



Conseil d'évaluation des
technologies de la santé
du Québec

THE SCREENING OF PRIMARY OPEN-ANGLE GLAUCOMA

Report submitted to the
Quebec Minister of Health and Social Services

by

the *Conseil d'évaluation des technologies de la santé du Québec*

August 1995

Legal deposit - Bibliothèque nationale du Québec, 1995
National Library of Canada

ISBN 2-550-29221-9

How to cite this report:

Conseil d'évaluation des technologies de la santé du Québec (CETS). The Screening of Primary

Open-Angle Glaucoma. Montreal: CETS, 1995, xvi, 93 pp.

SUMMARY

INTRODUCTION

This report on glaucoma screening is in response to a request for an assessment made to the *Conseil d'évaluation des technologies de la santé* by the Minister of Health and Social Services. Basically, it presents a cost-effectiveness analysis of a possible screening program.

Primary open-angle **glaucoma** is a disease of the eye resulting in the gradual destruction of the optic nerve fibres with a progressive loss of visual sensitivity that can lead to blindness.

In this report, screening refers to the examination and treatment when necessary of individuals ostensibly not affected by the condition in question, i.e. by glaucoma or high intraocular pressure. Screening is usually conducted in the context of a program targeting an entire defined population. Screening tests can also be administered in the context of visits to a health-care professional, those visits being motivated by some other reason than the pathology targeted by the screening; in this latter case, we speak of case finding.

There is no cure for glaucoma, but early diagnosis followed by appropriate treatment can, according to the medical consensus, arrest it or slow its progression.

The **objective of screening** is therefore to prevent or delay the onset of blindness through the early identification and treatment of cases of glaucoma and individuals at high risk for developing this disease because of ocular hypertension.

TREATMENT

The **objective of treating** glaucoma is to lower intraocular pressure. There are three main methods of lowering intraocular pressure: drugs; trabeculoplasty, which is performed with a laser; and trabeculectomy, a surgical procedure. Drugs are almost always used first.

Efficacy of treatment. It is well established that the various treatments available successfully lower intraocular pressure. However, the ability of the pressure reduction to prevent or slow the development of glaucoma is less well documented. Although it accepts the medical consensus that treatment is probably effective, the U.S. Office of Technology Assessment points out that this consensus is based on theoretical considerations, clinical experience, and postulates shared by physicians rather than on direct demonstrations. Actually, we do not have any rigorous data that would enable us to quantify this efficacy.

On the basis of an analysis of available information, we have to conclude that no demonstration of the efficacy of treatment currently exists. Nevertheless, because of the firm judgment of experts in the field, we also have to conclude that available treatments probably present a certain level of efficacy. The quantitative level of this efficacy is however unknown. On the basis of an assessment of the indirect data at our disposal, an efficacy estimate of 50% has been used for our main analyses and estimates of 30% and 70% for our sensitivity analyses.

DIAGNOSIS

Most physicians agree that at least two of the following three signs or symptoms must be present in order to make a diagnosis of glaucoma: a) changes in the optic disc; b) visual field defects; and c) high intraocular pressure.

The disc is observed by examining the optic fundus. To a large extent, the accuracy of the examination depends on the examiner's skill.

After a certain amount of time, the anatomical lesions associated with glaucoma cause function loss, i.e. visual field defects. These defects can be documented by manual or automated perimetry.

Intraocular pressure is measured with a Schiötz, Goldmann or air-puff tonometer. Despite an important association between high intraocular pressure and glaucoma, there are cases of glaucoma in the absence of high

pressure and cases of high pressure without glaucoma.

EPIDEMIOLOGY

The *main risk factors* for glaucoma are old age, high intraocular pressure and a family history of the disease. Glaucoma is more prevalent in blacks than in whites.

The role played by other factors, such as severe myopia, diabetes and high arterial blood pressure, is too small or not understood clearly enough to have an impact on the planning of a screening strategy.

Epidemiology in Quebec. There are very few direct data on the incidence and prevalence of high intraocular pressure, glaucoma and blindness due to glaucoma in Quebec. We therefore had to estimate these different parameters by applying data from studies conducted elsewhere, usually in the United States, to the Quebec population.

The prevalence of glaucoma. The prevalence rate of a disease is the proportion of the affected population at a given point in time. The number of cases affected at a given moment, rather than their proportion, is designated by the word prevalence. We obtained three estimates of the prevalence of glaucoma in Quebec by applying data from American studies to the age-and-sex structure of the Quebec population aged 40 to 79. These methods led to prevalence estimates of 1.57% and 1.31%. *In our calculations, we used a prevalence of 1.57%.*

The incidence of glaucoma. Incidence is a measure of the frequency of appearance of new cases of the disease during a given period of time, for example, a year. To estimate the incidence of glaucoma, we used data from a study conducted in Beaver Dam, Wisconsin, which, once again, we applied to the Quebec population. *We obtained a figure of 2,715 new cases of glaucoma a year in Quebec among people aged 40 to 79.*

The prevalence of high intraocular pressure. To estimate the prevalence of intraocular pressure in Quebec, we used the rates from different surveys,

including those conducted in Baltimore and Beaver Dam. *Our estimate for Quebec is 6%, or 156,433 cases among people aged 40 to 79.*

The prevalence and incidence of blindness attributable to glaucoma. There are very few data on the incidence and prevalence of blindness due to glaucoma. The data from the Canadian National Institute for the Blind suggest that in Quebec, the incidence is about 140 cases a year. *This corresponds to a prevalence, in Quebec, of approximately 1,260 cases.*

Based on a study conducted in England, *we also estimated that the number of new cases of **partial** blindness in Quebec is 114 per year.*

**EFFECTIVENESS
OF A SCREENING
PROGRAM**

The effectiveness of a screening program depends on several factors which cannot be estimated precisely. A screening program where the treatment efficacy level is 50%, the participation rate of the population aged 40 to 79 years is 75%, and the therapeutic compliance is 75% would result in preventing 39.4 cases of blindness per year. The average age at which these cases were diagnosed would be 78 years, at which age life expectancy is around nine years. As a result, the reduction of the prevalence of blindness in the population would be 354 cases; expressed on an annual basis, this corresponds to 354 person-years of blindness prevented.

**COST OF A
SCREENING
PROGRAM**

We determined the cost of a program that would be offered to the Quebec population aged 40 to 79 (in 1991, 2,670,210 people), assuming, to begin with, that there are no glaucoma-related diagnostic or therapeutic services in Quebec.

Using the fees for procedures performed in private offices, we calculated the costs at around \$36.4 million per year. More restricted programs targeting people from 65 to 79 years old would cost between \$11.1 and \$12.6 million per year.

**COST-
EFFECTIVENESS
RATIOS**

The scenarios based on screening that targets the population from 40 to 79 years of age, every three years, with a participation rate of 75%, therapeutic compliance of 75% and a treatment efficacy of 50%, lead to cost-effectiveness ratios of around \$100,000 per year of blindness prevented. All of these calculations have been made without discounting.

We conclude that this type of program is a very costly option, compared to other potential health benefits that can be derived from the same resources.

Reaching a better level of efficiency would require restricting screening to the 65 to 79 age bracket; even in these cases, the cost-effectiveness ratio would be from \$37,000 to \$42,000 per year of blindness prevented for a program presenting the same characteristics in terms of frequency, participation, compliance and effectiveness. Even these costs are high compared to the health benefits.

**RECOMMEN-
DATION NO 1**

Because establishing a health policy involves the investment of public resources, it should not be based only on the estimation of cost-effectiveness ratios, but also on a high degree of certainty. *Our analyses do not support the setting up of a formal glaucoma screening program in Quebec, both because of the high degree of uncertainty and because of the high cost such a program would entail.*

**CURRENT STATE
OF GLAUCOMA
SCREENING IN
QUEBEC**

However, there already exists a significant level of diagnostic activity leading to the early detection of high intraocular pressure or glaucoma. Although this activity is not systematically organized, it currently reaches and treats some 27,000 people aged 65 to 79. At the present time, the question in Quebec is not so much whether a screening program should be established as whether current activities should be maintained.

Three considerations should be taken into account regarding this decision:

- To abolish a health service normally requires a higher degree of scientific evidence than is available in the case at hand.
- Moreover, our estimates of the cost-effectiveness ratio take account neither of the years of partial blindness that would be prevented nor of the fact that examinations performed for the detection of primary open-angle glaucoma may lead to the detection of other eye diseases which can be treated. For these reasons, it is likely that our estimates of cost-effectiveness ratios somewhat exaggerate the costs compared to the positive effects on health.
- At the same time, a large proportion of the current costs of screening are already covered by an undetermined part of complete eye exams. It would therefore be difficult to isolate and de-insure the part of exams specifically designed to detect glaucoma.

**RECOMMEN-
DATION NO. 2**

For these reasons, we do not see any point in recommending that current screening activities be discontinued.

However, if these activities are maintained, it will be important to continue restricting them, the way they currently are, to the 65 to 79 age bracket.

Moreover, our analyses indicate that the screening tests should not be undertaken more often than every three years. It should be noted that perimetry is not included in our scenarios among the initial screening tests.

Finally, as in the case of all specialized professional procedures, it is essential to ensure the quality of those procedures and also the good degree of training of the professionals involved.

ACKNOWLEDGEMENTS

This report was prepared for the *Conseil d'évaluation des technologies de la santé du Québec* by Jean-François Boivin and Maurice M^cGregor.

The *Conseil* wishes to thank the following external reviewers for their numerous suggestions:

Marcel Amyot	Department of Ophthalmology, Hôpital Maisonneuve-Rosemont, Montreal
Jean-Louis Anctil	Department of Ophthalmology, Université Laval, Quebec City
Gordon Balaszi	Department of Ophthalmology, Royal Victoria Hospital, Montreal
Alain Béchetouille	Department of Ophthalmology, Centre hospitalier universitaire d'Angers, France
Hélène Boisjoly	Department of Ophthalmology, Hôpital Maisonneuve-Rosemont, Montreal
Jaime Caro	Caro Research, Lincoln, Massachusetts
Gilles Côté	Department of Ophthalmology, Université Laval, Quebec City
Jacques Gresset	School of Optometry, Université de Montréal

Lastly, the *Conseil* would also like to call attention to the contribution of its following staff members: Chantal Archer and Huguette Demers, for their part in preparing this report; Jacqueline Fiola, for her word processing; Adrian Levy, for operating the hospital discharge and medical-procedure databases; and Suzanne Tremblay, librarian. The English version was translated by Mark A. Wickens and George Tombs.

TABLE OF CONTENTS

	Page
SUMMARY	i
ACKNOWLEDGEMENTS	ix
TABLE OF CONTENTS	xi
LIST OF TABLES	xv
INTRODUCTION.....	1
1. EFFICACY OF TREATMENT	5
TREATMENT	5
EFFICACY OF TREATMENT.....	6
2. DIAGNOSIS.....	9
EXAMINATION OF THE OPTIC DISC	9
EXAMINATION OF THE VISUAL FIELD.....	9
MEASURING INTRAOCULAR PRESSURE	10
GONIOSCOPY	10
3. EPIDEMIOLOGY	11
RISK FACTORS	11
THE EPIDEMIOLOGY OF GLAUCOMA IN QUEBEC	12
THE EPIDEMIOLOGY OF HIGH INTRAOCULAR PRESSURE IN QUEBEC	12
PREVALENCE OF GLAUCOMA AND OF HIGH INTRAOCULAR PRESSURE	12
EPIDEMIOLOGY OF BLINDNESS ATTRIBUTABLE TO GLAUCOMA IN QUEBEC	13
4. EFFECTIVENESS OF A SCREENING PROGRAM	15
TOTAL BLINDNESS	15
PARTIAL BLINDNESS	16
5. COST OF A SCREENING PROGRAM	17
COSTS OF BLINDNESS	18
6. COST-EFFECTIVENESS	19
SCENARIO 1	19
SCENARIO 2.....	19
SCENARIOS 3 TO 9.....	19
SCENARIO 10.....	20

TABLE OF CONTENTS (continued)

	Page
SCENARIOS 11 AND 12	20
SCENARIOS 13 AND 14	21
TOTAL OR PARTIAL BLINDNESS	22
DISCOUNTING	22
 7. NUMBER OF DIAGNOSTIC AND THERAPEUTIC PROCEDURES PERFORMED IN QUEBEC IN 1991	 25
 8. RECOMMENDATIONS BY THE MAIN TASK FORCES	 27
 9. DISCUSSION AND RECOMMENDATIONS	 29
DEFINITIONS	29
LACK OF RELIABLE DATA	29
PRESUMED EFFICACY OF TREATMENT	29
COST-EFFECTIVENESS	30
RECOMMENDATION NO 1	30
CURRENT STATE OF GLAUCOMA SCREENING IN QUEBEC	31
RECOMMENDATION NO 2	31
 APPENDIX 1. RANDOMIZED STUDIES OF THE EFFICACY OF TIMOLOL	 33
 APPENDIX 2. RISK FACTORS	 37
PREVALENCE OF GLAUCOMA AS A FUNCTION OF AGE	37
PREVALENCE OF GLAUCOMA AS A FUNCTION OF INTRAOCULAR PRESSURE	37
PREVALENCE OF GLAUCOMA IN WHITES AND BLACKS	38
PREVALENCE OF GLAUCOMA AS A FUNCTION OF GENDER	38
OTHER RISK FACTORS	39
 APPENDIX 3. EPIDEMIOLOGY OF GLAUCOMA IN QUEBEC	 43
PREVALENCE OF GLAUCOMA	43
INCIDENCE OF GLAUCOMA	44
INCIDENCE OF GLAUCOMA AS A FUNCTION OF INTRAOCULAR PRESSURE	45
 APPENDIX 4. EPIDEMIOLOGY OF HIGH INTRAOCULAR PRESSURE	 53
INCIDENCE OF HIGH PRESSURE IN QUEBEC	54

TABLE OF CONTENTS (continued)

	Page
APPENDIX 5. EPIDEMIOLOGY OF BLINDNESS ATTRIBUTABLE TO GLAUCOMA	59
COMPLETE BLINDNESS.....	59
PARTIAL BLINDNESS	61
APPENDIX 6. COST OF A POSSIBLE SCREENING PROGRAM	67
COSTS ASSOCIATED WITH MONITORING AND DIAGNOSIS	67
COSTS ASSOCIATED WITH MONITORING AND TREATMENT	68
PROFESSIONALS OTHER THAN OPHTHALMOLOGISTS.....	69
COSTS ASSOCIATED WITH BLINDNESS	70
APPENDIX 7. SCREENING FREQUENCY	79
APPENDIX 8. DIAGNOSTIC AND THERAPEUTIC ACTIVITIES IN QUEBEC	83
REFERENCES	89

LIST OF TABLES

	Page
TABLE 1. Certain variables affecting the cost-effectiveness estimates for glaucoma screening.....	23
TABLE 2. Cost-effectiveness: sensitivity analysis according to different screening scenarios	24
TABLE A1.1 Randomized studies of the efficacy of timolol	35
TABLE A2.1 Prevalence of open-angle glaucoma by age	40
TABLE A2.2 Intraocular pressure and the prevalence of glaucoma at the time of pressure measurement, Baltimore survey	41
TABLE A2.3 Risk of glaucoma with visual field defects attributable in the population to high intraocular pressure	42
TABLE A3.1 Age-sex structure of the Quebec population aged 40-79 years, 1991.....	46
TABLE A3.2 Estimate of the prevalence of glaucoma in Quebec based on data from the Beaver Dam study	47
TABLE A3.3 Distribution of cases of primary open-angle glaucoma depending on diagnostic criteria, according to the Beaver Dam survey	48
TABLE A3.4 Estimated incidence of primary open-angle glaucoma in Quebec, on the basis of the Beaver Dam survey	49
TABLE A3.5 incidence of glaucoma in Quebec based on data from the Framingham study	50
TABLE A3.6 Incidence of glaucoma, Collaborative Glaucoma Study	51
TABLE A3.7 Incidence of glaucoma with visual field defects, Collaborative Glaucoma Study (actuarial method)	52
TABLE A4.1 Prevalence of high intraocular pressure (in presence or absence of glaucoma)	55
TABLE A4.2 Prevalence of high intraocular pressure as a function of age; estimates by Gottlieb et al. Applied to the Quebec population.....	56

LIST OF TABLES (continued)

	Page
TABLE A4.3 Estimate of the incidence of high intraocular pressure	57
TABLE A5.1 New entries to the Register of the Canadian National Institute for the blind: cases of blindness due to glaucoma, 1989.....	63
TABLE A5.2 Prevalence of blindness in Quebec as estimated from statistics for 14 American States, 1969 - 1970	64
TABLE A5.3 Incidence of total or partial blindness in Quebec as estimated from the rates for Avon County, England, 1984 - 1986.....	65
TABLE A6.1 Fees for different diagnostic acts, Régie de l'assurance-maladie du Québec	72
TABLE A6.2 The costs of diagnostic exams, annual screening	73
TABLE A6.3 Monitoring and treatments for 5 years for 100 patients with glaucoma	74
TABLE A6.4 Cost of monitoring and treatment.....	75
TABLE A6.5 Cost of visual aids program, Régie de l'assurance-maladie du Québec, 1992.....	76
TABLE A6.6 Typical service plan for rehabilitating a blind person	77
TABLE A6.7 Costs associated with blindness in Quebec	78
TABLE A7.1 Mean age of various categories of people participating in a screening program ..	81
TABLE A8.1 Diagnostic procedures performed by medical specialists in Quebec, 1991	85
TABLE A8.2 Diagnostic procedures performed by optometrists in Quebec, 1991	86
TABLE A8.3 Prescriptions for beta-blockers in the form of eyedrops in Quebec, 1992	87
TABLE A8.4 Glaucoma-related therapeutic procedures performed by medical specialists in Quebec, 1991	88

INTRODUCTION

In June of 1992, the Minister of Health and Social Services asked the *Conseil d'évaluation des technologies de la santé du Québec* for advice on glaucoma screening.

There are different forms of glaucoma, but the one of interest to us is primary open-angle glaucoma, or chronic glaucoma, which accounts for the vast majority of cases. The other forms are secondary since they result from infections, trauma or congenital malformations. Henceforth in this report, the word *glaucoma* will refer to primary open-angle glaucoma.

Primary open-angle glaucoma is a disease of the eye resulting in the progressive destruction of the optic nerve fibres[43]. It is characterized by an abnormal appearance of the optic disc and a slowly progressive loss of visual sensitivity that sometimes leads to blindness. The most important risk factor for the disease - and the only one that is modifiable - is high intraocular pressure, which is present in 50 to 65% of cases.

There is no cure for glaucoma, but early diagnosis followed by appropriate treatment can, according to the medical consensus, arrest or slow its progression. The objective of screening is therefore to prevent or delay the onset of blindness by identifying patients with glaucoma and treating them early. Such screening would also make it possible to identify people who, although they do not present a diagnosis of glaucoma, are at high risk for developing the disease because of high intraocular pressure. These individuals should also be followed and possibly treated, depending on their pressure level.

In this report, screening refers to the examination of asymptomatic individuals for the purpose of detecting a particular pathology, or even a risk factor of this pathology, in order to slow down or stop its progress. Screening can be performed in the context of an organized and systematic program. The word program in this context has been defined as "a set of resources brought together and put to use to provide organized services to a defined population in a coherent manner in time and space in order to achieve specific objectives with regard to a specific health problem"[40] Screening can also be undertaken in the context of visits to a health-care professional for another reason than the pathology targeted by the screening. This type of screening is generally referred to

as case finding [51]. This type of screening is therefore restricted to those people who consult their physician or other health-care professional.

Since the goal of screening is to proceed with early treatment, a screening program normally includes detection activities as well as treatment-related activities.

In the discussion that follows, we will assess a formal screening program for the early detection and treatment of glaucoma and high intraocular pressure.

The decision whether or not to proceed with a screening program depends on the relationship between the anticipated gains (the number of cases or of years of blindness prevented) and the disadvantages (the negative effects on health resulting from screening and treatment and the costs of such a program). The costs depend of the number of individuals who will be screened, the medical follow-up and the treatment. These estimates have to be considered in the context of diagnostic and therapeutic activities currently underway in Quebec.

The following questions must therefore be dealt with:

Efficacy of treatment. In the absence of effective treatment, screening would obviously be pointless. The first step is therefore to determine if there is a treatment that can arrest or slow the progression of glaucoma after it is detected or prevent its development in patients at high risk because of high intraocular pressure. (Chapter 1)

Diagnosis. If we assume that an effective treatment exists, what tests are required for glaucoma screening? Who is to be screened and how often? (Chapter 2)

Epidemiology. What is the frequency of detectable glaucoma in the population? What is the frequency of high intraocular pressure? And what is the frequency of blindness attributable to glaucoma? (Chapter 3)

Effectiveness of the program. What would the health benefits of instituting a glaucoma screening program be? How many cases or years of blindness would be prevented? (Chapter 4)

Cost. What would the cost of a glaucoma screening program be (i.e. the cost of the screening, patient follow-up and treatment)? (Chapter 5)

Cost-effectiveness. What would the cost-effectiveness, expressed in terms of dollars per year of blindness prevented, of such a program be? (Chapter 6)

Current situation. What is the current level of activities devoted to diagnosing and treating glaucoma? What is the outcome of these activities and what is their cost? (Chapter 7)

Recommendations of the main task forces

What are the conclusions of experts of other organizations who have studied the subject? (Chapter 8).

This study is based on a review of the literature since 1985 using the Medline, Embase and Pascal databases. We did updates on a regular basis with the aid of the reference journal *Current Contents*. The assessment of the costs and current diagnostic and therapeutic activities is based on data from the Régie de l'assurance-maladie du Québec (RAMQ).

Unless otherwise indicated, the population considered in this report is that 40 to 79 years of age. Under the age of 40, the prevalences of glaucoma and high intraocular pressure are very low. In cases detected after the age of 79, we believe that the very slow progression of the disease is such that only few of them would become blind before their death. However, it should be noted that in our analyses, we took into account the fact that cases detected between the ages of 40 and 79 would continue to be followed and treated as long as necessary, even after the age of 79.

1. EFFICACY OF TREATMENT (see also Appendix 1)

TREATMENT

The objective of all the forms of glaucoma treatment is to lower intraocular pressure, the ultimate goal being to prevent the onset or progression of glaucoma. Although the distribution of intraocular pressure in the population does not follow a normal curve, the cutoff point for high pressure is usually defined as being two standard deviations from the mean, or 21 or 22 mm Hg. However, this does not make it possible to determine a normal value defining the success or failure of treatment because visual field loss is observed at all pressure levels [32].

There are three main methods for lowering intraocular pressure: drugs; trabeculoplasty, which is performed with a laser; and trabeculectomy, which is a surgical procedure. Drugs are almost always used first, the main agents prescribed being beta-blockers. The other drugs available are adrenaline, or epinephrine, pilocarpine and carbonic anhydrase inhibitors, such as acetazolamide. New compounds, including alpha-blockers, such as apraclonidine, and prostaglandin analogs [43], are presently being evaluated.

Another strategy for lowering intraocular pressure is trabeculoplasty, which is usually reserved for patients in whom drugs have failed. Trabeculoplasty consists in creating, with the aid of a laser, small scars in the trabecular meshwork [15, 42]. Through a poorly understood mechanism possibly involving the production of factors that regulate cell function, these scars facilitate the flow of aqueous humor across the corneoscleral trabecula, thus promoting a decrease in pressure [1, 43]. However, most patients have to continue using drugs after the laser treatment. In about 50% of cases, the pressure reverts to elevated values in less than five years. Subsequent laser treatments are not as effective as the first one.

Surgical treatment by trabeculectomy is usually reserved for patients in whom drugs and trabeculoplasty have failed. Trabeculectomy consists in resecting a deep portion of the corneoscleral limbus containing the trabecular meshwork [17]. In principle, this produces a permanent channel for the drainage of aqueous humor [44]. According to Quigley, the five-year success rate is 75%. Trabeculectomy was popularized about 20 years ago, but the surgical methods continue to evolve. In cases where surgery is unsuccessful in lowering the intraocular pressure, consideration must be

given to performing another trabeculectomy or to using other surgical methods, such as implanting plastic tubing to form a shunt that would facilitate aqueous humor circulation, or, instead, decreasing the production of aqueous humor by selective destruction of the ciliary body. These treatments are accompanied by many harmful effects.

EFFICACY OF TREATMENT

It is well established that the various treatments available successfully lower intraocular pressure. For example, a meta-analysis of six randomized studies published between 1985 and 1991 showed that medical treatment leads to a modest but statistically significant reduction in intraocular pressure.

In the six therapeutic trials in question, each of which included a comparison group receiving placebo, the mean reduction in pressure was 4.9 mm Hg [49] .

However, the ability of this pressure reduction to prevent or slow the development of glaucoma is less certain. Although it accepts the medical consensus that glaucoma treatment is probably effective, the U.S. Office of Technology Assessment points out that this opinion is based on theoretical considerations, clinical experience, and postulates shared by physicians rather than on direct demonstrations [42].

In their meta-analysis, Rosetti et al. identified only three randomized trials of the treatment of high intraocular pressure with eyedrops, including visual field loss as a measure of effect. Two of these three studies suggested that the treatment was effective, but with a marginal level of statistical significance. The other study [53] did not show the treatment to be effective. This meta-analysis concluded that these studies, taken together, suggest an efficacy of 25% (odds ratio: 0.75, 95% confidence interval: 0.42 to 1.35) (see Appendix 1).

However, other, more indirect and less rigorous data support the hypothesis that treatment is effective. For example, in a non-randomized group of 20 patients treated for glaucoma, it was observed that the development or progression of the disease was less severe in those in whom the lowering of intraocular pressure was more successful [64]. Similarly, in 1992, the American Academy of Ophthalmology concluded that animal research and various clinical observations suggest that lowering intraocular pressure prevents or slows any new destruction of the optic nerve in most patients [1].

The randomized studies discussed above concerned the treatment of patients presenting only high

intraocular pressure, without having been diagnosed as having glaucoma. According to the American Academy of Ophthalmology, no randomized trial concerning the impact of the treatment of primary open-angle glaucoma has been conducted, and such a study would not be acceptable for ethical reasons. According to the Academy, however, the weight of the indirect evidence of the effectiveness of treatment continues to increase.

However, the ability of treatment to lower intraocular pressure apparently varies with the therapeutic agent, the state of the disease, the presence of aggravating factors, and the level of therapeutic compliance [1]. The following examples illustrate these various elements. It was reported that the success of trabeculoplasty, measured by the ability to maintain the intraocular pressure at the desired level, was 46% after five years [1], whereas for trabeculectomy, the figure was 75% (efficacy varying with the therapeutic agent) [43]. When a new operation is required, subsequent trabeculectomies are not as effective as the initial trabeculectomy (efficacy variation as a function of the state of illness) [1]. The trabeculectomy is also less effective in the case of people having had cataract surgery (efficacy variation as a function of the presence of aggravating factors) [1]. Finally, ophthalmic eye-drop therapeutic compliance was better among patients receiving a beta-blocker twice a day than among patients treated with pilocarpine 4 times a day (compliance variation as a function of the therapeutic agent) [43]. In the analysis of a screening program, one can surely not count on perfect therapeutic compliance on the part of patients. Treatment for glaucoma involves certain costs for patients, may require daily care, does not generally present obvious immediate effects, and is accompanied by harmful effects [18].

To sum up, although it has not been demonstrated, there is a strong medical consensus that the onset or progression of glaucoma can be prevented or slowed by considerably reducing the intraocular pressure by means of various treatments used alone or in different combinations. The only rigorous studies on the efficacy of treatment conducted thus far have been limited to determining the effect of eyedrops.

However, it is generally believed that pressure reductions larger than those obtained in the studies in question would be more effective. New studies that might clarify this matter are now under way. They include the Early Manifest Glaucoma Trial, in Sweden [22], and the Normal Tension Glaucoma Study [51].

However, while awaiting the completion of these studies, we have to take decisions on screening, on the basis of expert opinions and the very limited data described above. In the light of this uncertainty, and giving the benefit of the doubt to the idea that screening would be effective, we have assumed an efficacy of 50% for our main analyses, and estimates of 30% and 70% for our sensitivity analyses.

2. DIAGNOSIS

Glaucoma is characterized by anatomical changes affecting the optic disc and a function loss in the visual fields. The intraocular pressure is high in 50 to 65% of cases. Most authors agree that at least two of the following three elements must be present before one can make a diagnosis of glaucoma: a) changes in the optic disc; b) visual field defects; and c) high intraocular pressure.

EXAMINATION OF THE OPTIC DISC

The optic disc is observed by examining the optic fundus. The normal optic disc is the site of passage of more than a million axons which form at this point the end of the optic nerve and which connect the retina to the brain. It is often observed that the axons do not fill the entire optic disc, thus creating a physiologic depression at its centre called the cup. When, during the evolution of glaucoma, nerve fibres die, the rim of tissue formed by the optic nerve becomes thinner, causing the cup to enlarge. This cupping is characteristic of glaucoma. The ratio of the cup diameter to the diameter of the entire disc is used to assess the condition of the optic nerve. The normal cup-to-disc ratio is about 0.3. When the ratio reaches or exceeds 0.6, the likelihood of pathology increases rapidly.

When examining the fundus, one can also observe the nerve fibres outside the disc, in the retina. Decreases in the visibility of these nerve fibres are present in 90% of patients with glaucoma [43].

The accuracy of the examination depends mainly on the examiner's skill, but also on the type of ophthalmoscope used, i.e. monocular or stereoscopic, and on patient preparation, in particular, by pupillary dilation. Observing the optic disc is subject to a great deal of interobserver variability, and damage is difficult to detect during the onset of the disease, when the examination could be the most useful [37]. The subjectivity and variability of the examinations can be reduced by using fundus photographs read with a double-blind method [4]. With such photographs, one can measure and detect discrete damage and follow its evolution.

EXAMINATION OF THE VISUAL FIELD

After a certain amount of time, the anatomical lesions associated with glaucoma lead to function loss, i.e. visual field defects. These defects can be documented by mapping visual stimuli perceived by the patient. This procedure is known as *perimetry* and is performed with manual or automated

methods. The use of automated instruments has improved test precision and speed.

MEASURING INTRAOCULAR PRESSURE

Increased intraocular pressure alone does not permit a diagnosis of glaucoma, but it is an important risk factor for this disease. Intraocular pressure is measured with a Schiottz or Goldmann tonometer.

The Schiottz tonometer is an impression tonometer; the pressure is determined from the indentation made on the eye by a plunger. The Goldmann tonometer is an applanation tonometer; the pressure is measured as a function of the force applied and the resulting corneal deformation. A more recent apparatus, the air-puff tonometer, makes it possible to measure intraocular pressure using a jet of pressurized air, which eliminates direct contact with the cornea. The air-puff tonometer has a tendency to overestimate the pressure and loses some of its accuracy on rigid, scratched or edematous corneas. It is very useful in wide-scale screening programs because it involves very little risk of corneal lesions [50].

The mean intraocular pressure in patients who do not present any signs of glaucoma is about 16 or 17 mm Hg, and the pressure is not necessarily the same in both eyes. Generally, a diagnosis of high pressure is made when a pressure higher than 21 mm Hg is measured on three occasions, which reduces the effect of individual and nyctohemeral variations. This criterion of 21 mm Hg has been derived from epidemiologic studies of the distribution of intraocular pressure and is not a cut-off point separating the healthy population from the glaucomatous one. According to Leske, the distribution of intraocular pressure does not follow a normal curve; the pressure of 21 or 22 mm Hg is apparently two standard deviations above the population mean [32].

Despite an important association between high intraocular pressure and glaucoma, there are cases of glaucoma in the absence of high pressure and cases of high pressure without glaucoma. These relationships will be explored in greater detail below [17].

GONIOSCOPY

Open-angle glaucoma can be distinguished from narrow-angle glaucoma from the anatomical condition of the iridocorneal angle. Gonioscopy is an examination of the iridocorneal angle with a special contact lens, most often with the aid of a slit-lamp biomicroscope.

3. EPIDEMIOLOGY

To plan a screening program, one must have data on the prevalence and incidence of glaucoma, its risk factors and the resulting blindness. The data available for Quebec are very fragmentary. We therefore had to obtain estimates from the results of studies conducted elsewhere. The methods used are described in Appendices 2 to 5, the conclusions of which are presented below.

RISK FACTORS (see also Appendix 2)

The main risk factors affecting the prevalence and incidence of glaucoma are old age, high intraocular pressure and a family history of glaucoma. These factors and others that are less important or understood less clearly, such as the fact of being black, severe myopia, diabetes and high arterial blood pressure, form the subject of Appendix 2.

Briefly, according to published data, the prevalence increases with age. In whites, the prevalence rate is about 1% at age 40 and increases to about 5% or more in people aged 70 or older.

The frequency of glaucoma is also associated with intraocular pressure. Armaly et al. observed a 12.41% risk of glaucoma occurring after six years of follow-up in individuals presenting a pressure ≥ 20 mm Hg versus 1.46% when the pressure was lower. The Baltimore survey showed a continuous association between the prevalence rate and intraocular pressure, the prevalence rate ranging from 0.65% in individuals with an intraocular pressure ≤ 15 mm Hg to a rate of 26% in those with a pressure of about 35 mm Hg (Table A2.2).

Despite this association, one must take into account the fact that about 30 to 50% of the new cases of glaucoma appear in people who do not present high pressure. An effective screening program must therefore include detecting cases of glaucoma instead of focusing solely on the detection of cases of high pressure.

The prevalence of glaucoma varies between blacks and whites. It is high among West Indian and American blacks [31, 34, 61], for whom rates of 6.9% [31] to 8.8% in individuals aged 30 years or older have been reported.

The effect of other factors, such as severe myopia, diabetes and high arterial blood pressure, which is discussed in Appendix 2, is too weak or not understood well enough to have an impact on the planning of a screening strategy.

THE EPIDEMIOLOGY OF GLAUCOMA IN QUEBEC (see also Appendix 3)

To estimate the prevalence rate of glaucoma in Quebec, we applied data from two American studies, undertaken in Beaver Dam, Wisconsin and in Baltimore, Maryland [61], to the age and gender structure of the Quebec population aged 40 to 79 years. As a result, we obtained two quite similar estimates of 1.57% and 1.31%. For the reasons described in Appendix 3, we have used the rate estimated on the basis of data derived from the Beaver Dam study, or 1.57%, which represents 40,901 cases in Quebec, of which 28,588 had high intraocular pressure, and 12,313 had normal pressure. In the sub-category of people from 65 to 79 years of age, the prevalence of glaucoma was 19,506 cases, including 14,201 cases with high pressure, and 5,305 with normal pressure.

To estimate incidence, we once again used the data from the Beaver Dam study, which we applied to the Quebec population [41]. Consequently, we obtained a figure of 2,715 new cases of glaucoma per year in Quebec among people aged 40 to 79 years. An estimate on the basis of data from the Framingham study suggests a lower incidence, of the order of 1,733 cases per year. Once again, we used the Beaver Dam data in our subsequent calculations.

THE EPIDEMIOLOGY OF HIGH INTRAOCULAR PRESSURE IN QUEBEC (see also Appendix 4)

To estimate the prevalence rate of high intraocular pressure (> 21 mm Hg) in Quebec, we used the rates calculated by Gottlieb and those from the Baltimore and Beaver Dam studies. Our estimate for Quebec was 6% for people from 40 to 79 years of age, which amounts to 156,433 expected cases. We estimated above the prevalence of glaucoma with high pressure to be 28,588 cases; the prevalence of high pressure without glaucoma is therefore: 156,433 cases - 28,588 cases = 127,845 cases. Using the same calculation method, the prevalence of high pressure without glaucoma among people 65 to 79 years of age would be 44,075 cases (=58,276 - 14,201 cases).

PREVALENCE OF GLAUCOMA AND OF HIGH INTRAOCULAR PRESSURE

On the basis of estimates in the preceding paragraphs, we determined the prevalence of subjects

having either high intraocular pressure without glaucoma or glaucoma without high pressure, or both:

- a) High intraocular pressure without glaucoma:
40 - 79 years old: 127,845 cases
65 - 79 years old: 44,075 cases
- b) Glaucoma with high pressure:
40 - 79 years old: 28,588 cases
65 - 79 years old: 14,201 cases
- c) Glaucoma without high pressure:
40 - 79 years old: 12,313 cases
65 - 79 years old: 5,305 cases
- d) Total, high intraocular pressure, or glaucoma, or both:
40 - 79 years old: 168,746 cases
65 - 79 years old: 63,581 cases

EPIDEMIOLOGY OF BLINDNESS ATTRIBUTABLE TO GLAUCOMA IN QUEBEC

(see also Appendix 5)

There are very few data on the incidence and prevalence of blindness due to primary open-angle glaucoma. Statistics of the Canadian National Institute for the Blind, which are discussed in greater detail in Appendix 5, suggest that the incidence in Quebec among people 40 years and over is around 140 cases per year. Our estimate of prevalence is around 1,260 cases. Among people 65 to 79 years old, we estimated the incidence at 125 cases per year and the prevalence at 1,021 cases.

We estimated the average age at which blindness is diagnosed among people 40 years and over at 78 years; the life expectancy at this age is nine years. Among people 65 years and over, the average age at which blindness is diagnosed is 81 years, and the life expectancy at this age is approximately eight years.

We also estimated the frequency of partial blindness. The epidemiologic data on this question are

particularly weak. On the basis of a study undertaken in the United Kingdom, we estimated the number of new cases of partial blindness in Quebec at 114 per year, and the prevalence at 1,026 cases. The prevalence of blindness as a whole, whether complete or partial, represents 2,286 cases, of which 1,260 are cases of complete blindness and 1,026 cases of partial blindness.

4. EFFECTIVENESS OF A SCREENING PROGRAM

We already estimated the prevalence of blindness due to glaucoma in Quebec among people 40 years and older to be 1,260 cases, and among people from 65 to 79 to be 1,021 cases. The data of the Canadian National Institute for the Blind indicate that some 50% of cases of blindness due to glaucoma occur among people at or over the age of 80 years, and 9% among subjects at or over the age of 90 years. Because of the generally slow progression of glaucoma, we assumed in our analyses that all of these cases of glaucoma could be detected before the subjects reached the age of 80 years.

TOTAL BLINDNESS

The number of cases prevented by screening depends on the diagnostic tests used, the program's participation rate, therapeutic compliance and the efficacy of treatment. If, for example, diagnostic tests include a funduscopy and tonometry, while program participation and therapeutic compliance are each 75%, and the treatment efficacy is 50%, the number of cases of blindness prevented in a steady state would be $(1,260 \text{ cases}) \times (0.75) \times (0.75) \times (0.5) = 354 \text{ cases}$. On an annual basis, this would correspond to 354 person-years.

We can reach the same result by using the incidence rate of blindness as a point of departure for our calculations. The incidence of blindness was estimated earlier as being 140 cases/year. The number of new cases prevented each year in the conditions described in the preceding paragraph would then be $(140 \text{ cases}) \times (0.75) \times (0.75) \times (0.50) = 39.4 \text{ cases/year}$. The average age at which these cases were diagnosed would be 78 years, at which age life expectancy is around nine years. As a result, the reduction in the prevalence of blindness in the population would be $(39.4 \text{ cases/year}) \times (9 \text{ years}) = 354 \text{ cases}$.

The number of cases prevented by screening is affected by the diagnostic tests used. In the case of programs only including tonometry during the initial screening test, we have assumed that 70% of cases of glaucoma would be detected (Table A3.3). The number of cases of blindness prevented would then correspond to 70% of the number prevented when the funduscopy and tonometry are used during the initial exam. The prevalence calculated for screening offered to people from 40 to 79 years of age would then become $(0.7) \times (354 \text{ cases}) = 248 \text{ cases}$. Among people from 65 to 79 years of age, we have estimated that 73% of cases would be detected if tonometry alone were used (Table A3.3).

In all of our calculations, we assumed that people not participating in screening represent a random sample of the population. In that case, a participation rate of 75%, for example, will reduce costs and effectiveness by a factor of 25%, without affecting the cost-effectiveness ratio as a result. Analysing the impact of the participation rate can however be far more complex; we could take into account for example such factors as the relationship between the risk of glaucoma and the probability of participating in screening. These questions have not been considered in detail in the present study, because they are complex and we lack information about them.

PARTIAL BLINDNESS

It is difficult to incorporate both years of partial blindness and years of total blindness in a single index of effectiveness. Blindness is a gradual phenomenon, associated with varying degrees of handicap. In the calculations presented above, however, we confined ourselves to total blindness. In other analyses, we considered the prevention of complete or partial blindness as a criterion of effectiveness instead. Earlier on, we estimated prevalence at 2,286 cases, of which 1,260 were cases of complete blindness and 1,026 were cases of partial blindness. The prevalence of complete blindness therefore represents 55% of the prevalence of complete or partial blindness (1,260 cases divided by 2,286 cases). This percentage remains the same whatever scenario is used in terms of treatment efficacy, the frequency of screening, the rate of participation, therapeutic compliance and the diagnostic tests used in the screening examinations.

Consequently, to the years of total blindness prevented thanks to the different screening scenarios described in Table 2, we can add a certain number of years of partial blindness, representing a percentage estimated at 45% of the total years of total and partial blindness.

5. COST OF A SCREENING PROGRAM (see also Appendix 6)

All the costs mentioned in this report are expressed in 1994 Canadian dollars, from the point of view of the Quebec government, and, unless otherwise noted, of the Ministère de la Santé et des Services sociaux.

All of our calculations assume that each time screening is repeated, the population will have kept the same structure when it comes to age and gender. In fact, according to the projections of the Bureau de la statistique du Québec, the population aged 40 to 79 might be 28% larger in the year 2011 than it was in 1991, with a modified distribution by age. This will have an impact on the total costs of a screening program, something we have not taken into account here. However, the cost-effectiveness ratios discussed in the following section will remain the same, whatever Quebec's population structure.

We determined first of all the cost of a program that would be offered to the Quebec population aged 40 to 79 (in 1991, 2,607,210 people). First, we present here the cost of a screening program that would be carried out in toto by ophthalmologists and repeated every year. Since this cost includes items such as office overhead, we used the fees for procedures performed in offices, which are higher than those for procedures performed in hospitals. Unless otherwise indicated, we assumed in the calculation of costs, as we already did in the estimate of effectiveness, that no glaucoma-related diagnostic or therapeutic services are currently available to the Quebec population.

The calculations were made separately for the cost of diagnosis and that of monitoring and treatment. Details are presented in Appendix 6.

The costs of diagnostic tests associated with an annual screening program involving the entire population between the ages of 40 and 79, and including funduscopy and tonometry during the initial examination, have been estimated to be \$77,594,742. This represents the costs of visits to the doctor (which in turn includes tonometry and funduscopy), gonioscopy and perimetry. A program offered every three years, with 75% of the population participating, would cost \$19,668,325.

The cost of monitoring and treating patients with glaucoma or high intraocular pressure was estimated at \$29,718,651 a year, assuming 100% participation in screening and therapeutic

compliance. This includes the cost of the medical visits, retinophotography, perimetries, gonioscopies, fundus examinations with a contact lens and dilation, drugs, trabeculoplasties and trabeculectomies.

Appendix 6 presents other screening scenarios and gives details on the calculation of costs that correspond to these scenarios.

COSTS OF BLINDNESS

To calculate the direct net cost of screening, we should take account of the costs avoided thanks to the prevention of cases of blindness. We have therefore considered the costs associated with blindness itself. Indeed, blind people receive the benefits of care, services and equipment covered by the State. We identified three sources of costs: the Régie de l'assurance-maladie du Québec's visual aids program, the rehabilitative services offered to the visually handicapped, and the disability pensions from the Régie des rentes du Québec. Our estimate of these costs is \$3,000 per case of blindness per year. For individuals aged 65 years or older, our estimate is \$1,500. This latter figure may be exaggerated because the older a person is, the less he or she tends to resort to certain rehabilitative services, such as the teaching of braille. However, we were unable to include other costs, such as those of services provided by the local community service centres (CLSCs), which may have resulted in a certain underestimation of the costs.

6. COST-EFFECTIVENESS

Several variables would affect the cost-effectiveness (see Table 1). The effects of some of these variables on the cost-effectiveness estimates for the different hypothetical screening programs considered here are summarized in Table 2. The benefits and costs are once again estimated on the assumption that there are presently no glaucoma-related activities in Quebec and that the screening program has attained a steady state. We have taken account in these calculations of costs avoided thanks to the prevention of blindness, whether they be the costs of care, services or of equipment offered to blind people (Section 5 and Appendix 6).

SCENARIO 1

Table 2 presents, for scenario 1, estimates of the cost and results of screening performed every three years, assuming a screening participation rate of 75%, therapeutic compliance of 75% and treatment efficacy of 50%. Also, our calculations assume that treatment would be effective as soon as it is instituted, i.e. the progress of glaucoma is interrupted starting in the first year of the screening program. In this scenario, from the first year of the screening program, 39.4 new cases of blindness (rounded off to 39 cases in Table 2) will be prevented each year. We estimated earlier on that these subjects would have a life expectancy of nine years, which translates into a reduction of the prevalence of blindness in the population, in a steady state, of $(39.4 \text{ cases/year}) \times (9 \text{ years}) = 354$ cases. This scenario is associated with costs of \$36.4 million per year or \$100,000 per year of blindness prevented. This ratio was calculated using the following formula: $[(\text{total annual cost}) \div (\text{years of blindness prevented per year})] - (\text{annual cost of blindness}) = (\$36.4 \text{ million} \div 354 \text{ years}) - \$3,000$.

SCENARIO 2

Scenario 2 is based on the same assumptions as scenario 1, except that it depicts an annual screening program, which is the frequency recommended by some. In a steady state, this scenario would cost \$74.9 million a year with a cost-effectiveness of \$208,000 per year of blindness prevented.

SCENARIOS 3 TO 9

In scenarios 3 to 9, we examine the effect of different screening frequencies (scenario 3), screening participation rates (scenarios 4 and 5), rates of therapeutic compliance (scenarios 6 and 7) and levels of treatment efficacy (scenarios 8 and 9) on cost-effectiveness. If the treatment efficacy is 70% (scenario 9), the cost-effectiveness in a steady state would be \$70,000 per year of blindness avoided.

If it were shown that screening could be done only every five years without a loss of effectiveness (scenario 3), the cost-effectiveness in a steady state would be \$78,000 per year of blindness prevented (in all the calculations presented in Table 2, we assumed that the program's effectiveness was not affected by the frequency of screening, whether that screening be undertaken every year, every three years or every five years). However, as mentioned in Appendix 7, it would seem scarcely probable that screening undertaken every five years would actually be sufficient.

SCENARIO 10

The scenarios examined thus far pertain to the entire population aged 40 to 79. We also considered other types of programs aimed at higher-risk groups. The most important risk factor for glaucoma is age. In scenario 10, we examine the results of a screening program limited to people aged 65 to 79.

It is seen that the costs would decrease considerably. Such a program would cost, in a steady state, \$12.6 million a year. The cost-effectiveness in a steady state would therefore be \$42,000 per year of blindness prevented. However, since it would be limited to an older population, this program would succeed, in a steady state, in preventing 287 years of blindness a year, which is 81% of the figure given in scenario 1.

We also estimated the cost-effectiveness of a program restricted to people from 65 to 79 years of age and offered once every five years (the results are not included in Table 2). The total cost would be reduced to around \$10.8 million. We do not know in what way the effectiveness of the program would be affected, but if it is assumed that the effectiveness of such a program would be the same as for screening that was offered every three years, cost-effectiveness would be reduced to \$36,000 per year of blindness prevented. Spacing screening tests further and further apart clearly results in more and more limited gains in terms of cost-effectiveness. This can be explained by the fact that the portion of costs associated with monitoring and treatment (this portion amounts to \$8.1 million for people between the ages of 65 and 79) is not affected by the frequency of screening.

SCENARIOS 11 AND 12

Thus far, all the diagnosis cost estimates have been based on ophthalmologist's fees. Theoretically, we could envisage the involvement of other professionals, such as optometrists, general practitioners or other professionals adequately trained to perform certain tests (see Appendix 6). To examine this aspect, we used the costs of optometric procedures. In scenario 11, we explore the effect that this type of change in fees could have on the total cost. If the entire population aged 40 to 79 is included, we observe, in a steady state, a reduction of only 17% in the annual cost and in the cost-effectiveness in relation to the conditions defined in scenario 1. The same substitution of fees in a program aimed at people aged 65 to 79 (scenario 12) gives a cost-effectiveness of \$37,000 per year of blindness prevented, which is 12% lower in relation to scenario 10.

SCENARIOS 13 AND 14

We also analyzed screening programs aimed at detecting cases of high intraocular pressure. We first considered, in scenario 13, a screening program offered to people aged 40 to 79 that would consist in measuring their intraocular pressure every three years for the purpose of identifying those with a pressure higher than 21 mm Hg. Unlike the preceding scenarios, in this one, additional diagnostic tests, namely a fundus examination and perimetry, would only be administered to people presenting high pressure. Currently, there is no fee for tonometry performed by an ophthalmologist. For our analysis of these strategies, we arbitrarily assumed a cost of \$8 for this test. We assumed that the cases of high pressure in which no other abnormality was found would be looked after in the same manner as in scenario 1. In other words, these patients would be monitored by their physician, and some of them would be treated in order to lower their pressure (see Appendix 6).

This scenario would be less costly and would succeed in preventing 248 years of blindness per year in a steady state, which corresponds to a cost-effectiveness of \$74,000. For the purpose of these calculations, we considered the most favourable situation possible. In particular, we assumed that 70% of cases of glaucoma occur among people with high intraocular pressure. This percentage is in line with data in the scientific literature, but it is possible that the real percentage is lower, possibly below 50% [32]. If that were the case, then the cost-effectiveness of a screening program based on measuring high intraocular pressure would be less favourable than that presented in scenario 13.

In scenario 14, we modified this program, limiting it to people aged 65 to 79. Such a program would cost \$7.7 million in a steady state, with a cost-effectiveness of \$36,000 per year of blindness prevented. However, it would prevent only 209 years of blindness a year, which is 59% of the number that would be prevented with the scenario 1 program. However, even this estimate of 209 years of blindness prevented per year is surely overly optimistic, given the favourable assumptions that we made at several stages in our calculations.

TOTAL OR PARTIAL BLINDNESS

The scenarios presented above used total blindness as the sole effectiveness criterion. If, instead, all the cases of total and partial blindness are taken into consideration, the costs would be the same, but the cost-effectiveness would be 55% less than the estimates given in Table 2. However, this factor of 55% is applicable only if we attach the same importance to total blindness and partial blindness. More rationally, partial blindness should be weighted less, in which case the cost-effectiveness would tend to approach the values calculated for total blindness.

DISCOUNTING

In the analysis model we used, the discounting of costs and of effectiveness does not seem appropriate. Indeed, we assumed throughout that the efficacy of treatment was immediate, i.e., that treatment caused the progress of the illness to cease. Given the fact that every year, including the year in which the program started up, some people would go blind, interrupting the progression of their illness could prevent blindness as soon as the program begins. From this point of view, each annual investment made in the health-care system for a screening program would bring about an immediate reduction in the prevalence of blindness. The costs and effectiveness are both within the same time-frame, making discounting irrelevant.

TABLE 1. CERTAIN VARIABLES AFFECTING THE COST-EFFECTIVENESS ESTIMATES FOR GLAUCOMA SCREENING

VARIABLE	MAIN ESTIMATE CHOSEN	OTHER ESTIMATES	IMPACT ON COST-EFFECTIVENESS ESTIMATE
Screening frequency	Every 3 years	Every year; every 5 years	See Table 2
Screening participation rate	75%	60%; 90%	See Table 2
Therapeutic compliance	75%	60%; 90%	See Table 2
Efficacy of treatment	50%	30%; 70%	See Table 2
Prevalence of glaucoma	1.57%	1.31%	Higher % corresponds to higher treatment costs.
Incidence of total blindness due to glaucoma	140 cases/year	Not considered	---
Incidence of partial blindness due to glaucoma	114 cases/year	Not considered	---
Percentage of cases of glaucoma detectable by tonometry	70% (40-79 years) 73% (65-79 years)	Not considered	---
Total cost of treatments	\$353/person/year	Not considered	Conservative estimate: the cost would probably increase during the follow-up period.

TABLE 2. COST-EFFECTIVENESS: SENSITIVITY ANALYSIS ACCORDING TO DIFFERENT SCREENING SCENARIOS

Scenario	Screening frequency (years) and ages		Screening participation rate (%)	Therapeutic compliance (%)	Gross annual cost (\$ millions)			Efficacy of treatment (%)	Blindness prevented per year		Cost per year of blindness prevented ^a (\$)
					Diagnosis	Monitoring and treatment	Total		New cases prevented	Years prevented	
1	3	40-79	75	75	19.7	16.7	36.4	50	39	354	100 000
2	1	40-79	75	75	58.2	16.7	74.9	50	39	354	208 000
3	5	40-79	75	75	12.0	16.7	28.7	50	39	354	78 000
4	3	40-79	60	75	15.7	13.4	29.1	50	32	284	100 000
5	3	40-79	90	75	23.6	20.1	43.7	50	47	425	100 000
6	3	40-79	75	60	19.7	13.4	33.0	50	32	284	114 000
7	3	40-79	75	90	19.7	20.1	39.7	50	47	425	90 000
8	3	40-79	75	75	19.7	16.7	36.4	30	24	213	168 000
9	3	40-79	75	75	19.7	16.7	36.4	70	55	496	70 000
10	3	65-79	75	75	4.4	8.1	12.6	50	35	287	42 000
11	3	40-79	75	75	13.4	16.7	30.1	50	39	354	82 000
12	3	65-79	75	75	3.0	8.1	11.1	50	35	287	37 000
13	3	40-79	75	75	5.2	13.8	19.0	50	28	248	74 000
14	3	65-79	75	75	1.2	6.6	7.8	50	26	209	36 000

^a [(Total annual cost) ÷ (years of blindness prevented each year)] - (annual cost of blindness); rounded off to the nearest thousand.

Scenarios 11 and 12: screening as envisaged in scenario 1 but with lower fees for the initial diagnostic tests.

Scenarios 13 and 14: screening by means of tonometry, assuming a cost of \$8 per examination, every three years; people with high pressure would be looked after in the same manner as in the other scenarios.

7. NUMBER OF DIAGNOSTIC AND THERAPEUTIC PROCEDURES PERFORMED IN QUEBEC IN 1991 (see also Appendix 8)

Thus far, all our calculations have assumed that there are no glaucoma-related diagnostic or therapeutic activities in Quebec. In reality, there are currently several such activities, probably undertaken to a very large extent in a case finding context, i.e. visits to a physician or optometrist for other reasons than glaucoma. Since most people visit one or the other of these categories of professional on a more or less regular basis, we can expect the coverage of the population to be very great.

According to data from the Régie de l'assurance-maladie du Québec, in 1991, 966,618 people aged 40 to 79 underwent tonometry by an optometrist or a complete visual examination, including tonometry, by a medical specialist, whether an ophthalmologist or other specialist. There are approximately 2.6 million people aged 40 to 79 in Quebec. We do not know how often these examinations are repeated. However, if we assume an average interval of three years between them, we can conclude that most of the people in this age group are already covered periodically for an examination aimed at detecting glaucoma. However, this assumption has yet to be verified.

In terms of years of blindness prevented, the benefits of these activities are not known. However, we can estimate the number of cases of glaucoma or high intraocular pressure that are currently being treated. We know that in 1991, 26,840 people aged 65 to 79 received prescriptions for timolol, betaxolol or levobunolol eyedrops. These drugs are used only to lower intraocular pressure. The epidemiologic data that we have indicate that the number of people in this age group who should be under treatment is 25,334 (see Appendix 8). Therefore, these calculations suggest the possibility that most of the people aged 65 to 79 requiring treatment are presently being looked after, in a case finding context, and in the absence of a systematic screening program. However, based on the discussion in Appendix 8, these calculations are subject to error, so they should be considered with caution.

The cost of these activities cannot be estimated with precision. In 1991, the cost of all the diagnostic and therapeutic activities performed by optometrists or ophthalmologists, and which can be attributed almost exclusively to glaucoma, was \$16,817,469. This figure represents the cost of the visual field measurements effected by medical specialists and optometrists, the tonometries and biomicroscopies performed by optometrists, and all the costs of the drugs and therapeutic procedures covered by the Régie de l'assurance-maladie du Québec (Appendix 8). However, this figure is a minimum, for one would also have to attribute to glaucoma a portion of the cost of the complete examinations by optometrists and of the main visits to ophthalmologists. In 1991, the total cost of these complete examinations and main visits was \$25,651,146, although it is not known what proportion of this figure is directly attributable to glaucoma.

In comparison, the estimated annual cost of a planned program for people aged 40 to 79 with a three year frequency and 75% participation rate, after it has reached a steady state, would be \$36.4 million (scenario 1). Therefore, ignoring for the time being the whole question of the effectiveness of screening and treatment, glaucoma-related activities in Quebec in 1991 had already entailed costs of the same order of magnitude as our estimate of the cost associated with a planned program (i.e. almost 100% of \$16,817,469 plus an unknown portion of \$25,651,146). Even the planned program (scenario 1) would achieve a cost-effectiveness of only \$100,000 per year of blindness prevented. It should be noted that the current activities are probably less effective than a planned program would be. Therefore, the cost-effectiveness of these activities is even higher.

8. RECOMMENDATIONS BY THE MAIN TASK FORCES

In general, the different task forces believe that screening consisting solely in measuring intraocular pressure is not sufficient. Instead, they consider that a complete visual examination is necessary.

According to the U.S. Preventive Services Task Force, we do not have sufficient scientific evidence to recommend the regular use of tonometry by primary-care physicians. However, it would be a good idea to advise high-risk patients, such as those aged 65 or older, to be examined on a regular basis by an eye specialist, either an ophthalmologist or an optometrist. According to this task force, primary-care physicians often do not have the time or equipment that specialists have to perform tonometry correctly, to dilate the pupil to permit a thorough examination of the optic fundus, or to perform a precise visual-field examination [63].

The American Academy of Ophthalmology recommends, in the absence of symptoms or other indications, a complete examination whose frequency will depend on the patient's age, the level of risk for the disease and according to whether he or she is white or black. However, the Academy's recommendations are not limited to glaucoma screening. Rather, they pertain to the diagnosis and treatment of all eye diseases. Between the ages of 20 and 39, the Academy recommends an examination every three to five years for blacks and less frequently for whites. From the ages of 40 to 64, the examinations should be performed every two to four years. From the age of 65 on, an examination should be performed annually or every other year [2].

The American Optometric Association recommends that people above the age of 35 undergo tonometry on an annual basis as part of a complete eye and vision examination [63].

The Canadian Task Force on the Periodic Health Examination believes that there is not enough scientific evidence to justify including glaucoma screening in the periodic examination [11].

The U.S. Office of Technology Assessment does not make any recommendations. However, it does point out that a screening program for the elderly, for the purpose of identifying those with glaucoma or identifying those with high intraocular pressure, would be very expensive.

The following organizations do not make any recommendations: Statens Beredning för Utvärdering av Medicinsk Metodik (Swedish Evaluation Council), the French Agence nationale pour le développement de l'évaluation médicale, the Dutch Center for Medical Technology in the Netherlands, the Quebec Association of Ophthalmologists and the Quebec Association of Optometrists.

9. DISCUSSION AND RECOMMENDATIONS

DEFINITIONS

In this report, the word *screening* refers to the examination of asymptomatic individuals in order to detect a particular pathology, or a risk factor of this pathology, in order to slow down or stop its progress. A clinical examination performed because of a family history or the presence of signs or symptoms of these conditions is not considered a screening examination.

Screening normally takes place within a program, i.e. "a set of resources brought together and put to use to provide organized services to a defined population in a coherent manner in time and space in order to achieve specific objectives with regard to a specific health problem [40]." Screening can be carried out during visits to a health-care professional which are motivated by some other reason than the pathology targeted by the screening; in that case we speak of "case finding [26]."

LACK OF RELIABLE DATA

Several data essential for estimating the cost-effectiveness of a glaucoma screening program are not available. The most important element is the existence of a treatment for glaucoma or for high intraocular pressure, and an appraisal of the level of efficacy of this treatment. Such data on treatment are not available. Moreover, in order to assess such a screening program, it is important to know other factors such as the prevalence and incidence of glaucoma and of high intraocular pressure, and the incidence of blindness due to glaucoma in Quebec. We also need to know what proportion of people would agree to participate in the screening. Once the diagnosis is made, we must know how fast the untreated disease evolves into blindness and what proportion of the patients would comply with their treatment. But above all, we need to know how effective the different treatments are. None of these factors is known with accuracy.

PRESUMED EFFICACY OF TREATMENT

Although the majority of experts maintain that treatment is effective, an analysis of available information leads us to conclude that there is still some uncertainty. For this reason, in addition to the 50% estimate of efficacy which we have chosen for our main analyses, we have used estimates of 30% and 70% for our sensitivity analyses.

COST-EFFECTIVENESS

In the absence of solid information, we had to estimate the health effects and the costs of establishing a screening program, by exploring various hypothetical scenarios based on reasonable values of these parameters. The scientific data on which the choice of these values is based have always been presented explicitly. In addition, sensitivity analysis was abundantly used to test the robustness of our estimates of cost-effectiveness. In a first stage the assessment of the impact of the various screening scenarios assumed that the population did not have access to any diagnostic or therapeutic services for glaucoma. In the second stage, services currently offered were taken into account. Special attention was paid to the effect that the age of the population targeted by screening had on the efficiency of programs.

It is clear that the scenarios based on the screening of the entire population aged 40 to 79 involve high costs in relation to the benefits obtained. For example, a screening program with a three year frequency, a participation rate of 75% of the population aged 40 to 79, and an assumed therapeutic compliance of 75% (Table 2, scenario 1) would, in a steady state, cost \$36.4 million a year. If we assume a treatment efficacy of 50%, the cost-effectiveness of such a program would, once a steady state is reached, be \$100,000 per year of blindness prevented.

To obtain costs that are lower in relation to the anticipated benefits, more limited programs should be envisaged. For example, if screening is restricted to once in three years and only people from 65 to 79 years old are targeted (scenarios 10 and 12), then cost-effectiveness would be \$37,000 to \$42,000 per year of blindness prevented. Even these costs are high compared to the health benefits achieved, compared for example with estimates of \$4,500 and \$15,500 per year of life gained for breast-cancer screening and heart transplants, respectively.

RECOMMENDATION NO 1

Because establishing a health policy involves the investment of public resources, it should not be based only on the estimation of cost-effectiveness ratios, but also on a high degree of certainty. ***Our analyses do not support the setting up of a formal glaucoma screening program in Quebec, both because of the high degree of uncertainty with respect to benefits and because of the high cost such a program would entail.***

CURRENT STATE OF GLAUCOMA SCREENING IN QUEBEC

However, there already exists a significant level of diagnostic activity leading to the early detection of high intraocular pressure or glaucoma. Although this activity is not systematically organized, it currently reaches and treats some 27,000 people aged 65 to 79. At the present time, the question in Quebec is not so much whether a screening program should be established as whether current activities should be maintained.

Three considerations should be taken into account regarding this decision:

- To abolish a health service normally requires a higher degree of scientific evidence than is available in the case at hand.
- Moreover, our estimates of the cost-effectiveness ratio take account neither of the years of partial blindness that would be prevented nor of the fact that examinations performed for the detection of primary open-angle glaucoma may lead to the detection of other eye diseases which can be treated. For these reasons, it is likely that our estimates of cost-effectiveness ratios somewhat exaggerate the costs compared to the positive effects on health.
- At the same time, a large proportion of the current costs of screening are already covered by an undetermined part of complete eye exams. It would therefore be difficult to isolate and de-insure the part of exams specifically designed to detect glaucoma.

RECOMMENDATION NO 2

For these reasons, it does not seem appropriate to recommend that current screening activities be discontinued.

However, if these activities are maintained, it will be important to continue restricting them, the way they currently are, to the 65 to 79 age bracket.

Moreover, our analyses indicate that the screening tests should not be undertaken more often than every three years. It should be noted that perimetry is not included in our scenarios among the initial screening tests.

Finally, as in the case of all specialized professional procedures, it is essential to ensure the quality of those procedures and also the good degree of training of professionals involved.

APPENDIX 1. RANDOMIZED STUDIES OF THE EFFICACY OF TIMOLOL

Epstein et al. randomized 107 patients with pressures between 22 and 28 mm Hg to receive either timolol treatment or no treatment. After a mean follow-up of 53 months, the proportion of timolol-treated patients with an unsatisfactory evolution was 17.0% versus 28.8% of the untreated subjects. The criteria defining treatment failure were pressure > 32 mm Hg, optic disc deterioration, visual field loss, or a clinical judgment of vision at risk. The difference between the two groups was not statistically significant. However, an analysis taking the patients' therapeutic compliance into account showed that timolol had a protective effect. However, there is a much greater chance of bias in this type of analysis than in a simple comparison of the two randomized groups. The authors concluded that timolol is effective in patients with slightly high intraocular pressure [16].

Kass et al. observed 62 patients in whom one eye chosen at random was treated with topical timolol and the other eye with placebo. To be included in the study, the patients had to present an intraocular pressure between 25 and 34 mm Hg in both eyes. After a follow-up ranging from five to eight months, depending on the subject, visual field loss was observed in 6.5% of the treated eyes versus 16% of the untreated eyes. The difference between the two groups almost reached the conventional level of statistical significance [29].

The results of the study by Schulzer et al. differ from those of the two studies mentioned above. These authors studied 143 patients with an intraocular pressure above 22 mm Hg. The subjects were randomized to receive either timolol treatment or no treatment and were monitored for six years. An unsatisfactory clinical evolution was observed in 28.6% of the treated patients versus 30.1% of the untreated patients. Treatment failure was defined as visual field loss, disc hemorrhage or optic nerve damage. In this study, timolol was observed to lower intraocular pressure, but the drug did not modify the disease's clinical evolution [53].

Rosetti et al. performed a meta-analysis of the results of these three studies. The effect chosen was visual field loss. The combined data from these three studies indicated a rate of visual field loss in the treated subjects 25% lower than in the untreated subjects (odds ratio: 0.75). The 95% confidence interval ranged from 0.42 to 1.35, suggesting the possibility that the treatment had no effect. Therefore, at best, these data suggest modest treatment effectiveness, in the order of 25%.

Furthermore, the effect studied was visual field loss, whereas the ultimate goal of a screening program would be to prevent blindness. No randomized study evaluating blindness is presently available.

The randomized studies analyzed by Rosetti et al. only concerned timolol, not laser treatment or surgery. Furthermore, the average reduction in intraocular pressure achieved in these studies was only 3 mm Hg in the treated group in relation to the control group. According to some of the experts we consulted, it can be assumed that a treatment protocol aimed at maintaining the pressure at a lower level and which would use, if necessary, interventions more radical than drugs would lead to a higher rate of efficacy. Taking these considerations into account, as well as the significant medical consensus regarding the efficacy of treatment of glaucoma, we chose for our main analyses an estimate of efficacy of 50%. In the sensitivity analyses, we also considered estimates of 30% and 70%. We should remember, however, that the efficacy of treatment has never been demonstrated conclusively.

Another important question is therapeutic efficacy according to the pressure level treated. The three studies analyzed by Rosetti et al. only included patients with high pressure. However, patients whose pressure is considered normal are treated as well if they present other signs or symptoms of glaucoma, in order to further lower their pressure. Presently, we do not have any rigorous experimental data on this subject.

TABLE A1.1 RANDOMIZED STUDIES OF THE EFFICACY OF TIMOLOL

PARAMETERS	EPSTEIN (1989) [Erreur ! Signet non défini.]	KASS (1989) [Erreur ! Signet non défini.]	SCHULZER (1991) [Erreur ! Signet non défini.]
Groups compared	53 patients randomised to timolol; 54 not treated	62 patients : 1 eye randomized to timolol; 1 eye treated with placebo (However, according to the authors, the treatment of the other eye apparently had a pharmacologic effect on the placebo-treated eye.)	70 patients randomized to timolol; 73 not treated
<u>Inclusion criteria</u> Age in years Pressure (P) in mm Hg Visual fields Optic disc	Not specified $22 \leq P \leq 28$ in at least 1 eye Visual fields normal, Goldmann perimeter Excluded if: (1) abnormal disc cupping (2) asymmetry in cup-to-disc ratio ≥ 0.2 between the two eyes	≥ 40 $24 < P < 35$ in both eyes Visual fields normal in both eyes, Goldmann perimeter Excluded if: optic disc abnormal in at least 1 eye	45 - 70 $P > 22$ in 1 eye (?) Visual fields normal, automated perimetry Excluded if: (1) changes in the optic disc characteristic of glaucoma; (2) cup-to-disc ratio asymmetric (no exclusion on the basis of the cup-to-disc ratio itself)
Years subjects recruited	1979 - 1985	1980 - 1982	1980 - 1983
Length of follow-up	Mean follow-up: timolol, 56 months; untreated, 51 months	Minimum: 5 years in the patients who were not lost; maximum: 8 years	Minimum : 6 years in the patients who were not lost

TABLE A1.1 RANDOMIZED STUDIES OF THE EFFICACY OF TIMOLOL (Cont'd)

PARAMETERS	EPSTEIN (1989) [Erreur ! Signet non défini.]	KASS (1989) [Erreur ! Signet non défini.]	SCHULZER (1991) [Erreur ! Signet non défini.]
<u>Evaluation of effects</u> Visual fields	Goldmann perimeter: automated perimetry starting in 1982	Goldmann perimeter and automated perimetry of central field	Automated perimetry
Optic disc	Blind evaluation of photographs	Blind evaluation of photographs	Blind evaluation of photographs
<u>Main analysis</u> Definition of negative clinical events	Pressure > 32 mm Hg, deterioration of optic disc, visual field loss, or vision at risk according to clinical judgment	Visual field loss	Visual field loss, optic disc hemorrhage, or optic nerve damage
<u>Results</u> a) Difference between the treated group's pressure and that of the untreated group	Approximately 3.2	2.3	4.51
Treated group's pressure	20.2	21.6	21.77
b) <u>Proportion with unsatisfactory clinical evolution (crude %)</u>			
Treated	9/53 = 17.0%	4/62 = 6.5%	20/70 = 28.6%
Not treated	17/59 = 28.8%	10/62 = 16%	22/73 = 30.1%
Value of p (statistical test)	0.07	0.055 (one-sided)	Not significant

APPENDIX 2. RISK FACTORS

The epidemiologic literature on glaucoma has been reviewed and analyzed in detail by several authors [1,32,42,43]. The main recognized risk factors are old age, high intraocular pressure and a family history of glaucoma. The risk is higher in blacks than in whites. Other factors include severe myopia, diabetes and high arterial blood pressure.

PREVALENCE OF GLAUCOMA AS A FUNCTION OF AGE

Glaucoma is mainly a disease of the elderly. Table A2.1 presents age-specific glaucoma prevalence rate estimates according to American epidemiologic surveys conducted in Framingham, Massachusetts [41], Baltimore, Maryland [61] and Beaver Dam, Wisconsin [30]. The prevalence is observed to increase with age, hovering around 1% at about age 40 and increasing to over 5% or more in certain groups of very elderly individuals.

PREVALENCE OF GLAUCOMA AS A FUNCTION OF INTRAOCULAR PRESSURE

Several epidemiologic studies have shown that the prevalence of glaucoma is associated with the level of intraocular pressure at diagnosis. For example, Table A2.2 presents the data from the Baltimore survey [55]. The prevalence rate of glaucoma was observed to increase with high intraocular pressure. This tendency was the same in blacks and in whites.

The risk attributable to high intraocular pressure in the population is a function both of the level of risk increase in people with high pressure and of the proportion of the population with such pressure. In other words, a risk factor, even a very strong one, will, in practice, have little impact on the population if few people are exposed to it. Leske estimated the attributable risk in the population according to different situations (see Table A2.3). If we assume that the relative risk is fairly high, say, about 6, but that only 5% of the population has high pressure, the risk attributable to high pressure in the population would be 20%, which means that in the context of a screening program limited to measuring intraocular pressure, 80% of the cases would not be detected. Table A2.3 presents other scenarios as well. Even in a much more favourable situation where the relative risk is 10 and the proportion of people with high pressure 10%, the risk attributable to high intraocular pressure would only be 47.4%.

PREVALENCE OF GLAUCOMA IN WHITES AND BLACKS

In North America and in the West Indies, the prevalence of glaucoma is higher in blacks than in whites. This factor is noteworthy because there is a large African and West Indian population in the Montreal area. In a study conducted in Baltimore, the prevalence of glaucoma was observed to be four to five times higher in blacks than in whites [61]. In St. Lucia, the prevalence of glaucoma in blacks aged 30 or older was 8.8%. This estimate was based on the number of individuals who had undergone screening tests followed, where appropriate, by thorough visual-field examinations. Certain individuals referred for more thorough examinations did not complete these tests. When the results of their screening tests were taken into consideration, the prevalence estimate turned out to be 16% [34]. In Barbados, the prevalence was 6.9% in subjects aged 35 or older, most of whom were blacks, and reached 12.8% in people aged 55 or older. However, all black populations apparently do not present the same degree of risk. Thus, a study carried out in South Africa among a rural Tswana population indicated that the prevalence rate of glaucoma in people aged 30 or older [31]was 1.72% [14].

The criteria for defining glaucoma varied in the above-mentioned studies. In the Baltimore study, glaucoma was defined as visual field changes or the presence of abnormalities in the fundus in at least one eye. In the St. Lucia study, the narrow definition of glaucoma was visual field loss in at least one eye; a broader definition also included the presence of high intraocular pressure or an abnormal fundus in at least one eye. In the Barbados study, the definition included the presence of the following three criteria, presumably in at least one eye: high pressure, abnormal fundus examination and visual field changes. Lastly, in the South African study, the definition was limited to visual field abnormalities, presumably in at least one eye. In all these studies, the denominator consisted of people.

PREVALENCE OF GLAUCOMA AS A FUNCTION OF GENDER

The effect of gender has also been analyzed by several authors. The Beaver Dam study, data from which are presented in Table A2.1, provides separate estimates for men and women. The difference between the two sexes was not statistically significant, which is consistent with the overall conclusions in the literature. However, the epidemiologic data on this aspect are conflicting. For example, in the Framingham population, Kahn et al. observed that the prevalence was twice as high in men as in women [28].

OTHER RISK FACTORS

The other risk factors often discussed in the literature are a family history of glaucoma, myopia, diabetes and high arterial blood pressure.

Close relatives of people with glaucoma are at an increased risk for developing the disease. A prevalence study on the general population conducted in Baltimore indicated that the relative risk of glaucoma was 3.69 when a sibling was affected and 2.17 when a parent was affected [60].

Myopia

Myopia is considered a possible risk factor, but this has not been demonstrated [32,43]. The anatomical changes accompanying severe myopia could make the eye more susceptible to the harmful effect of high intraocular pressure [43]. However, Leske points out that methodological difficulties, mainly concerning the question of diagnosing glaucoma in these myopic individuals, make analysing this association difficult.

The Framingham study revealed an association between high intraocular pressure and diabetes. However [32], in their evaluation of the literature, Quigley and Leske indicate that the association between diabetes and glaucoma has not been convincingly demonstrated [32,43].

Several epidemiologic studies have reported a positive association between hypertension and intraocular pressure [32]. However, the investigators also observed an association between drops in blood pressure due, for example, to antihypertensive treatment and visual field loss. According to Leske, it is possible that visual field loss is associated both with high and low blood pressure. This matter warrants further research.

TABLE A2.1 PREVALENCE OF OPEN-ANGLE GLAUCOMA BY AGE

AGE	FRAMINGHAM (town) Whites Both sexes (%)	BALTIMORE (large city) Whites Both sexes (%)	BALTIMORE (large city) Blacks Both sexes (%)	BEAVER DAM (rural) White men (%)	BEAVER DAM (rural) White women (%)
40 - 44	N/E	0.92	1.60	N/E	N/E
45 - 49	N/E			(43 - 54 years) 0.55	(43 - 54 years) 1.38
50 - 54	N/E	0.41	4.67	1.30	1.28
55 - 59	0.5				
60 - 64	0.7	1.76	6.59	3.33	2.15
65 - 69	0.9				
70 - 74	1.7	3.47	10.51	4.53	4.81
75 - 79	2.0				
≥ 80	4.4 (80 - 84 years)	2.16	13.80		
TOTAL	1.2	1.70	5.59	1.99	2.21

N/E: Not estimated

Framingham:

Baltimore:

Beaver Dam:

Definition of the word "glaucoma"

1. Framingham: visual field changes in at least one eye.
2. Baltimore: visual field changes or fundus abnormalities in at least one eye.
3. Beaver Dam: at least two of the following three elements present in the same eye: abnormal visual field, high or asymmetric cup-to-disc ratio, and high pressure.

In all three studies, the denominator consisted of people.

TABLE A2.2 INTRAOCULAR PRESSURE AND THE PREVALENCE OF GLAUCOMA AT THE TIME OF PRESSURE MEASUREMENT, BALTIMORE SURVEY [Erreur ! Signet non défini.]

INTRAOCULAR PRESSURE (mm Hg)	PREVALENCE OF GLAUCOMATOUS EYES (%)
≤ 15	0.65
16 - 18	1.31
19 - 21	1.82
22 - 24	8.30
25 - 29	8.33
30 - 34	25.37
≥ 35	26.09

TABLE A2.3 RISK OF GLAUCOMA WITH VISUAL FIELD DEFECTS ATTRIBUTABLE IN THE POPULATION TO HIGH INTRAOCULAR PRESSURE [Erreur ! Signet non défini.]

RELATIVE RISK ^a OF GLAUCOMA, COMPARING HIGH PRESSURE WITH LOW PRESSURE	ATTRIBUTABLE RISK ^b IN A POPULATION WITH A PREVALENCE ^c OF HIGH INTRAOCULAR PRESSURE OF:			
	2.5%	5.0%	7.5%	10%
2	2.4%	4.8%	7.0%	9.1%
3	4.8%	9.1%	13.0%	16.7%
4	7.0%	13.0%	18.4%	23.1%
5	9.1%	16.7%	23.1%	28.6%
6	11.1%	20.0%	27.3%	33.3%
7	13.0%	23.1%	31.0%	37.5%
8	14.9%	25.9%	34.4%	41.2%
9	16.7%	28.6%	37.5%	44.4%
10	18.4%	31.0%	40.3%	47.4%

- ^a This is the relative risk obtained from epidemiologic studies comparing the risk of glaucoma in people with high intraocular pressure with that in people with a pressure considered normal.
- ^b This is the percentage of all the cases of glaucoma in the entire population that are associated with the presence of high intraocular pressure.
- ^c This is the proportion of people in the population with high intraocular pressure in at least one eye.

APPENDIX 3. EPIDEMIOLOGY OF GLAUCOMA IN QUEBEC

The prevalence rate of a given disease is the proportion of the population affected at a given point in time. *Prevalence* refers to the number of cases present in the population rather than the proportion. Incidence is a measure of the frequency of occurrence of new cases of the disease during a given period of time, for example, a year. Incidence can be expressed in several ways: the number of new cases during the period, the proportion of new cases, or the number of new cases divided by the number of person-years at risk. When it is expressed as a proportion, one can calculate a crude value, which does not take into account the fact that the length of patient follow-up is not necessarily the same in all cases, or one can use methods that take this varying length of follow-up into account, such as actuarial methods.

PREVALENCE OF GLAUCOMA

To estimate the prevalence rate of glaucoma in Quebec, we had to apply the prevalences found in the Beaver Dam (Wisconsin) and Baltimore (Maryland) studies to the Quebec population. Table A3.1 presents the age-and-sex structure of the Quebec population for 1991. The calculations based on Beaver Dam data (Table A3.2) give estimates of 17,203 cases for men and 23,698 cases for women, for a total of 40,901 cases for the Quebec population aged 40 to 79. This would translate into a prevalence of 1.57%. Similar calculations (not presented here), based on the Baltimore survey, suggest a prevalence rate of about 1.31% among people aged 40 to 79, or 34,266 cases. In both cases, our calculations involve certain approximations since the age groups in these two surveys did not correspond exactly to the age group under consideration here, namely 40 to 79. No prevalence calculations based on the Framingham study are presented here since it did not include subjects under 55.

To estimate the cost of the diagnostic tests, it was necessary to subdivide the cases into subcategories of glaucoma based on the presence of at least two of the three diagnostic criteria: high pressure, abnormal fundus and abnormal visual field; high pressure and abnormal fundus; high pressure and abnormal field; and abnormal fundus and abnormal field. For this calculation, we once again used estimates from the Beaver Dam study. The results are presented in Table A3.3.

In our calculations of the cost-effectiveness ratios of various screening scenarios proposed, we

always used prevalence estimates based on the Beaver Dam study. This latter study included a greater number of cases than the Baltimore study, and it provided the data needed in glaucoma diagnostic sub-categories.

INCIDENCE OF GLAUCOMA

Knowing the prevalence of a disease is not enough to plan a screening program. Upon implementing a program, a certain number of prevalent cases will be detected. However, afterwards, the screening will result in the detection of new cases, called "incident cases". The costs of the program will therefore depend in part on the disease's incidence. Unfortunately, since they are difficult to obtain, incidence data are encountered less frequently in the literature.

Leske et al. developed a method of estimating incidence using data on prevalence by age for irreversible illnesses presenting no differential mortality [33]. We used this method to estimate the incidence of glaucoma in Quebec, on the basis of prevalence data from Beaver Dam. The incidence rate for a period of 10 years was estimated using the following formula: $\text{incidence} = (P_{x+10} - P_x) \text{ divided by } (1 - P_x)$, where P_x represents the prevalence rate at a given age. Table A3.4 shows our calculations. Prevalence rates from the Beaver Dam survey are available for 10-year age groups. In our calculations, we have assumed that these rates corresponded to the midpoint of the interval. Moreover, we have defined the prevalence rate at the age of 40 as being 0%. In certain age groups, the estimate of incidence was negative. The most plausible explanation for this observation is that rates by age and by gender used in our calculations presented considerable statistical instability because of the small number of cases observed.

On the basis of the data in Table A3.4, we calculated that the average age at which glaucoma is diagnosed, among subjects between 40 and 79 years old, was 60 years. Among subjects from 65 to 79 years old, the average age was 71 years [42].

Table A3.5 presents incidence estimates for Quebec derived from the Framingham study. Since the latter did not provide any incidence estimates before the age of 55, we arbitrarily applied, starting at age 40, the estimate applicable to people aged 55. We thus estimated that 1,733 new cases of glaucoma occur in Quebec each year in persons aged 40 to 79. The extrapolation of the incidence observed in people aged 55 to those aged 40 to 54 may have biased the results. If, for example, the incidence in this age group was, on average, 0.02% rather than 0.04%, the number of new cases anticipated in Quebec would be 1,463 instead of 1,733. The Framingham study included far fewer cases than the Beaver Dam study, and in our subsequent calculations, we used the estimate of incidence calculated on the basis of the Beaver Dam data.

INCIDENCE OF GLAUCOMA AS A FUNCTION OF INTRAOCULAR PRESSURE

Some studies make it possible to obtain incidence data as a function of pressure. Armaly et al. calculated the incidence of glaucoma with visual field defects in individuals followed for up to 13 years and representing 5,886 eyes. Their data are presented in Table A3.6. Armaly et al. also calculated the incidence of glaucoma with visual field defects using the survival analysis technique. This method enables one to take into account varying lengths of follow-up in the individuals observed. Some of the results of these analyses are summarized in Table A3.7. After six years of follow-up in the subjects with a pressure ≥ 20 mm Hg, the incidence was 12.41% versus 1.46% when the pressure was lower.

Some investigators have measured the risk of glaucoma occurring up to 20 years after the diagnosis of high intraocular pressure. They noted that about a third of the individuals with high pressure will develop glaucoma during this period.

The data in Tables A3.6 and A3.7 enable us to compare the incidence of glaucoma in people who have high pressure with the incidence in those with a lower pressure. It is seen that the relative risk of glaucoma is very high in people with high intraocular pressure.

TABLE A3.1 AGE-SEX STRUCTURE OF THE QUEBEC POPULATION AGED 40-79 YEARS, 1991
[Erreur ! Signet non défini.]

AGE	MEN	WOMEN	TOTAL
	Number (%)	Number (%)	Number (%)
40 - 44	269,470 (10)	272,655 (10)	542,125 (20)
45 - 49	225,670 (9)	227,880 (9)	453,550 (18)
50 - 54	175,055 (7)	179,215 (7)	354,270 (14)
55 - 59	158,965 (6)	167,825 (6)	326,790 (12)
60 - 64	146,875 (6)	164,330 (6)	311,205 (12)
65 - 69	122,280 (5)	149,755 (6)	272,035 (11)
70 - 74	84,515 (3)	116,505 (4)	201,020 (7)
75 - 79	56,660 (2)	89,555 (3)	146,215 (5)
TOTAL	1,239,490 (48)	1,367,720 (52)	2,607,210 (100)

Mean age

$[(542,125)(42.5 \text{ years}) + \dots + (146,215)(77.5 \text{ years})] / 2,607,210 = 55.9 \text{ years.}$

(This is the mean age at the time of screening, obtained by multiplying the number of individuals in each age group by the age at the middle of this interval, then dividing by the total number of people.)

Note: In 1991, the population 80 years old and over comprised 48,590 men and 103,065 women.

TABLE A3.2 ESTIMATE OF THE PREVALENCE OF GLAUCOMA IN QUEBEC BASED ON DATA FROM THE BEAVER DAM STUDY [Erreur ! Signet non défini.]

AGE	MEN		WOMEN		MEN AND WOMEN
	RATE IN BEAVER DAM (%)	CASES EXPECTED IN QUEBEC ^c	RATE IN BEAVER DAM (%)	CASES EXPECTED IN QUEBEC ^c	CASES EXPECTED
40 - 54	0.55 ^a	3,753	1.38 ^a	9,381	13,134
55 - 64	1.30	3,976	1.28	4,285	8,261
65 - 74	3.33	6,907	2.15	5,725	12,632
75 - 79	4.53 ^b	2,567	4.81 ^b	4,307	6,874
TOTAL 40-79		17,203		23,698	40,901
80 +	4.53 ^b	2,201	4.81 ^b	4,958	7,159

Prevalence estimate for Quebec subjects 40-79 years old: $40,781/2,607,210 = 1.57\%$.

^a Rates for subjects aged 43 to 54 in Beaver Dam.

^b Rates for subjects aged 75 to 84 in Beaver Dam.

^c Rates by age and by gender in Beaver Dam, multiplied by the distribution by age and by gender in Quebec in 1991. The calculations were made using the rate for each of the four categories of glaucoma defined in Table A3.3. This led to some approximations, which in turn explain why some of the estimates cannot be obtained directly from the rates presented in the table.

**TABLE A3.3 DISTRIBUTION OF CASES OF PRIMARY OPEN-ANGLE GLAUCOMA
DEPENDING ON DIAGNOSTIC CRITERIA, ACCORDING TO THE BEAVER
DAM SURVEY [Erreur ! Signet non défini.]**

CRITERIA	PREVALENCE IN BEAVER DAM	CASES EXPECTED IN QUEBEC ^a		
		40-79 years	65-79 years	80 + years
1. Abnormal visual field; abnormal optic fundus; high pressure.	5 / 4,926	1, 555	1, 555	340
2. Abnormal visual field; abnormal optic fundus; normal pressure.	33 / 4,926	12,313	5,305	2,458
3. Abnormal visual field; normal optic fundus; high pressure.	45 / 4,926	16,978	9,730	3,227
4. Normal visual field; abnormal optic fundus; high pressure.	21 / 4, 926	10,055	2,916	1,134
TOTAL	104 / 4,926	40,901	19,506	7,159

^a Rate by age and gender in Beaver Dam multiplied by the distribution by age and gender in Quebec in 1991.

Definitions:

High intraocular pressure: ≥ 22 mm Hg.

High cup-to-disc ratio: ≥ 0.8 .

Asymmetric cup-to-disc ratio: ≥ 0.2 between the two eyes.

TABLE A3.4 ESTIMATED INCIDENCE OF PRIMARY OPEN-ANGLE GLAUCOMA IN QUEBEC, ON THE BASIS OF THE BEAVER DAM SURVEY [Erreur ! Signet non défini.]

GENDER	AGE	ALL CASES OF PRIMARY OPEN-ANGLE GLAUCOMA			CASES WITH NORMAL PRESSURE		
		PREVALENCE	INCIDENCE OVER 10 YEARS	CASES / YEAR IN QUEBEC ^a	PREVALENCE	INCIDENCE OVER 10 YEARS	CASES / YEAR IN QUEBEC ^a
MEN	40	0%	0.55%	272	0%	0.14%	69
	50	0.55%	0.75%	251	0.14%	0.67%	223
	60	1.30%	2.06%	546	0.81%	-0.07%	-19
	70	3.33%	1.24%	169	0.74%	0.65%	89
	80	4.53%	not estimated	not estimated	1.39%	not estimated	not estimated
WOMEN	40	0%	1.38%	691	0%	0.25%	125
	50	1.38%	-0.1%	-35	0.25%	0.32%	110
	60	1.28%	0.88%	273	0.57%	-0.32%	-9
	70	2.15%	2.72%	548	0.54%	1.21%	241
	80	4.81%	not estimated	not estimated	1.73%	not estimated	not estimated
TOTAL	40 - 79			2 715			829
TOTAL	65 - 79			1 127			316

^a Incidence divided by 10 (for approximation of yearly incidence) multiplied by the Quebec population at risk, for the appropriate agegroup.

TABLE A3.5 INCIDENCE OF GLAUCOMA IN QUEBEC BASED ON DATA FROM THE FRAMINGHAM STUDY [Erreur ! Signet non défini.]

AGE	QUEBEC POPULATION, 1991	ANNUAL INCIDENCE ^a (%)	NUMBER OF NEW CASES EXPECTED IN QUEBEC
40 - 44	542,125	0.04	217
45 - 49	453,550	0.04	181
50 - 54	354,270	0.04	142
55 - 59	326,790	0.04	131
60 - 64	311,205	0.06	187
65 - 69	272,035	0.10	272
70 - 74	201,020	0.14	281
75 - 79	146,215	0.22	322
TOTAL	2,607,210		1,733

^a Podgor et al. estimated incidences for 5 years using prevalences. For the purpose of subsequent calculations, we estimated incidences for 1 year, by dividing the values reported by Podgor et al. by 5. The result is an approximation with a negligible level of error for small percentages, such as the ones expressed here.

**TABLE A3.6 INCIDENCE OF GLAUCOMA, COLLABORATIVE GLAUCOMA STUDY [Erreur !
Signet non défini.]**

INTRAOCULAR PRESSURE (mm Hg)	PROPORTION OF EYES DEVELOPING GLAUCOMA (DEFINED AS INCLUDING VISUAL FIELD DEFECTS); MAXIMUM FOLLOW-UP OF 13 YEARS ^a (%)
≤ 16	0.8
16 – 19	1.4
20 – 23	3.1
≥ 24	8.4

^a Cumulative proportion for a maximum period of 13 years, not the proportion per year.

**TABLE A3.7 INCIDENCE OF GLAUCOMA WITH VISUAL FIELD DEFECTS,
COLLABORATIVE GLAUCOMA STUDY (ACTUARIAL METHOD) [Erreur ! Signet
non défini.]**

INTERVAL IN YEARS ^a	PRESSURE $\geq$ 20 mm Hg RISK (%)	PRESSURE $<$ 20 mm Hg RISK (%)
0 - 1	1.70	0.31
1 - 2	2.42	0.46
2 - 3	4.08	0.78
3 - 4	5.34	0.96
4 - 5	6.66	1.46
5 - 6	12.41	1.46

^a Results are presented here for the first six years of follow-up only. Beyond this point, only six patients remained under observation. This led to very imprecise estimates of incidence.

APPENDIX 4. EPIDEMIOLOGY OF HIGH INTRAOCULAR PRESSURE

A glaucoma screening program will detect cases of glaucoma and others who only present high intraocular pressure. However, the latter must be looked after by a physician in order to monitor the evolution of their pressure level and, if necessary, to treat them. This, too, will entail costs, which must be taken into account. We therefore estimated the number of cases that would thus be detected in Quebec. Table A4.1 presents estimates from the Baltimore, Beaver Dam, Ferndale and Dalby surveys. These studies covered large age groups; the prevalence rate estimates ranged from 4.7 to 9.4%. Table A4.1 also shows results for three age groups from the Framingham survey. The latter reported prevalences ranging from 18.4 to 24.6%.

To approximate the prevalence of high intraocular pressure in the Quebec population aged 40 to 79, we used age-specific intraocular pressure prevalence rate estimates published by Gottlieb et al. [18]. These estimates, which are presented in Table A4.2, were calculated by Gottlieb et al. by determining the mean results of a large number of studies published before 1983. By applying these rates to the Quebec population aged 40 to 79, we obtain a prevalence of 7.24%. The criterion used by Gottlieb et al. was a pressure ≥ 21 mm Hg. In more recent studies, this criterion was defined instead as > 21 mm Hg, which would have led to somewhat smaller prevalences.

The Baltimore [55] and Beaver Dam [30] studies had not yet been conducted when Gottlieb et al. performed their analysis. We compared the result obtained using the figures from Gottlieb et al. with the results of these more recent surveys. It was seen in Table A4.1 that these studies indicated prevalences of 7.4% and 4.7%, respectively. In both cases, high pressure was defined as being > 21 mm Hg, not ≥ 21 mm Hg as in Gottlieb et al. Moreover, the rates were established for populations of eyes rather than of people; thus the rate of people having at least one affected eye would be a little higher than the estimate of 4.7% (Beaver Dam) and a little lower than 7.4% (Baltimore). We did not obtain any age-specific prevalence rates for these two studies. Consequently, these prevalences are not directly applicable to the Quebec context. However, we did compare the age-sex structures of the populations in these two surveys with that of the Quebec population. We noted that these populations were older. This means that the estimates for Quebec, adjusted for age, would be somewhat lower than these non-adjusted values.

To sum up, we have three plausible estimates, i.e. the one derived from the data from Gottlieb et al. and those from the Baltimore and Beaver Dam studies. The mean value of these three estimates is 6.45%. Taking into account the fact that several sources of errors affect these estimates, probably exaggerating the prevalence rate, we rounded our estimate off to 6%. This translates into 156,433 people aged 40 to 79 having pressure > 21 mm Hg in Quebec. This estimate corresponds to 83% of the estimate calculated on the basis of rates published by Gottlieb et al., or 156,433 divided by 188,729. This figure of 156,433 cases with high pressure includes subjects with as well as without glaucoma. We calculated above (Table A3.3) that the prevalence of glaucoma with high pressure in Quebec was 28,588 cases. Our estimate of the prevalence of high pressure without glaucoma is therefore 156,433 cases - 28,588 cases = 127,845 cases. Among subjects aged 65 to 79, the prevalence of high pressure without glaucoma is estimated to be: 58,276 cases - 14,201 cases = 44,075 cases. Finally, among subjects 80 and over, the estimate is: 15,210 cases - 4,701 cases = 10,509 cases (Tables A3.3 and A4.2).

INCIDENCE OF HIGH PRESSURE IN QUEBEC

We did not find any studies on the incidence of high pressure in the literature. As a result, we used once again the method developed by Leske et al. to obtain estimates of incidence using data on prevalence by age. The rates available were for five-year age groups. For our calculations, we assumed that these prevalences corresponded to the midpoint of the interval. In addition, we defined the prevalence rate at 40 years of age as being 0%. These five-year incidence rates were calculated using the following formula: $\text{incidence} = (P_{x+5} - P_x) \text{ divided by } (1 - P_x)$; for the ages of 40 and of 77.5 years, rates for 2.5 years were calculated. Table A4.3 presents the results. The estimate of the number of new cases in Quebec is 8,159 per year. To calculate incidence among subjects 65 to 79 years old, we assumed that cases in the 62.5 - 67.5 year bracket were distributed equally between 62.5 to 64 years of age and 65 to 67.5 years of age. In our subsequent calculations, we assumed that the appearance of glaucoma never precedes the appearance of high intraocular pressure. In other words, we interpreted the incidence calculated in Table A4.3 as representing the incidence of high intraocular pressure alone, without glaucoma.

Using the data in Table A4.3, we calculated that the average age at which high intraocular pressure was diagnosed in the 40-79 age group, was 50 years. Among those from 65 to 79 years of age, the average age at diagnosis was 68 years.

TABLE A4.1 PREVALENCE OF HIGH INTRAOCULAR PRESSURE (IN PRESENCE OR ABSENCE OF GLAUCOMA)

SURVEY AND YEAR PUBLISHED	AGE	HIGH INTRAOCULAR PRESSURE		
		CRITERION (mm Hg)	DENOMINATOR	PREVALENCE (%)
BALTIMORE 1991	≥ 40	> 21	all eyes	7.4
BEAVER DAM 1992	43 - 84	> 21	right eye	4.7
FERNDALE 1966	40 - 74	> 20	people	9.4
DALBY 1981	55 - 70	> 20.5	probably people	7.3
FRAMINGHAM 1977	52 - 64	>20	people	18.4
FRAMINGHAM 1977	65 - 74	> 20	people	24.6
FRAMINGHAM 1977	75 - 84	> 20	people	24.1

Baltimore:[55
 Beaver Dam: [30
 Ferndale: [24
 Dalby: [6
 Framingham: [27

**TABLE A4.2 PREVALENCE OF HIGH INTRAOCULAR PRESSURE AS A FUNCTION OF AGE;
ESTIMATES BY GOTTLIEB ET AL. APPLIED TO THE QUEBEC POPULATION**
[Erreur ! Signet non défini.]

AGE	ESTIMATE # 1		ESTIMATE # 2	
	PREVALENCE OF PRESSURE ≥ 21 mm Hg (%)	CASES EXPECTED IN QUEBEC ^a	83% OF ESTIMATE #1 (SEE TEXT) (≥ 21 mg Hg)	CASES EXPECTED IN QUEBEC ^b
40 - 44	3.3%	17,890	2.7%	14,829
45 - 49	5.8%	26,306	4.8%	21,804
50 - 54	6.4%	22,673	5.3%	18,793
55 - 59	7.3%	23,856	6.1%	19,774
60 - 64	8.9%	27,697	7.4%	22,957
65 - 69	10.4%	28,292	8.6%	23,451
70 - 74	12.1%	24,323	10.0%	20,161
75 - 79	12.1%	17,692	10.0%	14,664
TOTAL 40 - 79		188,729		156,433
80 +	12.1% ^c	18,350	10.0%	15,210

^a Prevalence by age multiplied by population by age in Quebec, 1991.

^b $(156,433 \div 188,729) \times (\text{estimate \#1 by age})$.

^c Rate for subjects 75-79 years old in Gottlieb et al. [18].

TABLE A4.3 ESTIMATE OF THE INCIDENCE OF HIGH INTRAOCULAR PRESSURE

AGE ^a	PREVALENCE	INCIDENCE OVER 5 YEARS ^b	NUMBER OF CASES EXPECTED IN QUEBEC EACH YEAR ^c
40	0 %	2.7 %	2,927
42.5	2.7 %	2.2 %	2,091
47.5	4.8 %	0.5 %	403
52.5	5.3 %	0.8 %	545
57.5	6.1 %	1.4 %	829
62.5	7.4 %	1.3 %	700
67.5	8.6 %	1.5 %	662
72.5	10.0 %	0 %	0
77.5	10.0 %	0 %	0
80	10.0 %	not calculated	not calculated
TOTAL 40 - 79			8,159
TOTAL 65 - 79			1,012

^a Corresponds to the middle of the interval used to calculate prevalence.

^b Incidence over 2.5 years for the ages of 40 and of 77.5 years.

^c Incidence by age multiplied by the Quebec population by age, 1991.

APPENDIX 5. EPIDEMIOLOGY OF BLINDNESS ATTRIBUTABLE TO GLAUCOMA

COMPLETE BLINDNESS

Blindness is defined as visual acuity less than 6/60 or a visual field less than 20 degrees. There exist very few data on the incidence of blindness in people with glaucoma. Grant and Burke analyzed the files of patients followed at the Massachusetts Eye and Ear Infirmary for a period of 20 years or more. Of the 200 patients, which represent about 400 eyes, they observed, over 20 years of follow-up, 50 eyes that became blind [19]. The incidence and prevalence data for blindness in the general population are more relevant to our analyses. We examined data from Canada and the United States. Statistics from the Canadian National Institute for the Blind indicate that from 1985 to 1989, the number of new cases of blindness due to glaucoma ranged from 409 to 654 a year, the average being 533. This would mean about 150 cases per year in Quebec. Table A5.1 presents age-specific data from the Institute for the year 1989. Ninety-seven percent of these cases were found among patients 40 and over, which corresponds to 145 cases out of 150 in Quebec.

We do not know what proportion of cases registered at the National Institute could be attributed to primary open-angle glaucoma. An American study by Hiller and Kahn indicated that 90% of cases of primary glaucoma, or of cases that were not specified as being primary or secondary, were open-angle. In a study undertaken in Baltimore, 82% of all cases of glaucoma were primary open-angle [62]. In another study in Baltimore, Sommer et al. found 29 eyes that were blind because of glaucoma, including 21 (or 71%) because of primary open-angle glaucoma [56]. We know however that not all blind people are registered at the National Institute; for this reason we preferred subtracting only a small fraction of cases in order to take account in our estimate of primary open-angle glaucoma. We therefore chose as our final estimate 140 cases per year.

Table A5.1 shows that about 89% of new cases among subjects aged 40 and over (563 divided by 633) were found among people 65 and over. Our estimate of the incidence of blindness in this age group is therefore: $(0.89) \times (140 \text{ cases/year}) = (125 \text{ cases/year})$. In the United States, Power et al. estimated that in 1988, 4,600 people over 65 years of age were blind on account of glaucoma [42], which represents a rate of 0.15 per 1,000 people per year. Assuming that 90% of these cases could be attributed to primary open-angle glaucoma, we end up with an incidence

rate of 0.14 per 1,000 people per year among people over 65, which for Quebec represents $(0.00014) \times (770,925 \text{ people}) = 108 \text{ cases/year}$.

On the basis of the data in Table A5.1, we also calculated that the average age at which blindness was diagnosed, among subjects 40 years and over, was about 78 years. In 1985-87, the average life expectancy in Canada at 78 years, for both men and women, was approximately nine years. Our estimate of the prevalence of blindness caused by primary open-angle glaucoma is therefore: $(140 \text{ cases/year}) \times (9 \text{ years}) = 1,260 \text{ cases}$. This estimate is comparable to the estimate made by Battista et al. [5], i.e. 5,000 cases for all of Canada, which corresponds to about 1,250 cases for Quebec.

Data published by Hiller and Kahn and presented in Table A5.2, suggest that 81% of prevalent cases of blindness due to glaucoma are found among subjects 65 and over. If this percentage is applied to our estimate of 1,260 cases for Quebec, we obtain the following result: $(0.81) \times (1,260 \text{ cases}) = 1,021 \text{ cases}$. Among people 65 and over, the average age at which blindness was diagnosed would be 81 years. Life expectancy at this age is approximately eight years.

These estimates should be considered with caution. We know that the Quebec population already has access to a certain level of glaucoma screening and care. If we assume that these activities present a certain level of effectiveness, we can assume that the rates of blindness observed in Quebec do not represent all the gains that can be achieved in a population to which screening is not yet available.

However, it is unlikely that the glaucoma treatment dispensed in the past could have considerably reduced the current prevalence of blindness in Quebec and the data we have support instead the hypothesis that our estimate of the incidence and prevalence does represent the potential gains sought by a screening program. Hiller and Kahn [23] published incidence and prevalence estimates for blindness due to glaucoma in 14 American states for the years 1969 and 1970. Table A5.2 presents our estimate of the number of prevalent cases of blindness due to glaucoma in Quebec based on the rates in the American study. The number of cases in Quebec would be 1,385, which is practically the same as the estimate of 1,260 presented above. This estimate takes account of the fact that the authors indicate that their data were affected by

significant under-reporting, by a factor judged to be in the order of two. Hiller and Kahn also determined that the rates of blindness had been very stable in the United States since at least 1965. If we take into account the fact that the blind around 1965-1970 had been treated for glaucoma (if they had been treated) about 10 to 20 years earlier, it is very reasonable to consider these figures an estimate of the rates of blindness at a time when the modern treatments available in Quebec did not yet exist. In a study conducted in England, Grey et al. [20] observed that the rates of blindness due to glaucoma without distinguishing between categories of glaucoma remained stable between the 1960s and 1980s. They put forth the same hypothesis as we do, namely that the potential benefits of modern treatments are not yet reflected in the available statistics.

PARTIAL BLINDNESS

Glaucoma causes incapacities well before the criteria defining total blindness are met (visual acuity less than 6/60 or a visual field less than 20°). Thus, in Quebec, a horizontal stretch of the binocular visual field less than 100° means the loss of a class 5 driver's licence. The criteria for a chauffeur's licence are even more stringent. If the visual field of the better eye is less than 60° in the horizontal or vertical meridian, the individual experiences enough difficulty in his orientation and mobility for his visual deficiency to be considered a handicap. In Canada, if the visual field is less than 20°, the person is considered legally blind.

The incidence of partial blindness due to glaucoma is difficult to estimate. Table A5.3 summarizes statistics published by Grey et al. concerning the incidence of total and partial blindness in Avon County, England, from 1984 to 1986 [20]. If we apply these figures to Quebec, the incidence of total or partial blindness would be 254 cases a year. The number of cases of partial blindness would therefore be 114 cases a year, i.e. 254 minus 140. The mean age of these cases would be 79, which is nearly the same as the age calculated above for cases of total blindness. Assuming a nine-year life expectancy for these patients, the prevalence of partial blindness would be: (114 cases per year) x (9 years) = 1,026 cases. For subjects 65 and over, our estimate is: (0.81) x (1,026 cases) = 831 cases.

Among subjects 65 and over, these data indicate an incidence of complete or partial blindness of 239 cases per year. This corresponds to an incidence of 114 cases of partial blindness per year, i.e. 239 cases per year of partial or total blindness, less 125 cases of complete blindness.

These epidemiologic data are the best we have been able to find on this subject, but they are still very far from perfect. They are from a register whose accuracy was affected by various factors, including the patients' motivation to register, variability in the diagnostic criteria used by the physicians, and the fact that the disability pensions granted to the patients were larger in the cases of total blindness than in those of partial blindness. This could, in particular, explain the paradoxical observation of a lower incidence of partial blindness than total blindness in this population.

TABLE A5.1 NEW ENTRIES TO THE REGISTER OF THE CANADIAN NATIONAL INSTITUTE FOR THE BLIND: CASES OF BLINDNESS DUE TO GLAUCOMA, 1989 [Erreur ! Signet non défini.]

AGE (YEARS)	NUMBER OF NEW ENTRIES
0 - 5	4
6 - 17	4
18 - 29	7
30 - 39 ^a	6
40 - 49 ^a	7
50 - 59	32
60 - 64 ^b	31
65 - 69 ^b	32
70 - 79	203
80 - 89	270
90 +	58
TOTAL	654

^a The data for ages 30-39 and 40-49 were grouped together in the available statistics, showing a total of 13 cases for subjects between 30 and 49 years. We assumed that these cases were distributed approximately equally between the two age groups.

^b The data for ages 60-64 and 65-69 were grouped together in the available statistics, showing a total of 63 cases for subjects between 60 and 69 years. We assumed that these cases were distributed approximately equally between the two age groups.

TABLE A5.2 PREVALENCE OF BLINDNESS IN QUEBEC AS ESTIMATED FROM STATISTICS FOR 14 AMERICAN STATES, 1969 - 1970

AGE	MEN			WOMEN			MEN + WOMEN
	NUMBER	RATE (per 100,000)	CASES EXPECTED IN QUEBEC	NUMBER	RATE (per 100,000)	CASES EXPECTED IN QUEBEC	CASES EXPECTED
40 - 44	269,470	1.2	3.23	272,655	0.6	1.64	4.87
45 - 64	706,565	9.3	65.71	739,250	8.3	61.36	127.07
65 - 74	206,795	42.9	88.72	266,260	30.9	82.27	170.99
75 - 84	87,520	104.5	91.46	148,165	92.5	137.05	228.51
≥ 85	17,730	285.7	50.65	44,455	248.6	110.52	161.17
TOTAL	1,288,080		299.77	1,470,785		392.84	692.61

Definition of blindness: visual acuity of 20/200 or less in the better eye with the best correction possible or a visual field limited to 20° in its widest diameter. The cases of blindness due to primary glaucoma, open-angle or closed-angle, were included, as well as cases that were not specified to be primary or secondary; the cases of glaucoma specifically reported as being secondary or congenital were excluded.

Number of cases in Quebec: 692.61 cases, multiplied by a factor representing the estimated proportion of the under-reporting (x2) = 1,385 cases.

TABLE A5.3 INCIDENCE OF TOTAL OR PARTIAL BLINDNESS IN QUEBEC AS ESTIMATED FROM THE RATES FOR AVON COUNTY, ENGLAND, 1984 - 1986 [Erreur ! Signet non défini.]

AGE	QUEBEC POPULATION	RATE (per 100,000 per year)	CASES EXPECTED IN QUEBEC
40 - 49	995,675	0.9	8.96
50 - 59	681,060	0.0	0.0
60 - 64	311,205	1.9	5.91
65 - 69	272,035	5.2	14.15
70 - 79	347,235	27.5	95.49
80 - 84	89,465	64.7	57.89
≥ 85	62,185	115.5	71.82
TOTAL	2,758,860		254.22

Mean age of cases of total or partial blindness

$[(8.96)(45) + (5.91)(62.5) + (14.15)(67.5) + (95.49)(75) + (57.89)(82.5) + (71.82)(90)] \div 254.22 = 79.18$ years.

(See Table A3.1 for the method of calculating the mean age.)

Definition of partial blindness: visual acuity of at most 6/60 in the better eye, 6/24 if accompanied by moderate visual field loss, or 6/18 in the presence of considerable visual field loss.

APPENDIX 6. COST OF A POSSIBLE SCREENING PROGRAM

We determined the cost of a screening program including the costs of diagnosis and treatment that would be offered to the Quebec population aged 40 to 79 (in 1991, 2,607,210 people [58]). We first estimated the cost by assuming that there are currently, in Quebec, no glaucoma-related diagnostic or therapeutic activities. The calculations were made separately for the costs of diagnosis and for the costs of monitoring and treatment.

COSTS ASSOCIATED WITH MONITORING AND DIAGNOSIS

Table A6.1 presents the fees for different diagnostic procedures performed by medical specialists and optometrists in Quebec. In all of our calculations, we chose the fees for procedures performed in private offices. Table A6.2 presents the estimate of costs of diagnostic tests associated with an annual screening program including a funduscopy and tonometry during the initial exam.

We assumed in Table A6.2 that the entire population of Quebec aged 40 to 79 would be reached by the screening program and that this population was in a steady state regarding its size, its age-sex distribution and the incidence of high intraocular pressure and of glaucoma. At any given moment, a prevalence of 168,746 cases can be found of high intraocular pressure or glaucoma or both, already identified during previous screening examinations. This number of cases remains constant over time, since it is continually maintained at this level by a supply of new cases identified by annual screening tests, which make up for the disappearance, through death, of other cases.

Our estimate of the costs of the first visual exam is \$77,055,462 per year. If screening were offered less often, then the cost would be proportionately lower. For example, screening undertaken every three years would correspond to a cost for this first exam of \$25,685,154. However, the cost of gonioscopy and of the second visual exam would not be affected by the frequency of screening; when offered every three years, screening would lead to the detection of three times the incidence per screening cycle of the number of cases detected thanks to an annual program, leading to identical costs for the two programs for this portion of the diagnostic tests.

The costs of diagnostic tests are also proportional to the percentage of the population taking part in the screening program. If the participation was 75%, then the cost of screening offered every three

years would be $(0.75) \times (\$25,685,154) = \$19,263,865$ for the first visual exam, and $(0.75) \times (\$89,880 + \$449,400) = \$404,460$ for gonioscopy and the second exam. The total cost would therefore be $\$19,668,325 (= \$19,263,865 + \$404,460)$.

We also made the same calculations for persons between the ages of 65 and 79. This age bracket contained 619,270 people in Quebec in 1991. The cost of diagnostic tests administered every three years, assuming a participation rate of 75%, would be $\$4,449,703$.

Finally, we determined the cost of screening programs which would only include tonometry as an initial diagnostic exam, for the purpose of detecting subjects with pressure higher than 21 mm Hg. A complete visual examination as well as gonioscopy and perimetry would only be undertaken in the case of subjects having high pressure. There is currently no fee in Quebec for tonometry performed by an ophthalmologist. In our calculations, we arbitrarily chose a fee of \$8 for this test. Assuming once again a participation rate of 75%, the cost of diagnostic exams would be $\$5,370,289$ for subjects from 40 to 79 years old, and $\$1,180,127$ for those from 65 to 79 years.

COSTS ASSOCIATED WITH MONITORING AND TREATMENT

Table A6.3 shows the hypothetic evolution of the monitoring and treatment of 100 average patients over a five-year period. This table is based on several studies describing the evolution of patients treated for glaucoma [1, 38, 43, 45, 57, 65] as well as on expert opinion. According to this table, during the first year, the 100 patients will be treated using just one type of medication. During the second year, the treatment will have failed in 15 of these cases, and these latter patients will need two types of medication. During the third year, there will only remain 76 patients showing a good reduction of intraocular pressure with just one type of medication, while 24 others will need two types of medication. In the same way, the therapeutic needs of the patients will continue to evolve throughout years 4 and 5, according to the summary provided in Table A6.3. In addition to the costs indicated in Table A6.3, we included: a single retinophotography per patient at the beginning of monitoring; four main visits per year; two perimetries per year; a gonioscopy every two years; and examination with contact lens of fundus under dilation. To simplify our calculations, we assumed that a trabeculectomy would be performed as an out-patient procedure. The total cost for 100 patients is therefore calculated to be $\$176,576$ or $\$353$ per person per year. For each year beyond the fifth year, we also used the figure of $\$353$. We did not want to develop the tree shown in Table A6.3 beyond five

years, because of the high degree of imprecision that would have entailed. We believe however that the real costs of these subsequent years will be higher, because of the foreseeable increase in the frequency of surgery, among other things. Our approach probably therefore led to favourable cost-effectiveness ratios.

We also took account of patients with high intraocular pressure without glaucoma. According to Gottlieb et al. [18], between 10 and 30% of these patients have to be treated; we assumed that this proportion was 10%, which leads to more favourable cost-effectiveness ratios than higher percentages. We also assumed that the cost of treatment of these subjects was identical to the cost of treatment of those subjects suffering from glaucoma, or \$353 per year. Finally, we assumed that the other 90% of subjects with high intraocular pressure will require two visits per year to the ophthalmologist, at a cost of \$63.20 per year. Table A6.4 shows the final cost for the entire population of Quebec, namely \$29,718,651 per year. This represents the cost of treatment of patients detected between the ages of 40 and 79, but treated up to their death, whether these deaths occurred between 40 and 79 or afterwards. This cost is not affected by the frequency of screening; in a steady state, the number of subjects being monitored or treated will remain the same, whatever the frequency of the tests. The cost however will be affected by the participation in screening and therapeutic compliance. If for example these two parameters were 75%, the total cost of monitoring and treatment would be $(0.75) \times (0.75) \times (\$29,718,651) = \$16,716,741$.

PROFESSIONALS OTHER THAN OPHTHALMOLOGISTS

We reconsidered the costs by assuming that the initial diagnostic tests would be performed by professionals other than ophthalmologists, for a more advantageous fee. For these calculations, we used the fees of optometrists. In order to simplify the calculations, we assumed that the numbers of subjects detected and treated would be identical to the numbers shown in Table A6.2. We assumed a situation in which a first complete exam, including a funduscopy and tonometry, would be undertaken by a professional who was not an ophthalmologist. The subjects with at least one anomaly would then have manual perimetry of the central visual field and of the peripheral visual field. After these tests, patients with a presumed diagnosis of high intraocular pressure or of glaucoma would be referred to an ophthalmologist for more complete exams and, if necessary, for monitoring or treatments. In this scenario, we considered all costs related to care by ophthalmologists as costs of monitoring and treatment.

COSTS ASSOCIATED WITH BLINDNESS

An accurate calculation of the cost of a screening program should also take into account the costs associated with blindness. The blind receive certain care, services and equipment covered by the government. Preventing blindness reduces these expenses, which must therefore be subtracted from the cost of screening. However, accurate data are not available.

Table A6.5 presents the costs concerning the Régie de l'assurance-maladie du Québec's visual aids program for 1992. The program includes reading, writing and mobility aids, such as devices that convert optical impulses into tactile impulses, braille typewriters, canes and guide dogs. Our mean cost estimate is \$325 per case of blindness per year. It should be noted that the data from the Régie concern the costs for all the visually handicapped people covered by the program, not specifically blind people or people who are blind from glaucoma. We have therefore assumed here that the cost for patients with glaucoma was identical to the mean cost for all the program's beneficiaries.

The Régie also offers an ocular prosthesis program, but such prostheses are generally not required in cases of glaucoma.

Other costs are associated with rehabilitating people who have become blind. Table A6.6 presents a typical service plan for a 55-year-old who has become blind because of glaucoma [9]. This plan constitutes an ideal situation. We attempted to obtain a more empirical estimate of the cost of rehabilitative services in Quebec. To this end, we obtained the budget allotted to the visually handicapped for 10 of Quebec's rehabilitation agencies. The global budget for 1993-1994 was \$18,803,302, which involved 15,907 active files. This works out to a cost of \$1,182 a person.

Another cost is the disability pensions paid by the Régie des rentes du Québec. In 1993, the average disability pension paid to individuals with a visual handicap due to glaucoma was \$8,315 a year. The Régie does not pay any disability pensions after the age of 65, although most cases due to glaucoma occur after this age. According to the data in Table A5.2 on the age distribution of prevalent cases of blindness due to glaucoma, 19% of these cases occurred before the age of 65, and the average cost of a pension would therefore be $(\$8,315) \times (0.19) = \$1,580$.

Other costs were not estimated. For example, we do not have any cost data on paratransit or the home support services provided by the local community service centres. Nor did we estimate the governments' loss of revenue resulting from tax deductions granted to the blind.

Table A6.7 summarizes our blindness cost calculations. Our estimate is \$3,087 per year of blindness for all cases of all ages, and \$1,507 for people aged 65 or older. These are very rough figures. In our subsequent calculations, we rounded these figures to \$3,000 and \$1,500, respectively.

TABLE A6.1 FEES FOR DIFFERENT DIAGNOSTIC ACTS, RÉGIE DE L'ASSURANCE-MALADIE DU QUÉBEC [47,48]

CODE	CONSULTATION (IN A PRIVATE OFFICE)	FEES
Medical specialists		
9252	Main visit, ophthalmology	\$31.60
9129	Follow-up visit, ophthalmology	\$15.00
0543	Gonioscopy	\$10.00
0587	Static perimetry in both eyes	\$35.00
0553	Retinophotography	\$14.00
0576	Examination with contact lens of fundus under dilation	\$10.00
Optometrists		
9001	Complete examination	\$19.50
9024	Supplement for tonometry	\$2.25
9006	Examination of central visual field	\$8.00
9007	Examination of peripheral visual field	\$7.00

TABLE A6.2 THE COSTS OF DIAGNOSTIC EXAMS, ANNUAL SCREENING

A. Relevant populations 1. Population of Quebec, 40 - 79 years, 1991: 2,607,210 people. 2. Subjects 40 to 79 years old identified during previous screening tests as having high intraocular pressure, or glaucoma, or both: 168,746 people. 3. Subjects eligible for screening: (1) - (2) = 2,438,464 people. 4. Subjects with anomalies detected during the initial eye exam (i.e. annual incidence of high intraocular pressure without glaucoma (8,159 cases) and of glaucoma with normal intraocular pressure (829 cases): 8,988 cases ^a.
B. Costs 1. Initial eye exam (including funduscopy and tonometry): (2,438,464 people) x (\$31.60 per person) = \$77,055,462. 2. Gonioscopy performed on all subjects presenting an anomaly during the initial visual exam: (8,988 people) x (\$10 per person) = \$89,880. 3. Second visual exam, for subjects requiring perimetry because of the presence of anomalies detected during the initial exam (follow-up visit \$15; static perimetry, both eyes, \$35): (8,988 people) x (\$50 per case) = \$449,400. 4. Total cost: \$77,594,742.

^a We have not included here the incidence of glaucoma with high intraocular pressure: we have assumed that these cases would be detected during screening tests at an earlier stage of their natural development, at the time of the appearance of high intraocular pressure, which precedes the diagnosis of glaucoma by about 10 years.

TABLE A6.3 MONITORING AND TREATMENTS FOR 5 YEARS FOR 100 PATIENTS WITH GLAUCOMA

YEAR	PARAMETERS	NUMBER OF PATIENTS, NATURE OF MONITORING AND TREATMENT, AND COSTS							
1	Patients treatment drugs	100 medical 1 (\$123)							
2	Patients treatment drugs	85 medical 1 (\$123)					15 medical 2 (\$261)		
3	Patients treatment drugs	76 medical 1 (\$123)			9 medical 2 (\$261)		15 medical 2 (\$261)		
4	Patients treatment drugs	72 medical 1 (\$123)		4 medical 2 (\$261)	9 medical 2 (\$261)		7 laser (\$133) 0	8 laser (\$133) 1 (\$123)	
5	patients treatment drugs	68 medical 1 (\$123)	4 medical 2 (\$261)	4 medical 2 (\$261)	4 laser (\$133) 0	5 laser (\$133) 1 (\$123)	The 15 patients above redistributed as follows:		
							3 surgery (\$529) 0	7 post-laser 0	5 post-laser 1 (\$123)

Sum of costs for 100 patients for 5 years

(1) Drugs, laser and surgery, according to table above:	\$ 71,976
(2) Retinophotography: \$14 x 100 =	\$ 1,400
(3) Main visits: \$31.60 x (4/year) =	\$ 63,200
(4) Perimetries: \$35 (2/year) =	\$ 35,000
(5) Gonioscopies: \$10 x (1 every 2 years) =	\$ 2,500
(6) Examinations with contact lens: \$10 x (1 every 2 years) =	\$ 2,500
GRAND TOTAL =	\$176,576

TABLE A6.4 COST OF MONITORING AND TREATMENT

COST OF MONITORING AND TREATING PATIENTS FOR GLAUCOMA OR HIGH PRESSURE		COST OF MONITORING PATIENTS FOR HIGH PRESSURE ONLY	TOTAL
Glaucoma: 48,060	High pressure: (10%) x (138,354 cases)	(90%) x (138,354 cases)	186,414 cases
\$16,965,180	\$4,883,896	\$7,869,575	\$29,718,651

Note: The number of cases of glaucoma and of high pressure indicated in this table represents prevalence among people 40 years and over, including the population 80 and over; indeed, people detected between the ages of 40 and 79 will continue being treated after 79 years.

TABLE A6.5 COST OF VISUAL AIDS PROGRAM, RÉGIE DE L'ASSURANCE-MALADIE DU QUÉBEC, 1992 [Erreur ! Signet non défini.]

AGE	TOTAL COST (\$)	NUMBER OF BENEFICIARIES	COST PER BENEFICIARY (\$)	CASES OF BLINDNESS DUE TO GLAUCOMA ACCORDING TO TABLE A5.2
40 - 44	213,874	227	942	4.87
45 - 64	367,461	562	654	127.07
65 - 74	93,560	372	252	170.99
75 - 84	88,338	455	194	228.51
85 +	27,754	144	193	161.17
TOTAL				692.61

Average cost: calculated by multiplying the cost per beneficiary by the distribution of the cases of blindness due to glaucoma: $[(\$942) \times (4.87 \text{ cases}) + \dots + (\$193) \times (161.17 \text{ cases})] / 692.61 \text{ cases} = \298 .

One must add to the average cost calculated above the cost of maintaining guide dogs, i.e. \$27 per beneficiary. The total average cost is therefore $\$298 + \$27 = \$325$.

**TABLE A6.6 TYPICAL SERVICE PLAN FOR REHABILITATING A BLIND PERSON [Erreur !
Signet non défini.]**

SERVICE	HOURS	HOURLY RATE (\$)	TOTAL COST (\$)
Coordination of service plan	10	32	320
Low-vision evaluation	2	40	80
Orientation and mobility: teaching the person how to use a cane	80	32	2,560
Use of guide dog	92	32	2,944
Autonomy in daily activities	240	32	7,680
Functional communication			
■ tape recorder	5	32	160
■ calculator	3	32	96
■ complete braille	25	32	800
■ abridged braille	80	32	2,560
■ conventional typewriter	35	32	1,120
■ computer aid	30	32	960
Psychology	50	36	1,800
TOTAL			21,080

TABLE A6.7 COSTS ASSOCIATED WITH BLINDNESS IN QUEBEC

SERVICE	ANNUAL COST PER PERSON
Visual aids program Régie de l'assurance-maladie du Québec	\$325
Rehabilitation of a blind person	\$1,182
Disability pension, all ages ^a	\$1,580
Disability pension, after the age of 65	\$0
TOTAL, ALL AGES	\$3,087
TOTAL, 65 OR OLDER	\$1,507

^a There is no disability pension after the age of 65. The total indicated here is the average for all cases of glaucoma, regardless of age.

APPENDIX 7 SCREENING FREQUENCY

An important question in assessing the cost-effectiveness ratio of glaucoma screening is the frequency of screening. Indeed, the initial funduscopy and tonometry are an important factor in determining the cost. If the frequency of these exams is diminished, and if effectiveness is not affected, then the cost-effectiveness ratio improves considerably.

The optimum screening frequency depends on the natural history of the disease. The faster the progression between the onset of the disease and the onset of vision loss or blindness, the shorter the interval between the screening examinations should be. Unfortunately, our knowledge of the natural history of glaucoma is very limited. In three clinical trials of glaucoma treatment [16, 29, 53], it was observed that an average of 3% of the patients or, depending on the study, 3% of the eyes, presented visual field loss every year. In another randomized trial, the investigators reported that 32% of the patients who already presented visual field loss at the beginning of the study deteriorated during the year that followed, whereas 8% improved [1].

Other investigators have studied the progression of the disease in samples of patients followed at certain clinics. Hart and Becker followed a cohort of 73 patients with glaucoma for at least 10 years [21]. After 10 years of treatment, 78% of the eyes presenting only single hemifield involvement during the initial examination had developed dense or absolute involvement of their field, and 18% presented involvement described as intermediate. After 10 years, all 13 of the eyes that had presented simultaneous involvement of both horizontal hemifields during the initial examination developed dense or absolute loss in both hemifields.

Basing themselves on their clinical judgment and on a literature review, Gottlieb et al. [18] concluded that cases with untreated high intraocular pressure who subsequently develop visual field loss will become legally blind 12.5 years after they are detected during the screening process. This interval would include five years until the initial field loss, plus 7.5 years until legal blindness. The definition of legal blindness used by Gottlieb [18] was a visual field limited to 20° in its widest diameter.

However, these data should be interpreted with caution. All of these observations concern populations of patients chosen because they presented high intraocular pressure. It is plausible that in the general population, more than half of the cases of blindness will occur in patients whose pressure is not high. We do not know if the disease evolves in these patients as quickly as it does in those with high pressure. Various other selection biases may also affect the data from clinical samples, thus making interpretation difficult.

The epidemiologic data presented in Table A7.1 offer another perspective on this matter. The mean age of new cases of high pressure during screening will be 50 years, and that of cases of glaucoma, 60 years. The mean age at the time of the diagnosis of blindness is estimated to be 78 and the interval would therefore be about 18 to 28 years. But perhaps this type of analysis exaggerates the estimate of the length of this interval in that the estimate of the mean age at the time of the diagnosis of blindness is based on cases that were treated for glaucoma before they became blind. Despite all this, this calculation suggests a very long latency period. If the treatment is highly effective even when administered at an advanced stage of the disease and the objective of the screening is limited to preventing legal blindness, the screening interval could be quite long, perhaps about five to 10 years.

Briefly, the data that we have are fragmentary, possibly inaccurate and contradictory. We believe that an interval of three years between screening tests would be the best compromise. This seems justified because the screening should be done frequently enough to prevent not only blindness, but also visual field loss. It should probably not be done more frequently since the epidemiologic data, although far from rigorous, suggest that the disease does not evolve swiftly into blindness.

TABLE A7.1 MEAN AGE OF VARIOUS CATEGORIES OF PEOPLE PARTICIPATING IN A SCREENING PROGRAM

EVENT	SCREENING OFFERED TO PEOPLE 49 - 79	SCREENING OFFERED TO PEOPLE 65 - 79
	AGE	AGE
Screening begins	40	65
Mean age of new cases of high intraocular pressure ^a	50	68
Mean age of new cases of glaucoma ^b	60	71
Mean age of new cases of blindness due to glaucoma ^c	78	81

^a See Appendix 4.

^b See Appendix 3.

^c See Appendix 5.

APPENDIX 8. DIAGNOSTIC AND THERAPEUTIC ACTIVITIES IN QUEBEC

According to Régie de l'assurance-maladie du Québec data, in 1991, 966,618 people aged 40 to 79 underwent tonometry or biomicroscopy by an optometrist or a complete visual examination by a medical specialist, whether an ophthalmologist or other specialist. We obtained this figure by linking up the Régie's database concerning procedures performed by medical specialists (Table A8.1) with that concerning procedures performed by optometrists (Table A8.2). Tonometry is an examination solely for the purpose of diagnosing glaucoma or high intraocular pressure. We do not know how often these examinations are, on average, repeated in the population. If we assume that the average interval between these tests is three years, the potential population for this type of screening would be $3 \times 966,618$, or about 2.9 million, which is approximately the population aged 40 to 79 in Quebec. According to these calculations, up to 1993, almost the entire population was already undergoing examinations by optometrists or medical specialists.

How many cases are treated following these diagnostic activities? According to the Régie data presented in Table A9.3, 26,840 people aged 65 to 79 received prescriptions for timolol, betaxolol or levobunolol eyedrops in 1992. These drugs are used solely to lower intraocular pressure. The calculations presented earlier in Table A3.2 suggested that 19,506 Quebecers aged 65 to 79 have glaucoma. Table A4.2 indicates that there are 58,276 cases of high pressure in this population. Thus far, we have assumed that 10%, or 5,828 of these people need to be treated. According to these calculations, the grand total under treatment should therefore be $19,506 + 5,828 = 25,334$ people. This therefore suggests that all 65- to 79-year-olds requiring treatment are presently being looked after. However, these calculations should be considered with caution. The assumption that 10% of the cases of high pressure need to be treated has a considerable impact on our conclusions. If, as has also been suggested in the literature [18], this percentage were 30% instead, the estimate of the grand total requiring treatment would be $19,506 + 0.3(58,276) = 36,989$ people. We would thus conclude that $26,840/36,989 = 73\%$ of the population that should be treated is so already. Similarly, our estimate of the number of Quebecers who presently have glaucoma varies according to the data used (see Appendix 3).

We do not have any comparable data for estimating the number of 40- to 64-year-olds under

treatment.

What was the cost of these diagnostic and therapeutic activities in 1991? It may be impossible to obtain the exact answer to this question. Nonetheless, the data in Tables A8.1 to A8.4 may provide certain indications. Some of the costs given in these tables are largely attributable to glaucoma, namely the visual field measurements performed by medical specialists (codes 533, 534 and 538) and optometrists (codes 9006 and 9007), the tonometries and biomicroscopies performed by optometrists (code 9024) and all the costs of the drugs and therapeutic procedures indicated in Tables A8.3 and A8.4. The total cost for these different categories was \$16,817,469. The other very important cost category includes the main visits to ophthalmologists and the complete examinations by optometrists. In 1991, the cost of these procedures was \$25,651,146. We do not know what proportion of this total can be attributed specifically to diagnosing and treating glaucoma. At one extreme, we can attribute 100% of these procedures to glaucoma, at the other extreme 0%. This would give estimates ranging from \$16,817,469 to \$42,468,615. We have no idea what the correct value between these two extremes is. The cost of \$36.4 million attributed to scenario 1 shown in Table 2 is compatible with this range of estimates.

It should be borne in mind that these calculations are estimates. Visual field measurements, for example, are indicated for diseases other than glaucoma. Procedure 9024, which is performed by optometrists, includes not only tonometry, but also biomicroscopy, which is indicated in several eye diseases.

TABLE A8.1 DIAGNOSTIC PROCEDURES PERFORMED BY MEDICAL SPECIALISTS IN QUEBEC, 1991

CODE	PROCEDURE	AGE	NUMBER OF PROCESSES	NUMBER OF PATIENTS	COST
533	Peripheral and/or central visual field (1 variable)	40 - 79	3,783	3,552	\$50,645
		≥ 80	397	370	\$5,333
534	Peripheral and/or central visual field (several variables)	40 - 79	25,320	21,767	\$505,527
		≥ 80	3,173	2,650	\$63,246
538	Static perimetry	40 - 79	39,168	28,917	\$1,328,161
		≥ 80	3,704	2,810	\$125,974
9252	Main visit, ophthalmology Office	40 - 79	299,134	250,538	\$9,273,158
		≥ 80	38,607	29,371	\$1,196,814
9253	Outpatient	40 - 79	102,615	82,476	\$2,361,841
		≥ 80	16,200	12,634	\$372,886
	TOTAL	40 - 79	470,020	Not calculated ^a	\$13,519,332
		≥ 80	62,081		\$1,764,253

^a The figures in the "number of patients" column cannot be added up directly since some of the patients are in more than one diagnostic procedure category.

Source of data: Régie de l'assurance-maladie du Québec.

TABLE A8.2 DIAGNOSTIC PROCEDURES PERFORMED BY OPTOMETRISTS IN QUEBEC, 1991

CODE	PROCEDURE	AGE	NUMBER OF PROCEDURES	NUMBER OF PATIENTS	COST
9001	Complete examination (including funduscopy)	40 - 79	693,910	432,935	\$11,969,950
		≥ 80	27,623	26,679	\$476,497
9006	Examination of central visual field	40 - 79	586,279	563,520	\$4,690,231
		≥ 80	19,668	18,635	\$157,338
9007	Examination of peripheral visual field	40 - 79	172,876	169,185	\$1,115,050
		≥ 80	9,787	9,467	\$63,126
9024	Supplement for tonometry and/or biomicroscopy	40 - 79	717,772	630,624	\$1,722,653
		≥ 80	29,180	25,456	\$70,032
	TOTAL	40 - 79	2,170,837	Not calculated ^a	\$19,497,884
		≥ 80	86,258		\$766,993

^a The figures in the "number of patients" column cannot be added up directly since some of the patients are in more than one diagnostic procedure category.

Source of data: Régie de l'assurance-maladie du Québec.

TABLE A8.3 PRESCRIPTIONS FOR BETA-BLOCKERS IN THE FORM OF EYEDROPS IN QUEBEC, 1992

AGE	NUMBER OF PRESCRIPTIONS	NUMBER OF PATIENTS	COST
65 - 79	162,141	26,840	\$4,465,723
≥ 80	72,050	11,584	\$1,918,806
TOTAL	234,191	38,424	\$6,384,529

Note: For various calculations presented in this report, we assumed that the 1991 costs were the same as those presented here for 1992.

Source of data: Régie de l'assurance-maladie du Québec.

TABLE A8.4 GLAUCOMA-RELATED THERAPEUTIC PROCEDURES PERFORMED BY MEDICAL SPECIALISTS IN QUEBEC, 1991

CODE	PROCEDURE	AGE	NUMBER OF PROCEDURES	NUMBER OF PATIENTS	COST
7226	Sclerectomy for glaucoma	40 - 79	17	17	\$2,716
		≥ 80	5	4	\$970
7237	Trabeculectomy	40 - 79	605	524	\$232,896
		≥ 80	149	125	\$56,320
7802	Trabeculoplasty ^a	ALL	807	632	\$106,761
7811	Cyclodialysis	40 - 79	6	6	\$1,002
		≥ 80	0	0	\$0
7812	Cyclodiathermy	40 - 79	98	71	\$10,562
		≥ 80	17	17	\$1,853
7815	Reintervention within 4 months following a trabeculoplasty	40 - 79	1,444	1,002	\$102,120
		≥ 80	288	202	\$20,424
	TOTAL	≥ 40			\$535,624

^a Data on trabeculoplasty were available only for the period from June 1991 to May 1992 for all ages combined.

Source of data: Régie de l'assurance-maladie du Québec.

REFERENCES

1. American Academy of Ophthalmology. Primary open-angle glaucoma. San Francisco: American Academy of Ophthalmology, 1992. 37 p.
2. American Academy of Ophthalmology. Comprehensive adult eye evaluation. San Francisco: American Academy of Ophthalmology, 1992. 6 p.
3. Armaly MF, Krueger DE, Maunder L, et al. Biostatistical analysis of the collaborative glaucoma study: 1. Summary report of the risk factors for glaucomatous visual-field defects. Arch Ophthalmol 1980;98:2163-71.
4. Balaszi G. Personal Communication. 1994.
5. Battista RN, Huston P, Davis MWL. Changing concepts of primary open-angle glaucoma and early detection. Can Fam Physician 1986;32(Jul):1483-8.
6. Bengtsson B. Findings associated with glaucomatous visual field defects. Acta Ophthalmol 1980;58:20-32.
7. Bengtsson B. Aspects of epidemiology of chronic glaucoma. Acta Ophthalmol 1981;(Suppl 146):1-47.
8. Bengtsson B. The prevalence of glaucoma. Br J Ophthalmol 1981;65:46-9.
9. Benoit M. Personal communication. Longueuil: Institut Nazareth et Louis-Braille, 1994.
10. Canadian National Institute for the Blind (CNIB). Statistical information on the client population of the CNIB 1989. Montreal: CNIB, 1989. 4 p.
11. Canadian Task Force on the Periodic Health Examination. The periodic health examination: 2. 1985 update. Can Med Assoc J 1986;134(Apr 1):724-9.
12. Conseil d'évaluation des technologies de la santé du Québec (CETS). Cardiac transplantation in Quebec: survival, costs and cost-effectiveness (principal and technical reports). Montreal: CETS, 1992. 119 p.
13. Conseil d'évaluation des technologies de la santé du Québec (CETS). Screening for breast cancer in Quebec: estimates of health effects and of costs (reference documents in french only). Montreal: CETS, 1990. 78 p.
14. David R, Stone D. The prevalence of glaucoma in a homogenous African population. Recent Adv Glaucoma 1984:145-53.

15. Dorland WAN. Dorland's illustrated medical dictionary. (27th edition). Philadelphia: W.B. Saunders Co. 1988.
16. Epstein DL, Krug JH, Hertzmark E, Remis LL, Edelstein DJ. A long-term clinical trial of timolol therapy versus no treatment in the management of glaucoma suspects. *Ophthalmology* 1989;96:1460-7.
17. Flammarion Médecine-Sciences (ed). Dictionnaire de médecine Flammarion. Paris: Flammarion Médecine-Sciences, 1989.
18. Gottlieb LK, Schwartz B, Pauker SG. Glaucoma screening: a cost-effectiveness analysis. *Surv Ophthalmol* 1983;28:206-26.
19. Grant WM, Burke JF. Why do some people go blind from glaucoma? *Ophthalmology* 1982;89:991-8.
20. Grey RHB, Burns-Cox CJ, Hughes A. Blind and partial sight registration in Avon. *Br J Ophthalmol* 1989;73:88-94.
21. Hart WM, Becker B. The onset and evolution of glaucomatous visual field defects. *Ophthalmology* 1982;89:268-79.
22. Heijl A. Personal communication. 1994.
23. Hiller R, Kahn HA. Blindness from glaucoma. *Am J Ophthalmol* 1975;80(1):62-9.
24. Hollows FC, Graham PA. Intra-ocular pressure, glaucoma, and glaucoma suspects in a defined population. *Br J Ophthalmol* 1966;50:570-86.
25. Jay JL, Allan D. The benefit of early trabeculectomy versus conventional management in primary open angle glaucoma relative to severity of disease. *Eye* 1989;3:528-35.
26. Jenicek M. Introduction à l'épidémiologie. St-Hyacinthe: Edisem Inc., 1977. p. 201.
27. Kahn HA, Leibowitz HM, Ganley JP, et al. The Framingham Eye Study. I. Outline and major prevalence findings. *Am J Epidemiol* 1977;106(1):17-32.
28. Kahn HA, Milton RC. Alternative definitions of open-angle glaucoma: effect on prevalence and associations in the Framingham Eye Study. *Arch Ophthalmol* 1980;98:2172-7.

29. Kass MA, Gordon MO, Hoff MR, et al. Topical timolol administration reduces the incidence of glaucomatous damage in ocular hypertensive individuals: a randomized, double-masked, long-term clinical trial. *Arch Ophthalmol* 1989;107:1590-8.
30. Klein BEK, Klein R, Sponsel WE, Franke T, Cantor LB, Martone J, Menage MJ. Prevalence of glaucoma: the Beaver Dam Eye Study. *Ophthalmology* 1992;99:1499-1504.
31. Leske MC, Connell AMS, Kehoe R. A pilot project of glaucoma in Barbados. *Br J Ophthalmol* 1989;73:365-9.
32. Leske MC. The epidemiology of open-angle glaucoma: a review. *Am J Epidemiol* 1983;118(2):166-91.
33. Leske MC, Ederer F, Podgor M. Estimating incidence from age-specific prevalence in glaucoma. *Am J Epidemiol* 1981;113(6):606-13.
34. Mason RP, Kosoko O, Wilson MR, et al. National survey of the prevalence and risk factors of glaucoma in St. Lucia, West Indies. Part I. Prevalence findings. *Ophthalmology* 1989;96:1363-8.
35. Miettinen OS. Theoretical epidemiology: principles of occurrence research in medicine. New York: Wiley, 1985.
36. Ministère de la Santé et des Services sociaux (MSSS). Données de recensement. Info-Pop (Bulletin d'information sur les données de population du MSSS), Service des études opérationnelles et données statistiques. 1993 (Bulletin no. 1).
37. Montgomery DMI. Clinical disc biometry in early glaucoma. *Ophthalmology* 1993;100:52-6.
38. Moulin F, Ameline B, Redor Y, Boumerzag AB, Haut J. Trabéculorétraction au laser à l'argon (TRLA): résultats à cinq et huit ans. *J Fr Ophtalmol* 1992;15(8/9):463-8.
39. Patterson C. Visual impairment in the elderly: final draft. Hamilton (Ont): McMaster University, Department of Medicine, 1993. 46 p.
40. Pineault R, Daveluy C. La planification de la santé: concepts, méthodes, stratégies. Montréal: Agence d'ARC Inc. 1986. p. 58.
41. Podgor MJ, Leske MC, Ederer F. Incidence estimates for lens changes, macular changes, open-angle glaucoma and diabetic retinopathy. *Am J Epidemiol* 1983;118(2):206-12.

42. Power EJ, Wagner JL, Duffy BM. Screening for open-angle glaucoma in the elderly. Washington (DC): Office of Technology Assessment (OTA), 1988. 60 p.
43. Quigley HA. Open-angle glaucoma. *N Engl J Med* 1993;328(15):1097-1106.
44. Quigley HA, Addicks EM, Green WR. 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 Ophthalmol* 1982;100:135-46.
45. Quigley HA, Maumenee AE. Long-term follow-up of treated open-angle glaucoma. *Am J Ophthalmol* 1979;87:519-25.
46. Régie de l'assurance-maladie du Québec (RAMQ). Statistiques annuelles 1992. Québec: RAMQ, 1993, pp. 300-2.
47. Régie de l'assurance-maladie du Québec (RAMQ). Medical specialists' manual: health insurance plan. Québec: RAMQ, 1970-.
48. Régie de l'assurance-maladie du Québec (RAMQ). Optometrists' manual. Québec: RAMQ, 1970-.
49. Rossetti L, Marchetti I, Orzalesi N, Scorpiglioni N, Torri V, Liberati A. Randomized clinical trials on medical treatment of glaucoma: are they appropriate to guide clinical practice? *Arch Ophthalmol* 1993;11(Jan):96-103.
50. Rouhiainen H, Terasvirta M. Incidence of open-angle glaucoma and screening of the intraocular pressure with a non-contact tonometer. *Acta Ophthalmol* 1990;68:344-6.
51. Sacket DL, Haynes RB, Guyatt GH, Tugwell P. Clinical epidemiology. Boston (MA): Little, Brown and Company, 1991. p. 153.
52. Schulzer M. Intraocular pressure reduction in normal-tension glaucoma patients. *Ophthalmology* 1992;99:1468-70.
53. Schulzer M, Drance SM, Douglas GR. A comparison of treated and untreated glaucoma suspects. *Ophthalmology* 1991;98:301-7.
54. Schwartz B, Henson DB, Iwata K, LeBlanc R, Sommer A. Discussion: screening for glaucoma. *Surv Ophthalmol* 1989;33(Suppl):449-50.
55. Sommer A, Tielsch JM, Katz J, et al. Relationship between intraocular pressure and primary open angle glaucoma among white and black Americans: the Baltimore Eye Survey. *Arch Ophthalmol* 1991;109:1090-5.

56. Sommer A, Tielsch JM, Katz J, et al. Racial differences in the cause-specific prevalence of blindness in East Baltimore. *N Engl J Med* 1991;325:1412-7.
57. Sorensen PN, Nielsen NV, Norskov K. Ocular hypertension: a 15-year follow-up. *Acta Ophthalmol* 1978;56(Sept 1):363-72.
58. Statistics Canada. The nation. Ottawa: Statistics Canada, 1991, pp.108-15 (table 4) (Cat. 93-310).
59. Statistics Canada. Life tables, Canada and provinces. 1985-1987. *Health Reports* 1990;2(2 Suppl 13).
60. Tielsch JM, Katz J, Sommer A, Quigley HA, Javitt JC. Family history and risk of primary open angle glaucoma: the Baltimore Eye Survey. *Arch Ophthalmol* 1994;112:69-73.
61. Tielsch JM, Sommer A, Katz J, Royall RM, Quigley HA, Javitt J. Racial variations in the prevalence of primary open-angle glaucoma: the Baltimore Eye Survey. *JAMA* 1991;266(3):369-74.
62. Tielsch JM, Katz J, Singh K, Quigley HA, Gottsch JD, Javitt J, Sommer A. A population-based evaluation of glaucoma screening: the Baltimore Eye Survey. *Am J Epidemiol* 1991;134(10):1102-10.
63. U.S. Preventive Services Task Force. Guide to clinical preventive services: an assessment of the effectiveness of 169 interventions. Chapter 32: Screening for glaucoma. Baltimore: Williams & Wilkins, 1989:187-192.
64. Werner EB, Drance SM, Schulzer M. Trabeculectomy and the progression of glaucomatous visual field loss. *Arch Ophthalmol* 1977;95:1374-7.
65. Wilson RP. Glaucoma. *Year Book Ophthalmol* 1991:51-6.