologies:

- tonometry alone;
- ophthalmoscopy alone;
- both tonometry and ophthalmoscopy, referring for workup all persons testing positive on either test (henceforth designated "tonometry/ophthalmoscopy in parallel");
- both tonometry and ophthalmoscopy, referring for workup only persons positive on both tests (henceforth designated "tonometry/ophthalmoscopy in series"); or
- perimetry alone.

The sensitivity and specificity of OAG screening depend heavily on which technology is used, how it is used, and who uses it. There are, unfortunately, very few studies of the accuracy and predictive value of OAG screening tests, and the results of those studies cannot be inferred to different examiners and different settings. OTA has thus chosen only to examine the extremes of the values presented in the literature for these technologies, recognizing that the true value is unknown and greatly depends on who performs the screening and the conditions under which they do so. Table 11 lists the high and low bounds of sensitivity and specificity for each technology that OTA used in this analysis.

Tonometry, as a test for manifest OAG, has a natural limit to accuracy because most people with high IOPs do not have manifest OAG, and many people with OAG do not have high IOP when they are screened. OTA estimated a theoretical upper limit for the accuracy of tonometry (see box B) and used this as the upper bound in the analysis.

Table 10.--Calculation of Incidence of Open-Angle Glaucoma (OAG) in the Elderly Population

Age group	Population in 1990[a]	2-year OAG incidence per thousand	Total number of cases per 2 years	Number of OAG cases per year in screened population[c]
65-69	9,996,000	2.0	19,992	7,497
70-74	8,039,000	2.8	22,509	8,441
75-79	6,260,000	4.4	27,544	10,329
80-84	4,089,000	6.8	27,805	10,427
85+	3,313,000	10.0	33,130	12,424
TOTAL	31,697,000	4.1	130,980	49,118

[a] Estimates from U.S. Bureau of the Census, Current Population Reports, Series P-25, No. 952, Projections of the Population of the United States, by Age, Sex, and Race: 1983 to 2080 (Washington, DC: U.S. Government Printing Office, 1984).

[b] Cases per year of open-angle glaucoma in the relevant age group. Estimates for ages 65-79 from 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. Estimates forages 80 and over are undocumented assumptions of the Office of Technology Assessment.

[c] Assumes that 75 percent of the elderly in each age group would avail themselves of the screening benefit, and that half of this group would be screened each year.

SOURCE: Office of Technology Assessment.

Table 11.--Glaucoma Screening Test Accuracy Assumptions.

	Upper bound (Low cost)		Lower bound (High cost)		Source of figures	
	Specificity	Sensitivity	Specificity	Sensitivity	Upper bound	Lower bound
Tests for Open-angle Glaucoma						
Tonometry over 21 mm Hg)	0.76	0.78	0.72	0.30	see box B	Ford et al., 1982
Ophthalmoscopy	0.84	0.97	0.72	0.64	Hoskins and Gelber, 1975	Ford et al., 1982
Tonometry + ophthalmoscopy, dual positives referred	0.64	0.99	0.52	0.75	calculated from above	calculated from above
Tonometry + ophthalmoscopy, single positives referred	0.96	0.76	0.92	0.19	calculated from above	calculated from above
Automated perimetry	0.96	0.89	0.92	0.46	Rock et al., 1972	Ford et al 1982
Tests for High Intraocular Pressure						
om over 21 mm Hg	1 °°	1 °°	°.71	0.97	absolute maximum	Bengtsson, 1972

SOURCE Office of Technology Assessment, 1988. See references for sources of selected individual figures.

Box B--- Estimation of Theoretical Upper Limits of Accuracy of Tonometry (21 mm Hg or Greater) for Identifying People with Open-Angle Glaucoma

A natural upper bound to use for the accuracy of tonometry in identifying cases of manifest OAG is the theoretical maximum accuracy of high IOP in predicting manifest OAG. Since most people with high IOP do not have manifest OAG, and many people with OAG do not have high IOP, tonometry is clearly less than 100 percent sensitive and specific when used to identify cases of manifest OAG, even if the technology itself accurately identifies all people with high IOP.

To estimate the theoretical limits to accuracy of tonometry used for this purpose, first recall that approximately 24 percent of the elderly in one study were found to have IOPs of 20 mm Hg or greater. This figure provides a maximum--probably a considerable overestimate--for the proportion of elderly people in the United States as a whole who would test positive by tonometry at the slightly higher cutoff level of 21 mm Hg.

Next, one needs to know the proportion of this group that actually has OAG (true positives). Recall from table 4 (chapter 2) that approximately 3 to 10 percent of all individuals with IOP 20 mm Hg or greater will get manifest OAG within 5 years. This group therefore represents the absolute maximum number of people with high IOPs that actually have manifest OAG already. Take the higher end of this range and assume that, at the absolute maximum, 10 percent of the elderly with high IOPs also have manifest OAG. Multiplying .10 by .24 (the proportion of elderly people with high IOPs) gives a total of .024, the maximum proportion of all elderly who have high IOPs *and* manifest OAG.

Now, recall (also from table 4, chapter 2) that less than 1 percent of all individuals with normal IOPs will get OAG within 5 years. Again, assume that 1 percent therefore represents the absolute maximum number of elderly people with normal IOP that could have manifest OAG at the time of screening. Since 76 percent of elderly people have normal IOPs, the maximum rate of false negatives is (.76)*(.01), or .0076.

Adding false negatives and true positives yields the total proportion of elderly in the population with OAG. The maximum proportion of the elderly with OAG is thus (.024)+(.0076)=.0316; the proportion without OAG is (l)-(.0316)=.9684.

Lastly, one needs to know the proportion of true negatives (i.e., people with normal IOPs and no OAG). This proportion is all negatives minus false negatives, or (.76)-(.0076)=.7524. Then, the upper bounds of tonometry (cutoff 21 mm Hg) for detecting OAG are:

$$\text{Sensitivity} = \frac{\text{True positives}}{\text{All persons with OAG}} = \frac{.024}{.0316} = 76\%$$

$$\text{Specificity} = \frac{\text{True negatives}}{\text{All persons without OAG}} = \frac{.7524}{.9684} = 78\%$$

Cost

OTA analyzed five different potential screening settings: mass screening in community facilities (e.g., screening clinics at senior citizens' centers), and the offices of family practitioners, internists, ophthalmologists, and optometrists.

In the model, costs for services provided in offices settings are based on Medicare average allowed charges[1] for office visits and procedures. For the purpose of estimating the social costs of screening, these average allowed charges are assumed to represent real resource costs, although the extent to which this assumption is true is unknown.

The true cost of OAG screening done in physicians' or optometrists' offices depends on how much of the visit is due to the screening procedure. If screening is only one of many services performed during the visit, the cost of screening is only the cost of the screening procedure itself. If, on the other hand, the visit is made only for screening, then OAG screening must bear the entire cost of that visit. OTA thus tested two basic cost alternatives: one in which the screening cost is simply the Medicare average allowed charge for the procedure itself, and one in which the cost is the charge for a brief visit plus the charge for the screening procedure. Table 12 outlines these cost assumptions in greater detail.

Within either of these two basic assumptions, costs vary depending on who does the screening. A visit to a family practitioner, for example, costs less (on average) than a visit to an ophthalmologist. OTA used the examiner-specific charges when running the model to give the most accurate estimation of the extremes. However, *the true inter-examiner costs per case diagnosed cannot be compared with existing information.* An examiner who charges more for screening, for example, may also be more skilled, resulting in fewer false positives referred and consequent lower cost per diagnosed case overall. Since the actual relative accuracy of testing among examiners is unknown, specific inferences about which setting results in the overall lowest true costs cannot be drawn.

The use of Medicare average allowed charges applies only to office settings. For community facilities, OTA relied on a cost analysis of charitable glaucoma screening programs in northern California (56). These costs underestimate true resource costs, since the programs rely in part on volunteer labor. The baseline cost from this source was assumed to apply to either tonometry or ophthalmoscopy (see table 12). The programs do not currently use perimetry for screening; OTA assumed that, as with office-based examiners, perimetry would be about twice as expensive as the baseline cost. Since it was assumed that, in offices, the cost of performing both tonometry and ophthalmoscopy would be double the cost of providing either one alone, the same assumption was made for community facilities.

Followup rates

In the model, it was assumed that all persons with a positive screening test result would be referred to an ophthalmologist for a comprehensive visit, at which the definitive diagnosis (OAG/no OAG) would be made. (For patients screened by an ophthalmologist, it was assumed that the patient would return for a confirmatory comprehensive visit). OTA tested two extreme alternative assumptions of the rate at which people referred would actually show up for the visit: a 100 percent compliance rate, in which all people show up, and a 40 percent rate. The lower bound is slightly less than that reported for a current mass screening program (85). OTA assumed that compliance was independent of whether an individual had a true or false positive result on the screening test.

1 Medicare average allowed charges are used as the basis of Medicare payments to physicians; Medicare pays a proportion of the allowed charge for all covered services. Since the most recent charge data available are from 1985, OTA updated all charges by the Medicare Economic Index for participating primary-care physicians. Medicare average allowed charges underestimate actual average physician charges, since some physicians charge more than the level allowed for Medicare payment.

Table 12.--Cost Assumptions

Service	Low-cost estimate		High cost estimate	
	Proxy measure	value	Proxy measure	value
Screening episode				
Tonometry Ophthalmoscopy	Medicare average allowed charge for serial tonometry, by specialty	$12.63 (FP) $16.52 (Int) $10.55 (Opt) $19.07 (Oph)	Medicare average allowed charge for limited visit + charge for serial tonometry, by specialty	$30.36 (FP) $39.34 (Int) $29.96 (Opt) $40.34 (Oph)
	Average screening cost in Northern California mass screening programs	$ 5 75 (Comm)	Average screening cost in Northern California mass screening program	$ 5.75 (Comm)
Tonometry + ophthalmoscopy	2 x (Medicare average allowed charge for serial tonometry, by specialty)	$25.26 (FP) $33.04 (Int) $21.10 (Opt) $38.14 (Oph)	Medicare average allowed charge for limited visit + (2 x charge for serial tonometry), by specialty	$42.99 (FP) $55.86 (Int) $40.51 (Opt) $59.41 (Oph)
	2 x (average screening cost in Northern California mass screening programs	$11 50 (Comm)	2 x (average screening cost in Northern California screening programs)	$11.50 (Comm
Automated perimetry	Medicare average allowed charge for diagnostic perimetry, by specialty	$28.59 (FP) $30.22 (Int) $23.81 (Opt) $34.38 (Oph)	Medicare average allowed charge for limited visit + charge for automated perimetry, by specialty	$46.32 (FP) $53.04 (Int) $43.22 (Opt) $55.65 (Oph)
	2 x (average screening cost in Northern California mass screening programs)	$11.50 (Comm)	2 x (average screening cost in Northern California mass screening programs)	$11.50 mm
Followup visit				
Visit to ophthalmologist	Medicare average allowed charge for a comprehensive visit + diagnostic perimetry (ophthalmologist only	$75 85	Medicare average allowed charge for a comprehensive visit + diagnostic perimetry (ophthalmologist only	$75 85

ABBREVIATIONS: FP--family practitioner; Int--internist; Opt--optometrist; Oph--ophthalmologist; mm screening in community settings

SOURCE: Office of Technology Assessment. Values for office practitioners are 1985 national average Medicare allowed charges from Health Care Financing Administration BMAD database, inflated to 1988 dollars. Values for mass screening in community settings are from P. Jamgochian, "Northern California Society to Prevent Blindness, 1984 Glaucoma Program, Cost Benefit Analysis," unpublished paper, May 1986. These values are also inflated to 1988 dollars.

Results

Number of OAG Cases Diagnosed

As shown in table 13, the number of cases that might be diagnosed annually by an every-other- year screening program range from approximately 50,000 to 340,000 cases **in initial years and from 10,000 to 90,000 cases in later years.** The actual numbers depend heavily on the true prevalence and incidence of OAG in the elderly.

In addition, the effectiveness of a screening program in identifying cases depends on the sensitivity of the screening procedure in whatever setting it is used. Perimetry and tonometry/opthalmoscopy in parallel (anyone testing positive on either test referred for follow up) are equal in their potential to detect a maximum number of cases. Tonometry/ophthalmoscopy in series is likely to detect the least number of cases under anyone set of assumptions. This result leads to the conclusion that, while tonometry and ophthalmoscopy used in combination have the potential to be highly effective in identifying previously unknown cases of OAG, maximum effectiveness is likely to be achieved only if all persons testing positive on either test are referred for followup.

cost

Tables 14 and 15 set out the high and low estimates of the model for total screening program costs and for average cost per case of manifest OAG detected, respectively, in the initial years of a screening program. Tables 16 and 17 present the same information for subsequent years. In the tables, setting-specific charges were used, resulting in five double columns for the five settings. In each double column, the low-cost estimate assumes:

- 100 percent followup rate for people with positive tests,
- maximum test accuracy for the respective screening procedure,
- high incidence (4 per thousand per year) or prevalence (3 percent), and
- screening episode costs that include only a procedure-specific charge.

The high-cost estimate assumes:

- *40* percent followup rate for people with positive tests,
- minimum test accuracy for the respective screening procedure,
- low incidence (2 per thousand per year) or prevalence (2 percent), and
- screening episode costs that include a visit charge as well as a procedure-specific charge.

Table 13--- Number of Open-Angle Glaucoma Cases Diagnosed Under Extreme Assumptions of Test Accuracy and Followup Rates

	Low-cost model: 100% followup, high prevalence/incidence, high test accuracy		High-cost model: 40% followup, low prevalence/incidence, low test accuracy	
Technology	Initial years	Later years	Initial years	Later years
Tonometry	271,000	72,300	68,500	13,700
Ophthalmoscopy	300,000	80,000	68,500	13,700
Tonometry/ophthalmoscopy in series	228,000	60,700	49,300	9,900
Tonometry/ophthalmoscopy in parallel	343,000	91,400	87,600	17,500
Perimetry	342,000	91,300	87,500	17,500

SOURCE : Office of Technology Assessment, 1988.

Table 14--- High and Low Bounds[a] of Total Costs of Screening and Confirmatory Followup for Open-Angle Glaucoma in Initial Years of a Screening Program (In millions of dollars)

Technology	Family Practice		Internist		Optometrist		Ophthalmologist		Community Facility[b]	
	Low	High	Low	High	Low	High	Low	High	"Low"	"High"
Tonometry	$363	$613	$409	$720	$338	%09	$440	$732	$700	$321
Ophthalmoscopy	(276)[c]	493	(276)[c]	600	(276)[c]	489	276	612	403	201
Tonometry/ophthalmoscopy in series	(476)[c]	604	(476)[c]	757	(476)[c]	574	476	799	371	229
Tonometry/ophthalmoscopy in parallel	(692)[c]	803	(692)[c]	956	(692)[c]	774	692	998	868	429
Perimetry	462	748	481	828	405	711	531	859	634	334

[a] High bound assumes lowest relevant reported sensitivities and specificities of the respective screening procedure, 40% followup rate for positive cases referred, prevalence rate of 2 percent per year, and screening episode costs that include both visit and procedure-specific charges (for office settings). Low bound assumes highest relevant reported sensitivities and specificities of the respective screening procedure, 100% followup rate for positive cases referral, prevalence rate of 3 per thousand per year, and b screening episode costs that include only procedure-specific charges (for office settings).

High and low bounds for community facilities vary only by assumptions regarding followup rates and incidence rates assumed; costs per screening episode and test specificities and sensitivities did not vary. Because of this, the average per-case cost varies little between the bounds, but the total number of cases varies drastically. Thus, unlike the other settings, the model variant producing the most number of cases diagnosed ("low" variant) actually produces much higher total costs than does the model variant producing the least number of cases ("high").

[c] For procedures involving ophthalmoscopy, OTA assumed that only very experienced ophthalmologists could attain the levels of sensitivity and specificity used for the low bound. Thus, despite the fact that ophthalmologists' charges for ophthalmoscopy are higher than charges of other professionals, OTA assumed that other specialties could perform the procedure no less cheaply overall than could opthalmologists. The lowest cost per case found for ophthalmologists was thus assumed to be also the lowest attainable cost per case for any other profession.

SOURCE: Office of Technology Assessment, 1988.

Table 15.--High and Low Bounds[a] of Cost Per Confirmed Case of Open-Angle Glaucoma in Initial Years of a Screening Program

Technology	Family Practice		Internist		Optometrist		Ophthalmologist		Community Facility[b]	
	Lou	High	Lou	High	Lou	High	Low	High	"Low"	"High"
Tonometry	$1,300	$9,000	$1,500	$10,500	$1,200	$8,900	$1,600	$10,700	$2,700	$4,700
Ophthalmoscopy[c]	(900)	7,200	(900)	8,800	(900)	7,100	900	8,900	1,600	2,900
Tonometry/ophthalmoscopy[c] in series	(2,100)	12,200	(2,100)	15,400	(2,100)	11,700	2,100	16,200	2,000	4,700
Tonometry/ophthalmoscopy[c] in parallel	(2,000)	9,200	(2,000)	10,900	(2,000)	8,800	2,000	11,400	2,600	4,900
Perimetry	1,300	8,600	1,400	9,500	1,200	8,100	1,600	9,800	1,900	3,800

[a] High bound assumes lowest relevant reported sensitivities and specificities of the respective screening procedure, 40% followup rate for positive cases referred, incidence rate of 2 per thousand per year, and screening episode costs that include both visit and procedure-specific charges (for office settings). Low bound assumes highest relevant reported sensitivities and specificities of the respective screening procedure, 100% followup rate for positive cases referred, incidence rate of 4 per thousand per year, and screening episode costs that include only procedure-specific charges (for office settings).

[b] High and low bounds for community facilities vary only by assumptions regarding followup rates and incidence rates assumed; costs per screening episode and test specificities and sensitivities did not vary.

[c] For procedures involving ophthalmoscopy, OTA assumed that only very experienced ophthalmologists could attain the levels of sensitivity and specificity used for the low bound. Thus, despite the fact that opthalmologists' charges for ophthalmoscopy are higher than charges of other professionals, OTA assumed that other specialties could perform the procedure no less cheaply overall than could opthalmologists. The lowest cost per case found for ophthalmologists was thus assumed to be also the lowest attainable cost per case for any other profession.

SOURCE: Office of Technology Assessment, 1988.

Table 16--- High and Low Bounds[a] of Total Costs of Screening and Confirmatory Followup for Open-Angle Glaucoma in Later Years of a Screening Program (In millions of dollars)

Technology	Family Practice		Internist		Optometrist		Ophthalmologist		Community Facility[b]	
	Low	High	Low	High	Lou	High	Lou	High	"Low"	"High"
Tonometry	$231	$613	$277	$720	$206	$609	$308	$732	$700	$321
Ophthalmoscopy	(240)[c]	491	(240)[c]	598	(240)[c]	486	240	610	396	199
Tonometry/ophthalmoscopy in series	(458)[c]	602	(458)[c]	755	(458)[c]	573	458	797	366	228
Tonometry/ophthalmoscopy in parallel	(543)[c]	802	(543)[c]	956	(543)[c]	773	543	998	866	428
Perimetry	382	746	401	826	325	709	451	857	626	333

[a] High bound assumes lowest relevant reported sensitivities and specificities of the respective screening procedure, 40% followup rate for positive cases referred, incidence rate of 2 per thousand per year, and screening episode costs that include both visit and procedure-specific charges (for office settings). Low bound assumes highest relevant reported sensitivities and specificities of the respective screening procedure, 100% followup rate for positive cases referred, incidence rate of 4 per thousand per year, and screening episode costs that include only procedure-specific charges (for office settings).

High and low bounds for community facilities vary only by assumptions regarding followup rates and incidence rates assumed; costs per screening episode and test specificities and sensitivities did not vary. Because of this, the average per-case cost varies little between the bounds, but the total number of cases varies drastically. Thus, unlike the other settings, the model variant producing the most nun-bet- of cases diagnosed ("low" variant) actually produces much higher total costs than does the model variant producing the least number of cases ("high").

[c] For procedures involving ophthalmoscopy, OTA assumed that only very experienced ophthalmologists could attain the levels of sensitivity and specificity used for the low bound. Thus, despite the fact that opthalmologists' charges for ophthalmoscopy are higher than charges of other professionals, OTA assumed that other specialties could perform the procedure no less cheaply overall than could opthalmologists. The lowest cost per case found for ophthalmologists was thus assumed to be also the lowest attainable cost per case for any other profession.

SOURCE: Office of Technology Assessment, 1988.

Table 17--- High and Low Bounds[a] of Cost Per Confirmed Case of Open-Angle Glaucoma in Later Years of a Screening Program

Technology	Family Practice		Internist		Optometrist		Ophthalmologist		Community Facility[b]	
	Low	High	Low	High	Low	High	Low	High	"Low"	"High"
Tonometry	$4,900	$44,800	$5,500	$52,600	$4,500	$44,400	$5,900	$53,500	$10,200	$23,400
Ophthalmoscopy	(3,200)[c]	35,900	(3,200)[c]	43,700	(3,200)[c]	35,500	3,200	44,500	5,800	14,500
Tonometry/ophthalmoscopy in series	(7,600)[c]	61,100	(7,600)[c]	76,600	(7,600)[c]	58,100	7,600	80,900	7,400	23,100
Tonometry/ophthalmoscopy in parallel	(7,400)[c]	45,800	(7,400)[c]	54,500	(7,400)[c]	44,100	7,400	56,900	9,900	24,400
Perimetry	4,900	42,600	5,100	47,200	4,300	40,500	5,600	49,000	7,200	19,000

[a] High bound assumes lowest relevant reported sensitivities and specificities of the respective screening procedure, 40% followup rate for positive cases referred, incidence rate of 2 per thousand per year, and screening episode costs that include both visit and procedure-specific charges (for office settings). Low bound assumes highest relevant reported sensitivities and specificities of the respective screening procedure, 100% followup rate for positive cases referred, incidence rate of 4 per thousand per year, and screening episode costs that include only procedure-specific charges (for office settings).

[b] High and low bounds for community facilities vary only by assumptions regarding followup rates and incidence rates assumed; costs per screening episode and test specificities and sensitivities did not vary.

[c] For procedures involving ophthalmoscopy, OTA assumed that only very experienced ophthalmologists could attain the levels of sensitivity and specificity used for the low bound. Thus, despite the fact that ophthalmologists' charges for ophthalmoscopy are higher than charges of other professionals, OTA assumed that other specialties could perform the procedure no less cheaply overall than could opthalmologists. The lowest cost per case found for ophthalmologists was thus assumed to be also the lowest attainable cost per case for any other profession.

SOURCE: Office of Technology Assessment, 1988.

For procedures involving ophthalmoscopy, it was assumed that only a few ophthalmologists who were glaucoma specialists might actually attain the test accuracies implicit in the lowest-cost estimate. Thus, despite the higher charges of ophthalmologists, OTA assumed that the lowest-cost estimate for procedures involving ophthalmoscopy could be no lowe r for non - ophthalmologists than for ophthalmologists.

As the tables 14 and 16 demonstrate, **total annual health care costs of a screening program would be somewhere between $200 million and $1 billion.** Clearly, the benefit derived from such a program--the number of OAG cases identified--vary greatly within these bounds. A more accurate reflection of how efficiently the program might detect cases can be expressed in the average amount of money that must be spent to identify and confirm a case of OAG. As tables 15 and 17 show, **this amount lies somewhere between approximately $1,000 and $16,000 per case of OAG detected through the program in initial years and between approximately $3,000 and $81,000 per case in later years.** The actual cost, within these ranges, depends upon the variables listed above and upon the examiner and the screening procedure used. These costs do not include the costs associated with treatment.

The wide ranges of the above estimates--nearly 30-fold, in the last case--is indicative of the uncertainty surrounding the estimates. For example, in order to know more about the relative costs of screening as performed by different examiners in different sites, one must know not only their relative charges but their relative accuracies in identifying cases when using the different screening procedures. Since almost nothing about the relative accuracies of different examiners is known, OTA can conclude only that the true costs associated with each type of examiner probably lie within the extremes above. It is not known whether, on average, screening would be cheaper if done by optometrists, ophthalmologists, or other physicians. Nor is it known which procedure would, on average, be cheapest. At best, some hypotheses can be suggested - -for example, that if both tonometry and ophthalmoscopy are performed, there may be a substantial difference in cost in some settings depending on the referral criterion. The results of OTA's model suggest that referring for followup any person testing positive on either test results in more cases found and lower per-case costs than referring only those testing positive on both. The model results also suggest that mass screening in community facilities is not necessarily the least expensive method of screening; if office-based examiners can perform screening more accurately and/or have higher followup rates, the cost per OAG case detected in these settings would be lower.

Applying the Model to Screening for High Intraocular Pressure (IOP)

The model described above to estimate the costs and yield of a screening program for manifest OAG can also be applied to a program whose goal is detecting high IOP. The population with high IOP consists primarily of people with ocular hypertension (OH) --high IOP but no other signs of OAG--but includes a minority of people who, at the confirmatory visit, would be found to have manifest OAG.

Estimating the screening program cost per confirmed case of high IOP involves uncertainties similar to those for manifest OAG screening. Both the accuracies of the tests and the settings in which they would most often be performed (and, hence, the cost of the screening episode and the type of tonometer used) are largely unknown. The precise incidence and prevalence of high IOP in the U.S. elderly population is also still uncertain.

OTA estimated the likely upper and lower bounds of the costs of a screening program to detect elderly people with high IOP using the same basic model as for manifest OAG screening. Assumptions regarding population size, utilization of the program, and frequency with which screening would occur are the same as for the OAG screening model. Again, OTA calculated the average cost per confirmed case of high IOP (i.e., all persons with high IOP at the screening episode would be referred for a confirmatory, comprehensive visit; total costs are divided by

confirmed high IOP cases to yield the average cost of detecting a case of high IOP). Costs and medical benefits occurring after the confirmatory visit were not calculated due to the uncertainty regarding the likely benefits of treatment. Tonometry was the only screening technology considered. Table 18 presents other assumptions for the high and low bounds of the estimated cost per confirmed case of high IOP and the rationale for each assumption.

OTA estimates that **a program to screen elderly people for high IOP with tonometry would cost between $100 and $1,700 per confirmed case of high IOP in initial years, and between $300 and $14,600 in later years. Total costs of such a program would likely be between $100 million and $300 million initially and between $250 million and $500 million in later years of an ongoing program.[2] Because the cost of the confirmatory visit is so great compared to the screening visit, and because high IOP is fairly common (with a large number of positive tests), the proportion of people testing positive who actually show up for the confirmatory visit is especially crucial to costs and to the number of cases identified.**

This screening program would detect between 300,000 and 3 million people with high IOP per year in initial years and between 30,000 and 350,000 per year in later years. The cases of confirmed high IOP would consist primarily of people with OH but would include a minority of individuals who had manifest OAG.

2 Here, as with a program to detect only manifest OAG, high per-case costs do not lead to proportionately high total costs, because the highest per-case costs occur when there are relatively few cases detected.

Table 18--- Assumptions for Low- and High-Cost Bounds of a Model for Estimating Costs of Screening for High Intraocular Pressure

Component	Low-cost bound	High-cost bound	Rationale
Prevalence of high IOP (21 mm Hg or more)	24%	9%	Percent of elderly with IOPs equal to or over 20 and 22 mm Hg, respectively (based on Framingham, MA data)
Incidence of high IOP (21 mm Hg or more)	3%	1%	Assume that incidence is roughly 10 percent of prevalence
Cost of screening episode	$5.75	$40.34	Low figure is per-person cost of mass screening (based on Northern California data); high figure is Medicare average allowed charge for brief visit + tonometry by internist (based on HCFA data, updated for inflation)
Cost of followup visit	$75.85	$75.85	Medicare average allowed charge for comprehensive visit + perimetry by ophthalmologist (based on HCFA data, updated for inflation)
Rate of compliance with followup visit (if positive test)	100%	40%	High figure is absolute maximum; low figure is slightly lower than the experience of the National Society to Prevent Blindness programs
Sensitivity (tonometry, cutoff 21 mm Hg)	100%	71%	High figure is absolute maximum; low figure is based on accuracy of Schiotz compared with Goldmann tonometry
Specificity (tonometry, cutoff 21 mm Hg)	100%	97%	High figure is absolute maximum; low figure is based on accuracy of Schiotz compared with Goldmann tonometry

SOURCE: Office of Technology Assessment, 1988. Data for individual assumptions from: B. Bengtsson, "Comparison of Schiotz and Goldman Tonometry in a Population," Acta Ophthalmologica 50(4):445-457, 1972; H.A. Kahn and R. C Milton, "Alternative Definitions of Open-Angle Galucoma," Arch. Ophthalmol. 98:2172-2177, 1980; P. Jamgochian, "Northern California Society to Prevent Blindness, 1984 Glaucoma Program, Cost Benefit Analysis," unpublished paper, May 1986; National Society to Prevent Blindness, "Highlights of the 1985 NSPB Sponsored Glaucoma Screening Program," unpublished paper, 1986; 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; unpublished data from the Health Care Financing Administration BMAD database (T. Kay, HCFA, Baltimore, MD, personal communication, 1988).

1. Airaksinen, P. J., Vane, O., Takki, K. K., et al., "Timolol Treatment of Chronic Open-Angle Glaucoma and Ocular Hypertension," Graefes Arch. Clin. Exp. Ophthalmol., 219(2):68-71, August 1982.

2. Allen, R. C., Hertzmark, E., Walker, A. M., et al., "A Double-Masked Comparison of Betaxolol vs. Timolol in the Treatment of Open-Angle Glaucoma," Am. J. Ophthalmology 101(5):535-541, May 1986.

3. American Medical Association, Physicians' Current Procedural Terminology, 4th edition (Chicago, IL: American Medical Association, November 1987).

4. Armaly, M. F., "Ocular Pressure and Visual Fields," Arch. Ophthalmology 81(1):25-40, January 1969.

5. Armaly, M. F., "Lessons To Be Learned From the Collaborative Glaucoma Study," Survey of Ophthalmology 25(3):139- 144, November-December 1980.

6. Ashburn, F., Goldberg, I., and Kass, M. A., "Compliance With Ocular Therapy," Survey of Ophthalmology 24(4):237-248, January-February 1980.

7. Asregadoo, E. R., "Blood Levels of Thiamine and Ascorbic Acid in Chronic Open-Angle Glaucoma," Annals of Ophthalmology 11(7) :1095-1100, July 1979.

8. Axelsson, U., and Holmberg, A., "The Frequency of Cataract Surgery After Miotic Therapy," Acta Ophthalmologica 44(3):421-429, 1966.

9. Bankes, J. L. K., Perkins, E. S., Tsolakis, S., et al., "Bedford Glaucoma Survey," Brit. Med. J. 1(595):791-796, March 30, 1968.

10. Becker, B., and Morton, W. R., "Topical Epinephrine in Glaucoma Suspects," Am. J. Ophthalmology 62(2):272-277, August 1966.

11. Bengtsson, B., "Comparison of Schiotz and Goldmann Tonometry in a Population," Acta Ophthalmologica 50(4):445-457, August 1972.

12. Bengtsson, B., "The Prevalence of Glaucoma," Brit. J. Ophthalmogy 65(1):46-49, January 1981.

13. Bengtsson, B., "Manifest Glaucoma in the Aged I: Occurrence Nine Years After a Population Survey," Acta Ophthalmologica 59(3):321-335, June 1981.

14. Bengtsson, B., and Krakau, C. E. T., "Automatic Perimetry in a Population Survey," Acta Ophthalmologica 57(5):929-937, October 1979.

15. Bensinger, R. E., Keates, U., Gofman, J. D., et al., "Levobunolol: A Three-Month Efficacy Study in the Treatment of Glaucoma and Ocular Hypertension," Arch. Ophthalmology 103(3):375-378, March 1985.

16. Berkow, R., cd., The Merck Manual, 15th edition (Rahway, NJ: Merck & Co., 1987).

17. Berson, F. G., Cohen, H. B., Roerster, R. J., et al., "Levobunolol Compared With Timolol for the Long-Term Control of Elevated Intraocular Pressure," Arch. Ophthalmology lo3(3):379-382, March 1985.

18. Bigger, J. F., "A Comparison of Patient Compliance in Treated vs. Untreated Ocular Hypertension," Trans. Am. Acad. Ophth. & Otol. 81: OP277-OP285, March-April 1976.

19. Boston, L., American Academy of Ophthalmology, San Francisco, CA, personal communication, March 1988.

20, Campos-Outcalt, D., and Carmichael, J. M., "New Perspectives on Glaucoma Screening," J. Family Practice 12(3):451-457, March 1981.

21. Canadian Department of National Health and Welfare, Periodic Health Examination Task Force, The Periodic Health Examination. 1979 (Hull, Quebec, Canada: The Canadian Government Publishing Office, 1979).

22. Cinotti, A., Cinotti, D., Grant, W., et al., "Levobunolol vs. Timolol for Open-Angle Glaucoma and Ocular Hypertension," Am. J. Ophthalmology 99(1):1 1-17, January 1985.

23. Cochrane, A. L., Graham, P. A., and Wallace, J., "Glaucoma," in Screening in Medical Care, C. Birkenhead, E.T. Williams, and G. McLachlan (eds.) (New York, NY: Oxford University Press, 1968).

24. Cockburn, D. M., "The Prevalence of Ocular Hypertension in Patients of an Optometrist and the Incidence of Glaucoma Occurring During Long-Term Follow-Up of Ocular Hypertensives," Am. J. Optometry & Physiological Optics 59(4):330-337, April 1982.

25. Cockburn, D. M., "Does Reduction of Intraocular Pressure (IOP) Prevent Visual Field Loss in Glaucoma?" Am. J. Optometry & Physiological Optics 60(8):705-710, August 1983.

26. Cohen, M. F., Feldman, R., Siegelaub, A. B., "Dollar Cost per Positive Test for Automated Multiphasic Screening," New Eng. J. Med. 283:459-463, Aug. 27, 1970.

27. David, R., Livingston, D. G., and Luntz, M. H., "Ocular Hypertension--A Long-Term Follow-up of Treated and Untreated Patients," Brit. J. Ophthalmology 61(1 1):668-674, November 1977.

28. David, R., Zangwill, L. M., Tessler, Z., et. al., "The Correlation Between Intraocular Pressure and Refractive Status," Arch. Ophthalmology 103(12):1812-1815, December 1985.

29. Drance, S. M., "Correlation Between Optic Disc Changes and Visual Field Defects in Chronic Open-Angle Glaucoma," Trans. Am. Acad. Ophth. & Otol. 81: OP224-OP225, March-April 1976.

30. Drance, S. M., "Low-Tension Glaucoma: Enigma and Opportunity," Arch. Ophthalmology 103(8):1 131-1133, August 1985.

31. Eddy, D. M., Sanders, L. E., and Eddy, J. F., "The Value of Screening for Glaucoma With Tonometry," Survey of Ophthalmology 28(3):194-205, November-December 1983.

32. Eddy, D. M., and Billings, J., "The Quality of Medical Evidence and Medical Practice," paper prepared for the National Leadership Commission on Health Care, 1987.

33. Eifrig, D. E., and Simons, K.B. "An Overview of Common Geriatric Ophthalmologic Disorders," Geriatrics 38(4):55-77, April 1983.

34. Epstein, D.L. (cd,), Chandler & Grant's Glaucoma, 3rd edition (Philadelphia, PA: Lea & Febiger, 1986).

35. Ford, V. J., Zimmerman, T. J., and Kooner, K., "A Comparison of Screening Methods for the Detection of Glaucoma," (abstract) Invest. Ophthalmol. & Visual Science 22(suppl):257, 1982.

36. Gaasterland, D. E., "A Review of Surgical Alternatives to Medical Therapy for Glaucoma," J. National Med. Assn. 80(7):721-723, July 1988.

37. Gaasterland, D. E., Georgetown University Center for Sight, Washington, DC, personal communication, March 1988.

38. Gaasterland, D., and Kupfer, C., "Experimental Glaucoma in the Rhesus Monkey," Invest. Ophthalmology 13(6):455-457, June 1974.

39. Goldbloom, R., and Battista, R. N., "The Periodic Health Examination: 2. 1985 Update," Can. Med. Assoc. J. 134:724-727, April 1, 1986.

40. Goldberg, I., Hollows, F. C., Kass, M. A., et al., "Systemic Factors in Patients With Low-Tension Glaucoma," Brit. J. Ophthalmology 65(1):56-62, January 1981.

41. Gottlieb, L. K., Schwartz, B., and Pauker, S. G., "Glaucoma Screening: A Cost-Effectiveness Anal ysis," Survey of Ophthalmology 28(3):206-226, November-December 1983.

42. Graham, P. A., "The Definition of Pre-Glaucoma a Prospective Study," Trans. Ophthal. Soc. U.K. 88(1968):153-165, 1969.

43. Grant, W. M., and Burke, J. F., "Why Do Some People Go Blind From Glaucoma?" Ophthalmology 89(9):991 -998, September 1982.

44. Greenridge, K. C., and Spaeth, G. L., "Change in Appearance of the Optic Disc Associated With Lowering of Intraocular Pressure," Ophthalmology 92(7):897-903, July 1985.

45. Harbin, T. S., Podos, S. M., Kolker, A. E., et al., "Visual Field Progression in Open-Angle Glaucoma Patients Presenting With Monocular Field Loss," Trans. Am. Acad. Ophthalmol. & Otol. 81(2):253-256, 1976.

46. Hart, W. M., and Becker, B., "The Onset and Evolution of Glaucomatous Visual Field Defects," Ophthalmology 89(3):268-279, March 1982.

47. Hildreth, H. R., and Becker, B., "Routine Tonometry," Trans. Am. Ophthalmol. Soc. 54:55-61, 1956.

48. Hiller, R., and Kahn, H. A., "Blindness From Glaucoma," Am. J. Ophthalmology 80(1):62-69, July 1975.

49. Hiller, R., Sperduto, R. D., and Krueger, D. E., "Race, Iris Pigmentation, and Intraocular Pressure," Am. J. Epidemiology 115(5):674-683, May 1982.

50. Hitchings, R. A., and Spaeth, G. L., "The Optic Disc in Glaucoma, II: Correlation of the Appearance of the Optic Disc With the Visual Field," Brit. J. Ophthalmology 61(1):107- 113, January 1977.

51. Hoff, M., Parkinson, J. M., Kass, M. A., et al., "Long-Term Trial of Unilateral Timolol Treatment in Ocular Hypertensive Subjects," (abstract) Invest. Ophthalmol. & Visual Science 29(suppl):16, 1988.

52. Hollows, F. C., and Graham, P. A., "The Ferndale Glaucoma Survey," in Glaucoma, L.B. Hunt (cd.) (London: E. & S. Livingtone Ltd., 1966).

53. Holmin, C., "Optic Disc Evaluation Versus the Visual Field in Chronic Glaucoma," Acta Ophthalmologica 60(2):275-283, April 1982.

54. Hoskins, H. D., and Gelber, E. C., "Optic Disk Topography and Visual Field Defects in Patients With Increased Intraocular Pressure," Am. J. Ophthalmology 80(2):284-290, August 1975.

55. Hovding, G., and Aasved, H., "Prognostic Factors in the Development of Manifest Open-Angle Glaucoma," Acta Ophthalmologica 64(16):601-608, Dec. 1986.

56. Jamgochian, P., "Northern California Society to Prevent Blindness, 1984 Glaucoma Program, Cost Benefit Analysis," unpublished paper, May 1986.

57. Johnson, D. H., and Brubaker, R. F., "Glaucoma: An Overview," Mayo Clinic Proceedings 61:59-67, January 1986.

58. Kahn, H. A., Leibowitz, H. M., Ganley, J. P., et al., "The Framingham Eye Study 1. Outline and Major Prevalence Findings," Am. J. Epidemiology 106(1)17-32, July 1977.

59. Kahn, H. A., and Milton, R. C., "Alternative Definitions of Open-Angle Galucoma," Arch. Ophthalmology 98(12):2172-2177, December 1980.

60. Kahn, H. A., and Milton, R. C., "Revised Framingham Eye Study Prevalence of Glaucoma and Diabetic Retinopathy," Am. J. Epidemiology 11 1(6):769-776, June 1980.

61. Kass, M. A., Gordon, M., Morley, R. E., et al., "Compliance With Topical Timolol Treatment," Am. J. Ophthalmology 103(2):188- 193, February 1987.

62. Katz, L. J., Cantor, L. B., Spaeth, G. L., et al., "Perimetry in Glaucoma Patients With Reversible Disc Cupping," Invest. Ophthalmol. & Visual Science 27(3, suppl):41, March 1986.

63. Keltner, J. L., and Johnson, C. A., "Screening for Visual Field Abnormalities With Automated Perimetry," Survev of Ophthalmology 28(3):175-183, November-December, 1983.

64. Kitazawa, Y., "Prophylactic Therapy of Ocular Hypertension: A Prospective Study," Trans. Ophthalogy Soc. New Zealand 33:30-32, 1981.

65. Kitazawa, Y., Horie, T., Aoki, S., et al., "Untreated Ocular Hypertension," Arch. Ophthalmology 95(7):1 180-1184, July 1977.

66. Kolker, A. E., "Visual Prognosis in Advanced Glaucoma: A Comparison of Medical and Surgical Therapy for Retention of Vision in 101 Eyes With Advanced Glaucoma," Trans. Am. Ophthalmol. Soc. 75:539-555,1977.

67. Kolker, A. E., and Hetherington Jr., J. (eds.), Becker-Shaffer's Diagnosis and Therapy of the Glaucomas, 5th edition (St. Louis, MO: C.V. Mosby Co., 1983).

68. Kolker, A. E., Washington University Medical School, St Louis, MO, personal communication, June 1988.

69. Kronfeld, P. C., and McGarry, H. I., "Five Year Follow-up of Glaucomas," J. A.M.A. 136(15):957-964, April 10, 1948.

70. Krug, J. H., Hertzmark, E., Remis, L. L., et al., "Long Term Study of Timolol vs. No Treatment in the Management of Glaucoma Suspects," (abstract) Invest. Ophthalmol. & Visual Science 28(3, suppl):148, March 1987.

71. Krug, J. H., Massachusetts Eye & Ear Infirmary, Boston, MA, personal communication, June 1988.

72, Leske, M. C., "The Epidemiology of Open-Angle Glaucoma: A Review," Am. J. Epidemiol- ~ 118(2):166-191, August 1983.

73. Leske, M. C., and Hawkins, B. S., "Screening: Relationship to Diagnosis and Therapy," in Clincal Ophthalmology, T.D. Duane (cd.) (Philadelphia, PA: Harper & Row, 1984).

74. Leske, M. C., and Podgor, M., "Intraocular Pressure, Cardiovascular Risk Variables, and Visual Field Defects," Am, J. Epidemiology 118(2):280-287, August 1983.

75. Leske, M, C., Podgor, M., and Ederer, F., "An Evaluation of Glaucoma Screening Methods," (abstract) Invest. Ophthalmol. & Visual Science 22(3, suppl):128, March 1982.

76. Leske, M. C., and Rosenthal, J., "Epidemiological Aspects of Open-Angle Glaucoma," Am. J. Epidemiology 109(3):250-272, March 1979.

77. Levene, R. Z., "Uniocular Miotic Therapy," Trans. Am. Acad. Ophthalmol. & Otol. 79(2):376-380, 1975.

78. Levi, L., and Schwartz, B., "Glaucoma Screening in the Health Care Setting," Survey of Ophthalmology 28(3):164-174, November-December 1983.

79. Linner, E., "Diagnostic and Therapeutic Aspects of Early Chronic Simple Glaucoma," Israel J. Med. Sci. 8(8-9):1394-1396, August-September 1972.

80. Linner, E., and Stromberg, U., "Ocular Hypertension: A Five-Year Study of the Total Population in a Swedish Town, Skovde," in Glaucoma Tutzing Symposium (Karger, Basel: New York, NY, 1967), 187-214.

81. Lundberg, L., Wettrell, K., and Linner, E., "Ocular Hypertension," Acta Ophthalmologica 65(6):705-708, December 1987.

82. Markowitz, S., and Morin, J. D., "Timolol: A 4-Year Follow-up Study," Can. J. Ophthalmol- ~ 18(6):278-280, 1983.

83. Mikelberg, F. S., Schulzer, M., Drance, S, M., et al., "The Rate of Progression of Scotomas in Glaucoma," Am. J. Ophthalmology 101(1):1-6, January 1986.

84. National Society to Prevent Blindness, Vision Problems in the U.S. (New York, NY: NSPB, 1980).

85. National Society to Prevent Blindness, "Highlights of the 1985 NSPB Sponsored Glaucoma Screening Program," unpublished paper, 1986.

86. Nelson, W. L., Fraunfelder, F. T., Sills, J. M., et al., "Adverse Respiratory and Cardiovascular Events Attributed to Timolol Ophthalmic Solution, 1978- 1985," Am. J. Ophthalmology 102(5):606-61 1, November 1986.

87. Nielsen, J. V., "The Ocular Hypotensive Effect of Timolol in Long-Term Treatment of Glaucoma: A 4-Year Study," Acta Ophthalmologica 60(6):961-966, December 1982.

88. Norskov, K., "Routine Tonometry in Ophthalmic Practice: II. Five-Year Followup," Acta Ophthalmologica 48(5):873-895, October 1970.

89. Packer, H., Deutsch, A. R., Deweese, M. W., et al., "Frequency of Glaucoma in Three Population Groups," J. A.M.A. 188(2):1 15-119, Apr. 13, 1964.

90. Packer, H., Deutsch, A. R., and Deweese, M. W., "Efficiency of Screening Tests for Glaucoma," J. A.M.A. 192(8):693-696, May 1965.

91. Pederson, J. E., and Herschler, J., "Reversal of Glaucomatous Cupping in Adults," Arch. Opthalmology 100(3):426-431, March 1982.

92. Perkins, E. S., "The Bedford Glaucoma Survey: I. Long-Term Follow-Up of Borderline Cases," Brit. J. Ophthalmology 57(3):179-185, March 1973.

93. Peters, P., Associate Director, National Society to Prevent Blindness, Schaumburg, IL, personal communication, March 1988.

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

95. Pohjanpelto, P. E. J., and Palva, J., "Ocular Hypertension and Glaucomatous Optic Nerve Damage," Acta Ophthalmologica 52:194-200, 1974.

96. Pollack, I. P., "The Challenge of Glaucoma Screening," Survey of Opthalmology 13:4-22, 1968-1969

97. Quigley, H. A., and Maumenee, A. E., "Long-Term Follow-Up of Treated Open-Angle Glaucoma," Am. J. Ophthalmolog 87(4):519-525, April 1979.

98. Quigley, H. A., Addicks, E. M., and Green, R., "Optic Nerve Damage in Human Glaucoma III. Quantitative Correlation of Nerve Fiber Loss and Visual Field Defect in Glaucoma, Ischemic Neuropathy, Papilledema, and Toxic Neuropathy," Arch. Ophthamology 100(1):135-146, January 1982.

99. Rock, W. J., Drance, S. M., and Morgan, R. W., "Visual Field Screening in Glaucoma," Arch. Ophthalmology 89(4):287-290, April 1983.

100. Schappert-Kimmijser, J., "A Five-Year Follow-Up of Subjects With Intra-Ocular Pressure of 22-30 mm Hg Without Anomalies of Optic Nerve and Visual Field Typical for Glaucoma at First Investigation," Acta Ophthalmologica 162(1):289-295, February 1971.

101. Shaffer, R. N., and Hetherington, J., "Anticholinesterase Drugs and Cataracts," Am. J. Ophthalmology 62(4):613-618, October 1966.

102. Shin, D. H., Kolker, A. E., Kass, M. A., et al., "Long-Term Epinephrine Therapy of Ocular Hypertension," Arch. Ophthalmology 94(12):2059-2060, December 1976.

103. Sommer, A., Enger, C., and Witt, K., "Screening for Glaucomatous Visual Field Loss With Automated Threshold Perimetry," Am. J. Ophthalmology 103(5):681-684, May 1987.

104. Sorensen, P. N., Nielsen, N. V., and Norskov, K., "Ocular Hypertension. A 15-Year Followup," Acta Ophthalmologica 56(3):363-372, June 1978.

105. Spaeth, G. L., Wills Eye Hospital, Philadelphia, PA, personal communication, July 1988.

106. Spaeth, G. L., "Treatment for Glaucoma is Beneficial," unpublished paper, 1988.

107. Spaeth, G. L., "Visual Loss in a Glaucoma Clinic, I. Sociological Considerations," Invest. Ophthalmol. 9(1):73-82, January 1970.

108. Spector, R., Lightfoote, J. B.. Cohen, P., et al., "Should Tonometry Screening Be Done by Technicians Instead of Physicians?" Arch. Intern. Med. 135(9):1260-1263, September 1975.

109. Sponsel, W. E., Dallas, N. L., and Burbridge, L., "Visual Field Survival: The Response to Timolol Therapy in Open-Angle Glaucoma," Brit. J. Ophthalmology 67(4):220-227, April 1983.

110. Sugar, H. S., "Postoperative Cataract in Successfully Filtering Glaucomatous Eyes," Am. J. Ophthalmology 69(5):740-746, May 1970.

111. Thorburn, W., "The Accuracy of Clinical Applanation Tonometry," Acta Ophthalmologica 56(1):1-5, February 1978.

112. Tielsch, J. M., Royall, R. M., Quigley, H. A., et al., "Baltimore Eye Survey: Design and Preliminary Results," Invest. Ophthal. & Visual Science 27(3, suppl):44, March 1986.

113. Tucker, J. B., "Glaucoma Detection in Family Practice Residencies," J. Family Practice 12(3):656-566, March 1981.

114. Tuulonen, A., Niva, A., and Alanko, H. I., "A Controlled Five-Year Follow-up Study of Laser Trabeculoplasty as Primary Therapy for Open-Angle Glaucoma," Am. J. Ophthalmology 104(11):334-338, October 1987.

115. U.S. Department of Commerce, Bureau of the Census, Current Population Reports, Series P-25, No. 952, Projections of the Population of the United States, by Age, Sex, and Race: 1983 to 2080 (Washington, DC: U.S. Government Printing Office, 1984).

116. U.S. Department of Health and Human Services, Health Care Financing Administration, Office of Research and Demonstrations, Findings From the National Kidney Dialysis and Kidney Transplantation Study (Baltimore, MD: U.S. DHHS, HCFA, October 1987).

117. U.S. Department of Health and Human Services, Public Health Service, National Center for Health Services Research, Laser Trabeculoplasty for Open-Angle Glaucoma, Health Technology Assessment Report No. 23 (Rockville, MD: U.S. DHHS, PHS, 1984.
118. U.S. Department of Health and Human Services, Public Health Service, National Center for Health Statistics, Vital & Health Statistics, Series 10, No. 150, "Current Estimates from the National Health Interview Survey: United States, 1982," DHHS Pub. No. (PHS)85-1578 (Hyattsville, MD: U.S. DHHS, PHS, NCHS, September 1985).

119. U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, Vision Research--A National Plan: 1983-1987 (vol. 2 part 4: Report of the Glaucoma Panel), NIH Pub. No. 84-2474 (Bethesda, MD: U.S. DHHS, PHS, NIH, 1984).

120. U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, Clinical Trials Supported by the National Eye Institute, NIH Pub. No. 87-2910 (Bethesda, MD: U.S. DHHS, PHS, NIH, November 1987).

121. Van Buskirk, E. M., Weinreb, R. N., Berry, D. P., et al., "Betaxolol in Patients With Glaucoma and Asthma," Am. J. Ophthalmology 101(5):531-534, May 1986.

122. Whitener, J., American Optometric Association, Alexandria, VA, personal communication, August 1988.

123. Wilensky, J. T., Podos, S. M., and Becker, B., "Prognostic Indicators in Ocular Hypertension," Arch. Ophthalmology 91(3):200-202, March 1974.

124. Wilson, M. R., Hertzmark, E., Walker, A. M., et al., "A Case-Control Study of Risk Factors in Open-Angle Glaucoma," Arch. Ophthalmology 105(8):1066-1071, August 1987

125. Wilson, J. M. G., and Junger, G., Principles and Practice of Screening for Disease (Geneva, Switzerland: World Health Organization, 1968).

126. Wood, C. M., and Bosanquet, R. C., "Limitations of Direct Ophthalmoscopy in Screening for Glaucoma," Br. Med. J. 294(6587):1587-1588, June 20, 1987.

127. Worthen, D., "Economic Aspects of the Management of Ocular Hypertension," Survey of Ophthalmology 25(3):206-214, November-December 1980.

128. Worthen, D. M., "Significance of Intraocular Pressure in the Therapy of Glaucoma," in Symposium on Glaucoma (St. Louis, MO: The C.V. Moseby Company, 1981).

129. Zammataro, A., American Academy of Ophthalmology, San Francisco, CA, personal communication, March 1988.

130. Zimmerman, T. J., University of Louisville, Louisville, KY, personal communication, March 1988.